Title: STENT WITH THERAPEUTICALLY ACTIVE DRUG COATED THEREON

Abstract: Delivery of a Janus Kinase 3 (JAK3) inhibitor locally, particularly from an intravascular stent, directly from micropores in the stent body or mixed or bound to a polymer coating applied on stent, to inhibit neointimal tissue proliferation and thereby prevent restenosis. This invention also facilitates the performance of the stent in inhibiting restenosis.
STENT WITH THERAPEUTICALLY ACTIVE DRUG COATED THEREON

FIELD OF THE INVENTION

Delivery of a Janus Kinase 3 (JAK3) inhibitor locally, particularly from an intravascular stent, directly from micropores in the stent body or mixed or bound to a polymer coating applied on stent, to inhibit neointimal tissue proliferation and thereby prevent restenosis. This invention also facilitates the performance of the stent in inhibiting restenosis.

BACKGROUND OF THE INVENTION

Re-narrowing (restenosis) of an atherosclerotic coronary artery after percutaneous transluminal coronary angioplasty (PTCA) occurs in 10-50% of patients undergoing this procedure and subsequently requires either further angioplasty or coronary artery bypass graft. While the exact hormonal and cellular processes promoting restenosis are still being determined, our present understanding is that the process of PTCA, besides opening the atherosclerotically obstructed artery, also injures resident coronary arterial smooth muscle cells (SMC). In response to this injury, adhering platelets, infiltrating macrophages, leukocytes, or the smooth muscle cells (SMC) themselves release cell derived growth factors with subsequent proliferation and migration of medial SMC through the internal elastic lamina to the area of the vessel intima. Further proliferation and hyperplasia of intimal SMC and, most significantly, production of large amounts of extracellular matrix over a period of 3-6 months results in the filling in and narrowing of the vascular space sufficient to significantly obstruct coronary blood flow.

Several recent experimental approaches to preventing SMC proliferation have shown promise although the mechanisms for most agents employed are still unclear.

Heparin is the best known and characterized agent causing inhibition of SMC proliferation both in vitro and in animal models of balloon angioplasty-mediated injury. The mechanism of SMC inhibition with heparin is still not known but may be due to any or all of the following: 1) reduced expression of the growth regulatory protooncogenes c-fos and c-myc, 2) reduced cellular production of tissue plasminogen activator; are 3) binding and dequstration of growth regulatory factors such as fibrovalent growth factor (FGF).

Other agents which have demonstrated the ability to reduce myointimal thickening in animal models of balloon vascular injury are angiopeptin (a somatostatin analog), calcium channel blockers, angiotensin converting enzyme inhibitors (captopril, cilazapril), cyclosporin A, trapidil (an antianginal, antiplatelet agent),
terbinafine (antifungal), colchicine and taxol (antitubulin antiproliferatives), and c-myc and c-myb antisense oligonucleotides.

Additionally, a goat antibody to the SMC mitogen platelet derived growth factor (PDGF) has been shown to be effective in reducing myointimal thickening in a rat model of balloon angioplasty injury, thereby implicating PDGF directly in the etiology of restenosis. Thus, while no therapy has as yet proven successful clinically in preventing restenosis after angioplasty, the in vivo experimental success of several agents known to inhibit SMC growth suggests that these agents as a class have the capacity to prevent clinical restenosis and deserve careful evaluation in humans.

Coronary heart disease is the major cause of death in men over the age of 40 and in women over the age of fifty in the western world. Most coronary artery-related deaths are due to atherosclerosis. Atherosclerotic lesions which limit or obstruct coronary blood flow are the major cause of ischemic heart disease related mortality and result in 500, 000-600,000 deaths in the United States annually. To arrest the disease process and prevent the more advanced disease states in which the cardiac muscle itself is compromised, direct intervention has been employed via percutaneous transluminal coronary angioplasty (PTCA) or coronary artery bypass graft (CABG).

PTCA is a procedure in which a small balloon-tipped catheter is passed down a narrowed coronary artery and then expanded to re-open the artery. It is currently performed in approximately 250,000-300,000 patients each year. The major advantage of this therapy is that patients in which the procedure is successful need not undergo the more invasive surgical procedure of coronary artery bypass graft. A major difficulty with PTCA is the problem of post-angioplasty closure of the vessel, both immediately after PTCA (acute reoclusion) and in the long term (restenosis).

The mechanism of acute reocclusion appears to involve several factors and may result from vascular recoil with resultant closure of the artery and/or deposition of blood platelets along the damaged length of the newly opened blood vessel followed by formation of a fibrin/red blood cell thrombus. Recently, intravascular stents have been examined as a means of preventing acute reclosure after PTCA. Restenosis (chronic reclosure) after angioplasty is a more gradual process than acute reocclusion: 30% of patients with subtotal lesions and 50% of patients with chronic total lesions will go on to restenosis after angioplasty. While the exact mechanism for restenosis is still under active investigation, the general aspects of the restenosis process have been identified.
In the normal arterial wall, smooth muscle cells (SMC) proliferate at a low rate (<0.1%/day; ref). SMC in vessel wall exists in a 'contractile' phenotype characterized by 80-90% of the cell cytoplasmic volume occupied with the contractile apparatus. Endoplasmic reticulum, golgi bodies, and free ribosomes are few and located in the perinuclear region. Extracellular matrix surrounds SMC and is rich in heparin-like glycosylaminoglycans which are believed to be responsible for maintaining SMC in the contractile phenotypic state.

Upon pressure expansion of an intracoronary balloon 55 catheter during angioplasty, smooth muscle cells within the arterial wall become injured. Cell derived growth factors such as platelet derived growth factor (PDGF), basic fibroblast growth factor (bFGF), epidermal growth factor (EGF), etc. released from platelets (i.e., PDGF) adhering to the 60 damaged arterial luminal surface, invading macrophages and/or leukocytes, or directly from SMC (i.e., BFGF) provoke a proliferation and migratory response in medial SMC. These cells undergo a phenotypic change from the contractile phenotyope to a 'synthetic' phenotype characterized by 65 only few contractile filament bundles but extensive rough endoplasmic reticulum, golgi and free ribosomes. Proliferation/migration usually begins within 1-2 days post injury and peaks at 2 days in the media, rapidly declining thereafter (Campbell et al., in: Vascular Smooth Muscle Cells in Culture, Campbell, J. H. and Campbell, G. R., Eds, CRC Press, Boca Ration, 1987, pp. 39-55); Clowes, A. W. and Schwartz, S. M., Circ. Res. 56:139-145, 1985).

Finally, daughter synthetic cells migrate to the intimal layer of arterial smooth muscle and continue to proliferate. Proliferation and migration continues until the damaged luminal endothelial layer regenerates at which time proliferation ceases within the intima, usually within 7-14 days postinjury. The remaining increase in intimal thickening which occurs over the next 3-6 months is due to an increase in extracellular matrix rather than cell number. Thus, SMC migration and proliferation is an acute response to vessel injury while intimal hyperplasia is a more chronic response. (Liu et al., Circulation, 79:1374-1387, 1989).

Patients with symptomatic reocclusion require either repeat PTCA or CABG. Because 30-50% of patients undergoing PTCA will experience restenosis, restenosis has clearly limited the success of PTCA as a therapeutic approach to coronary artery disease. Because SMC proliferation and migration are intimately involved with the pathophysiological response to arterial injury, prevention of SMC proliferation and
migration represents a target for pharmacological intervention in the prevention of restenosis.

SUMMARY OF THE INVENTION
Novel Features and Applications to Stent Technology

Currently, attempts to improve the clinical performance of stents have involved some variation of either applying a coating to the metal, attaching a covering or membrane, or embedding material on the surface via ion bombardment. A stent designed to include reservoirs is a new approach which offers several important advantages over existing technologies.

The present invention relates to a stent having a coating containing a compound of the formula

\[
\text{I}
\]

or the pharmaceutically acceptable salt thereof; wherein

- \( R^1 \) is a group of the formula

\[
\text{II}
\]

wherein \( y \) is 0, 1 or 2;

- \( R^4 \) is selected from the group consisting of hydrogen, \((C_1-C_6)\)alkyl, \((C_1-C_6)\)alkylsulfonyl, \((C_2-C_6)\)alkenyl, \((C_2-C_6)\)alkynyl wherein the alkyl, alkenyl and alkynyl groups are optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, \((C_1-C_4)\)alkoxy, \((C_1-C_6)\)acyloxy, \((C_1-C_6)\)alkylamino, \((C_1-C_6)\)(alkyl)\(_2\)amino, cyano, nitro, \((C_2-C_6)\)alkenyl, \((C_2-C_6)\)alkynyl or \((C_1-C_6)\)acylamino; or \( R^4 \) is \((C_3-C_{10})\)cycloalkyl wherein the cycloalkyl group is optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, \((C_1-C_6)\)acyloxy, \((C_1-C_6)\)acylamino, \((C_1-C_6)\)alkylamino, \((C_1-C_6)\)(alkyl)\(_2\)amino, cyano, cyano\((C_1-C_6)\)alkyl, trifluoromethyl\((C_1-C_6)\)alkyl, nitro, nitro\((C_1-C_6)\)alkyl or \((C_1-C_6)\)acylamino;

- \( R^5 \) is \((C_2-C_6)\)heterocycloalkyl wherein the heterocycloalkyl groups must be substituted by one to five carboxy, cyano, amino, deuterium, hydroxy, \((C_1-C_6)\)alkyl,
(C₁₋C₆)alkoxy, halo, (C₁₋C₆)acyl, (C₁₋C₆)alkylamino, amino(C₁₋C₆)alkyl, (C₁₋C₆)alkoxy-CO-NH, (C₁₋C₆)alkylamino-CO-NH₂, (C₁₋C₆)alkenyl, (C₂₋C₆)alkynyl, (C₁₋C₆)alkylamino, amino(C₁₋C₆)alkyl, hydroxy(C₁₋C₆)alkyl, (C₁₋C₆)alkoxy(C₁₋C₆)alkyl, (C₁₋C₆)acyloxy(C₁₋C₆)alkyl, nitro, cyano(C₁₋C₆)alkyl, halo(C₁₋C₆)alkyl, nitro(C₁₋C₆)alkyl, trifluoromethyl, trifluoromethyl(C₁₋C₆)alkyl, (C₁₋C₆)acyl, amino(C₁₋C₆)alkyl, (C₁₋C₆)acyloxy(C₁₋C₆)acylamino, amino(C₁₋C₆)acyl, amino(C₁₋C₆)acyl(C₁₋C₆)alkyl, (C₁₋C₆)alkylamino(C₁₋C₆)acyl, ((C₁₋C₆)alkyl)ₙamino(C₁₋C₆)acyl, R¹⁵R¹⁶N-CO-O-, R¹⁵R¹⁶N-CO-(C₁₋C₆)alkyl, (C₁₋C₆)alkyl-S(O)ₖ, R¹⁵R¹⁶NS(O)ₖ, R¹⁵R¹⁶NS(S)ₖ, R¹⁵S(O)ₖR¹⁶N(C₁₋C₆)alkyl wherein m is 0, 1 or 2 and R¹⁵ and R¹⁶ are each independently selected from hydrogen or (C₁₋C₆)alkyl; or a group of the formula

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  R²ₙ₋₁BBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBBR²
   )       )       )       )       )       )       )       )       )       )       )       )
      (X)ₙ       (Y)ₙ       (Z)ₙ       (CR₆R₇)ₙ       (CR₆R₇R¹⁰)ₙ
    )       )       )       )       )       )       )       )       )       )       )       )
       N       N       N       N       N       N       N       N       N       N       N
    )       )       )       )       )       )       )       )       )       )       )       )
      R₆       R₆       R₆       R₆       R₆       R₆       R₆       R₆       R₆       R₆       R₆

wherein a is 0, 1, 2, 3 or 4;

b, c, e, f and g are each independently 0 or 1;

d is 0, 1, 2, or 3;

X is S(O)ₖ, wherein n is 0, 1 or 2; oxygen, carbonyl or -C(=N-cyano);

Y is S(O)ₖ, wherein n is 0, 1 or 2; or carbonyl and

Z is carbonyl, C(O)O-, C(O)NRₖ- or S(O)ₖ, wherein n is 0, 1 or 2;

R₄, R₇, R₈, R₁⁰ and R¹¹ are each independently selected from the group consisting of hydrogen or (C₁₋C₆)alkyl optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C₁₋C₆)acyloxy, (C₁₋C₆)acylamino, (C₁₋C₆)alkylamino, ((C₁₋C₆)alkyl)₂amino, cyano, cyano(C₁₋C₆)alkyl, trifluoromethyl(C₁₋C₆)alkyl, nitro, nitro(C₁₋C₆)alkyl or (C₁₋C₆)acylamino;

R¹² is carboxy, cyano, amino, oxo, deuterium, hydroxy, trifluoromethyl, (C₁₋C₆)alkyl, trifluoromethyl(C₁₋C₆)alkyl, (C₁₋C₆)alkoxy, halo, (C₁₋C₆)acyl, (C₁₋C₆)alkylamino, ((C₁₋C₆)alkyl)₂amino, amino(C₁₋C₆)alkyl, (C₁₋C₆)alkoxy-CO-NH, (C₁₋C₆)alkylamino-CO-NH₂, (C₂₋C₆)alkenyl, (C₂₋C₆)alkynyl, (C₁₋C₆)alkylamino, hydroxy(C₁₋C₆)alkyl, (C₁₋C₆)alkoxy(C₁₋C₆)alkyl, (C₁₋C₆)acyloxy(C₁₋C₆)alkyl, nitro, cyano(C₁₋C₆)alkyl.
C₆alkyl, halo(C₁-C₆)alkyl, nitro(C₁-C₆)alkyl, trifluoromethyl, trifluoromethyl(C₁-C₆)alkyl, (C₁-C₆)acylamino, (C₁-C₆)acylamino(C₁-C₆)alkyl, (C₁-C₆)alkoxy(C₁-C₆)acylamino, amino(C₁-C₆)acyl, amino(C₁-C₆)acyl(C₁-C₆)alkyl, (C₁-C₆)alkylamino(C₁-C₆)acyl, ((C₁-C₆)alkyl)₂amino(C₁-C₆)acyl, R¹(R¹N-CO-O⁻), R⁵R¹₈N-CO-(C₁-C₆)alkyl, R¹₅C(O)NH, R¹₅NHC(O)NH, (C₁-C₆)alkyl-S(Ο)m, (C₁-C₆)alkyl-S(Ο)m(C₁-C₆)alkyl, R⁵R¹₅₈NₕS(Ο)mR¹₆₅NₕS(Ο)mR¹₅₈Nₕ(C₁-C₆)alkyl

wherein m is 0, 1 or 2 and R¹₅ and R¹₆ are each independently selected from hydrogen or (C₁-C₆)alkyl;

R² and R³ are each independently selected from the group consisting of hydrogen, deuterium, amino, halo, hydroxy, nitro, carboxy, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, trifluoromethyl, trifluoromethoxy, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, (C₃-C₁₀)cycloalkyl wherein the alkyl, alkoxy or cycloalkyl groups are optionally substituted by one to three groups selected from halo, hydroxy, carboxy, amino (C₁-C₆)alkylthio, (C₁-C₆)alkylamino, ((C₁-C₆)alkyl)₂amino, (C₅-C₉)heteroaryl, (C₂-C₉)heterocycloalkyl, (C₃-C₆)cycloalkyl or (C₆-C₁₀)aryl; or R² and R³ are each independently (C₃-C₁₀)cycloalkyl, (C₃-C₁₀)cycloalkoxy, (C₁-C₆)alkylamino, ((C₁-C₆)alkyl)₂amino, (C₆-C₁₀)arylamino, (C₁-C₆)alkylthio, (C₅-C₁₀)arylamino, (C₁-C₆)alkylsulfinyl, (C₁-C₆)arylsulfinyl, (C₁-C₆)alkylsulfonyl, (C₅-C₁₀)arylsulfonyl, (C₁-C₆)acyl, (C₁-C₆)alkoxy, CO-NH₅, (C₁-C₆)alkyamino-CO⁻, (C₅-C₉)heteroaryl, (C₂-C₉)heterocycloalkyl or (C₆-C₁₀)aryl wherein the heteroaryl, heterocycloalkyl and aryl groups are optionally substituted by one to three halo, (C₁-C₆)alkyl, (C₁-C₆)alkyl-CO-NH⁻, (C₁-C₆)alkoxy-CO-NH⁻, (C₁-C₆)alkyl-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkoxy-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkoxy-CO-NH-(C₁-C₆)alkoxy, carboxy, carboxy(C₁-C₆)alkyl, carboxy(C₁-C₆)alkoxy, benzoxycarbonyl(C₁-C₆)alkoxy, (C₁-C₆)alkoxycarbonyl(C₁-C₆)alkoxy, (C₆-C₁₀)aryl, amino, amino(C₁-C₆)alkyl, (C₁-C₆)alkoxycarbonylamino, (C₆-C₁₀)aryl(C₁-C₆)alkylamino, (C₁-C₆)alkylamino, ((C₁-C₆)alkyl)₂amino, (C₁-C₆)alkylamino(C₁-C₆)alkyl, ((C₁-C₆)alkyl)₂amino(C₁-C₆)alkyl, hydroxy, (C₁-C₆)alkoxy, carboxy, carboxy(C₁-C₆)alkyl, (C₁-C₆)alkoxycarbonyl, (C₁-C₆)alkoxycarbonyl(C₁-C₆)alkyl, (C₁-C₆)alkoxy-CO-NH₂, (C₁-C₆)alkyl-CO-NH₂, cyano, (C₅-C₉)heterocycloalkyl, amino-CO-NH₂, (C₁-C₆)alkylamino-CO-NH₂, ((C₁-C₆)alkyl)₂amino-CO-NH₂, (C₆-C₁₀)arylamino-CO-NH₂, (C₅-C₉)heteroarylamino-CO-NH₂, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₅-C₉)heteroarylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylsulfonyl, (C₁-C₆)alkylsulfonyl, (C₁-C₆)alkylamino-CO-NH₂, (C₁-C₆)alkylamino-CO-NH₂, (C₁-C₆)alkylamino-CO-NH₂, (C₆-C₁₀)arylamino-CO-NH₂, (C₅-C₉)heteroarylamino-CO-NH₂, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₅-C₉)heteroarylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH₂, (C₁-C₆)alkylamino-CO-NH₂.
C₆)alkylsulfonylamino, (C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, (C₆-C₁₀)arylsulfonyl, (C₆-C₁₀)arylsulfonylamino(C₁-C₆)alkyl, (C₁-C₆)alkylsulfonylamino, (C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, (C₅-C₉)heteroaryl or (C₂-C₅)heterocycloalkyl,

said coating formed from a polymer mixed carrier containing the compound of Formula I; and said coating applied to said stent.

Local Drug Delivery from a Stent to Inhibit Restenosis

In this application, it is desired to deliver a therapeutic agent to the site of arterial injury. The conventional approach has been to incorporate the therapeutic agent into a polymer material which is then coated on the stent. The ideal coating material must be able to adhere strongly to the metal stent both before and after expansion, be capable of retaining the drug at a sufficient load level to obtain the required dose, be able to release the drug in a controlled way over a period of several weeks, and be as thin as possible so as to minimize the increase in profile. In addition, the coating material should not contribute to any adverse response by the body (i.e., should be non-thrombogenic, non-inflammatory, etc.).

An alternative would be to design the stent to contain reservoirs which could be loaded with the drug. A coating or membrane of biocompatible material could be applied over the reservoirs which would control the diffusion of the drug from the reservoirs to the artery wall.

One advantage of this system is that the properties of the coating can be optimized for achieving superior biocompatibility and adhesion properties, without the addition requirement of being able to load and release the drug. The size, shape, position, and number of reservoirs can be used to control the amount of drug, and therefore the dose delivered.

DESCRIPTION OF THE DRAWINGS

The invention will be better understood in connection with the following figures in which:

FIGS. 1 and 1a are top views and section views of a stent containing reservoirs as described in the present invention;

FIGS. 2a and 2b are similar views of an alternate embodiment of the stent with open ends;
FIGS. 3a and 3b are further alternate figures of a device containing a grooved reservoir; and
FIG. 4 is a layout view of a device containing a reservoir as in FIG. 3.

DETAILED DESCRIPTION OF THE INVENTION

The following reaction Schemes illustrate the preparation of the compounds of the present invention. Unless otherwise indicated \( R^2 \), \( R^3 \), \( R^4 \) and \( R^5 \) in the reaction Schemes and the discussion that follow are defined as above.
PREPARATION B

Cl

Cl

Cl

R

R

R

R

R

R

R

R

XXI

XXII

XVI
SCHEME 2
SCHEME 3

$\text{XVII}$

$\text{I}$
In reaction 1 of Preparation A, the 4-chloropyrrolo[2,3-d]pyrimidine compound of formula XXI, wherein R is hydrogen or a protecting group such as benzenesulfonyl or benzyl, is converted to the 4-chloro-5-halopyrrolo[2,3-d]pyrimidine compound of formula XX, wherein Y is chloro, bromo or iodo, by reacting XXI with N-chlorosuccinimide, N-bromosuccinimide or N-iodosuccinimide. The reaction mixture is heated to reflux, in chloroform, for a time period between about 1 hour to about 3 hours, preferably about 1 hour. Alternatively, in reaction 1 of Preparation A, the 4-chloropyrrolo[2,3-d]pyrimidine of formula XXI, wherein R is hydrogen, is converted to the corresponding 4-chloro-5-nitropyrrrolo[2,3-d]pyrimidine of formula XX, wherein Y is nitro, by reacting XXI with nitric acid in sulfuric acid at a temperature between about -10°C to about 10°C, preferably about 0°C, for a time period between about 5 minutes to about 15 minutes, preferably about 10 minutes. The compound of formula XXI, wherein Y is nitro, is converted to the corresponding 4-chloro-5-aminopyrrolo[2,3-d]pyrimidine of the formula XX, wherein Y is amino, by reacting XXI under a variety of conditions known to one skilled in the art such as palladium hydrogenolysis or tin(IV)chloride and hydrochloric acid.

In reaction 2 of Preparation A, the 4-chloro-5-halopyrrolo[2,3-d]pyrimidine compound of formula XX, wherein R is hydrogen, is converted to the corresponding compound of formula XIX, wherein R² is (C₁₋₇)alkyl or benzyl, by treating XX with N-butyllithium, at a temperature of about -78°C, and reacting the dianion intermediate so formed with an alkylhalide or benzyhalide at a temperature between about -78°C to room temperature, preferably room temperature. Alternatively, the dianion so formed is reacted with molecular oxygen to form the corresponding 4-chloro-5-hydroxypyrrolo[2,3-d]pyrimidine compound of formula XIX, wherein R² is hydroxy.

The compound of formula XX, wherein Y is bromine or iodine and R is benzenesulfonate, is converted to the compound of formula XIX, wherein R² is (C₆₋₁₂)aryl or vinyl, by treating XX with N-butyllithium, at a temperature of about -78°C, followed by the addition of zinc chloride, at a temperature of about -78°C. The corresponding organo zinc intermediate so formed is then reacted with aryliodide or vinyl iodide in the presence of a catalytic quantity of palladium. The reaction mixture is stirred at a temperature between about 50°C to about 80°C, preferably about 70°C, for a time period between about 1 hour to about 3 hours, preferably about 1 hour.

In reaction 3 of Preparation A, the compound of formula XIX is converted to the corresponding compound of formula XVI by treating XIX with N-butyllithium, lithium
diisopropylamine or sodium hydride, at a temperature of about -78°C, in the presence of a polar aprotic solvent, such as tetrahydrofuran. The anionic intermediate so formed is further reacted with (a) alkylhalide or benzylhalide, at a temperature between about -78°C to room temperature, preferably -78°C, when R³ is alkyl or benzyl; (b) an aldehyde or ketone, at a temperature between about -78°C to room temperature, preferably -78°C, when R³ is alkoxy; and (c) zinc chloride, at a temperature between about -78°C to room temperature, preferably -78°C, and the corresponding organozinc intermediate so formed is then reacted with arylliodide or vinyl iodide in the presence of a catalytic quantity of palladium. The resulting reaction mixture is stirred at a temperature between about 50°C to about 80°C, preferably about 70°C, for a time period between about 1 hour to about 3 hours, preferably about 1 hour. Alternatively, the anion so formed is reacted with molecular oxygen to form the corresponding 4-chloro-6-hydroxyprolo[2,3-d]pyrimidine compound of formula XVI, wherein R³ is hydroxy.

In reaction 1 of Preparation B, the 4-chloropyrrolo[2,3-d]pyrimidine compound of formula XXI is converted to the corresponding compound of formula XXII, according to the procedure described above in reaction 3 of Preparation A.

In reaction 2 of Preparation B, the compound of formula XXII is converted to the corresponding compound of formula XVI, according to the procedures described above in reactions 1 and 2 of Preparation A.

In reaction 1 of Scheme 1, the 4-chloropyrrolo[2,3-d]pyrimidine compound of formula XVII is converted to the corresponding compound of formula XVI, wherein R is benzenesulfonyl or benzyl, by treating XVII with benzenesulfonyl chloride, benzylchloride or benzylbromide in the presence of a base, such as sodium hydride or potassium carbonate, and a polar aprotic solvent, such as dimethylformamide or tetrahydrofuran. The reaction mixture is stirred at a temperature between about 0°C to about 70°C, preferably about 30°C, for a time period between about 1 hour to about 3 hours, preferably about 2 hours.

In reaction 2 of Scheme 1, the 4-chloropyrrolo[2,3-d]pyrimidine compound of formula XVI is converted to the corresponding 4-aminopyrrolo[2,3-d]pyrimidine compound of formula XV by coupling XVI with an amine of the formula HNR³R⁵. The reaction is carried out in an alcohol solvent, such as tert-butanol, methanol or ethanol, or other high boiling organic solvents, such as dimethylformamide, triethylamine, 1,4-dioxane or 1,2-dichloroethane, at a temperature between about 60°C to about 120°C,
preferably about 80°C. Typical reaction times are between about 2 hours to about 48 hours, preferably about 16 hours. When R^5 is a nitrogen containing heterocycloalkyl group, each nitrogen must be protected by a protecting group, such as benzyl. Removal of the R^5 protecting group is carried out under conditions appropriate for that particular protecting group in use which will not affect the R protecting group on the pyrrolo[2,3-d]pyrimidine ring. Removal of the R^5 protecting group, when benzyl, is carried out in an alcohol solvent, such as ethanol, in the present of hydrogen and a catalyst, such as palladium hydroxide on carbon. The R^5 nitrogen containing heterocycloalkyl group so formed may be further reacted with a variety of different electrophiles of formula II. For urea formation, electrophiles of formula II such as isocyanates, carbamates and carbamoyl chlorides are reacted with the R^5 nitrogen of the heteroalkyl group in a solvent, such as acetonitrile or dimethylformamide, in the presence of a base, such as sodium or potassium carbonate, at a temperature between about 20°C to about 100 °C for a time period between about 24 hours to about 72 hours. For amide and sulfonamide formation, electrophiles of formula II, such as acylchlorides and sulfonyl chlorides, are reacted with the R^5 nitrogen of the heteroalkyl group in a solvent such as methylene chloride in the presence of a base such as pyridine at ambient temperatures for a time period between about 12 hours to about 24 hours. Amide formation may also be carried out by reacting a carboxylic acid with the heteroalkyl group in the presence of a carbodiimide such as 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide in a solvent such as methylene chloride at ambient temperatures for 12-24 hours. For alkyl formation, electrophiles of formula II, such as α,β-unsaturated amides, acids, nitriles, esters, and α-halo amides, are reacted with the R^5 nitrogen of the heteroalkyl group in a solvent such as methanol at ambient temperatures for a time period between about 12 hours to about 18 hours. Alkyl formation may also be carried out by reacting aldehydes with the heteroalkyl group in the presence of a reducing agent, such as sodium cyanoborohydride, in a solvent, such as methanol, at ambient temperature for a time period between about 12 hours to about 18 hours.

In reaction 3 of Scheme 1, removal of the protecting group from the compound of formula XV, wherein R is benzenesulfonyl, to give the corresponding compound of formula I, is carried out by treating XV with an alkali base, such as sodium hydroxide or potassium hydroxide, in an alcohol solvent, such as methanol or ethanol, or mixed solvents, such as alcohol/tetrahydrofuran or alcohol/water. The
reaction is carried out at room temperature for a time period between about 15 minutes to about 1 hour, preferably 30 minutes. Removal of the protecting group from the compound of formula XV, wherein R is benzyl, is conducted by treating XV with sodium in ammonia at a temperature of about -78°C for a time period between about 15 minutes to about 1 hour.

In reaction 1 of Scheme 2, the 4-chloropyrrolo[2,3-d]pyrimidine compound of formula XX is converted to the corresponding 4-aminopyrrolo[2,3-d]pyrimidine compound of formula XXIV, according to the procedure described above in reaction 2 of Scheme 1.

In reaction 2 of Scheme 2, the 4-amino-5-halopyrrolo[2,3-d]pyrimidine compound of formula XXIV, wherein R is benzenesulfonate and Z is bromine or iodine, is converted to the corresponding compound of formula XXIII by reacting XXIV with (a) aryloboronic acid, when R² is aryl, in an aprotic solvent, such tetrahydrofuran or dioxane, in the presence of a catalytic quantity of palladium (0) at a temperature between about 50°C to about 100°C, preferably about 70°C, for a time period between about 2 hours to about 48 hours, preferably about 12 hours; (b) alkynes, when R² is alkynyl, in the presence of a catalytic quantity of copper (I) iodide and palladium (0), and a polar solvent, such as dimethylformamide, at room temperature, for a time period between about 1 hour to about 5 hours, preferably about 3 hours; and (c) alkenes or styrenes, when R² is vinyl or styrenyl, in the presence of a catalytic quantity of palladium in dimethylformamide, dioxane or tetrahydrofuran, at a temperature between about 80°C to about 100°C, preferably about 100°C, for a time period between about 2 hours to about 48 hours, preferably about 48 hours.

In reaction 3 of Scheme 2, the compound of formula XXIII is converted to the corresponding compound of formula XV, according to the procedure described above in reaction 3 of Preparation A.

In reaction 1 of Scheme 3, the compound of formula XVII is converted to the corresponding compound of formula I, according to the procedure described above in reaction 2 of Scheme 1.

The compounds of the present invention that are basic in nature are capable of forming a wide variety of different salts with various inorganic and organic acids. Although such salts must be pharmaceutically acceptable for administration to animals, it is often desirable in practice to initially isolate the compound of the present invention from the reaction mixture as a pharmaceutically unacceptable salt and then
simply convert the latter back to the free base compound by treatment with an alkaline reagent and subsequently convert the latter free base to a pharmaceutically acceptable acid addition salt. The acid addition salts of the base compounds of this invention are readily prepared by treating the base compound with a substantially equivalent amount of the chosen mineral or organic acid in an aqueous solvent medium or in a suitable organic solvent, such as methanol or ethanol. Upon careful evaporation of the solvent, the desired solid salt is readily obtained. The desired acid salt can also be precipitated from a solution of the free base in an organic solvent by adding to the solution an appropriate mineral or organic acid.

Those compounds of the present invention that are acidic in nature, are capable of forming base salts with various pharmacologically acceptable cations. Examples of such salts include the alkali metal or alkaline-earth metal salts and particularly, the sodium and potassium salts. These salts are all prepared by conventional techniques. The chemical bases which are used as reagents to prepare the pharmaceutically acceptable base salts of this invention are those which form non-toxic base salts with the acidic compounds of the present invention. Such non-toxic base salts include those derived from such pharmacologically acceptable cations as sodium, potassium calcium and magnesium, etc. These salts can easily be prepared by treating the corresponding acidic compounds with an aqueous solution containing the desired pharmacologically acceptable cations, and then evaporating the resulting solution to dryness, preferably under reduced pressure. Alternatively, they may also be prepared by mixing lower alkanolic solutions of the acidic compounds and the desired alkali metal alkoxide together, and then evaporating the resulting solution to dryness in the same manner as before. In either case, stoichiometric quantities of reagents are preferably employed in order to ensure completeness of reaction and maximum yields of the desired final product.

Pharmacological attempts to prevent restenosis by pharmacologic means have thus far been unsuccessful and all involve systemic administration of the trial agents. Neither aspirin-dipyridamole, ticlopidine, acute heparin administration, chronic warfarin (6 months) nor methylprednisolone have been effective in preventing restenosis although platelet inhibitors have been effective in preventing acute reocclusion after angioplasty. The calcium antagonists have also been unsuccessful in preventing restenosis, although they are still under study. Other agents currently under study include thromboxane inhibitors, prostacyclin mimetics, platelet
membrane receptor blockers, thrombin inhibitors and angiotensin converting enzyme inhibitors. These agents must be given systemically, however, and attainment of a therapeutically effective dose may not be possible; antiproliferative (or anti-restenosis) concentrations may exceed the known toxic concentrations of these agents so that levels sufficient to produce smooth muscle inhibition may not be reached (Lang et al., 42 Ann. Rev. Med., 127-132 (1991); Popma et al., 84 Circulation, 1426-1436 (1991)).

Additional clinical trials in which the effectiveness for preventing restenosis of dietary fish oil supplements, thromboxane receptor antagonists, cholesterol lowering agents, and serotonin antagonists has been examined have shown either conflicting or negative results so that no pharmacological agents are as yet clinically available to prevent post-angioplasty restenosis (Franklin, S. M. and Faxon, D. P., 4 Coronary Artery Disease, 232-242 (1993); Serruys, P. W. et al., 88 Circulation, (part 1) 1588-1601, (1993)).

Conversely, stents have proven useful in preventing reducing the proliferation of restenosis. Stems, such as the stent 40, seen in layout in FIG. 4, balloon-expandable slotted metal tubes (usually but not limited to stainless steel), which when expanded within the lumen of an angioplastied coronary artery, provide structural support to the arterial wall. This support is helpful in maintaining an open path for blood flow. In two randomized clinical trials, stents were shown to increase angiographic success after PTCA, increase the stenosed blood vessel lumen and to reduce the lesion recurrence at 6 months (Serruys et al., 331 New Eng Jour. Med, 495, (1994); Fischman et al., 331 New Eng Jour. Med. 496-501 (1994). Additionally, in a preliminary trial, heparin coated stents appear to possess the same benefit of reduction in stenosis diameter at follow-up as was observed with non-heparin coated stents. Additionally, heparin coating appears to have the added benefit of producing a reduction in sub-acute thrombosis after stent implantation (Serruys et al., 93 Circulation, 412-422 (1996). Thus, 1) sustained mechanical expansion of a stenosed coronary artery has been shown to provide some measure of restenosis prevention, and 2) coating of stents with heparin has demonstrated both the feasibility and the clinical usefulness of delivering drugs to local, injured tissue off the surface of the stent.
Experiments

Agents: 3-((3R,4R)-4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidin-1-yl)-3-oxo-propionitrile

Delivery Methods:

These can vary:

Local delivery of such agents (3-((3R,4R)-4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidin-1-yl)-3-oxo-propionitrile) from the struts of a stent, from a stent graft, grafts, stent cover or sheath.

Involving comixture with polymers (both degradable and nondegrading) to hold the drug to the stent or graft.

or entrapping the drug into the metal of the stent or graft body which has been modified to contain micropores or channels, as will be explained further herein.

or including covalent binding of the drug to the stent via solution chemistry techniques (such as via the Carmeda process) or dry chemistry techniques (e.g. vapour deposition methods such as rf-plasma polymerization) and combinations thereof.

Catheter delivery intravascularly from a tandem balloon or a porous balloon for intramural uptake

Extravascular delivery by the pericardial route

Extravascular delivery by the advential application of sustained release formulations.

Uses: for inhibition of cell proliferation to prevent neointimal proliferation and restenosis.

prevention of tumor expansion from stents

prevent ingrowth of tissue into catheters and shunts inducing their failure.

1. Experimental Stent Delivery Method-Delivery from Polymer Matrix

   Solution of 3-((3R,4R)-4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidin-1-yl)-3-oxo-propionitrile, prepared in a solvent miscible with polymer carrier solution, is mixed with solution of polymer at final concentration range 0.001 weight % to 30 weight % of drug. Polymers are biocompatible (i.e., not elicit any negative tissue reaction or promote mural thrombus formation) and degradable, such as lactone-based polyesters or copolyesters, e.g., polylactide, polycaprolactone-glycolide,polyorthoesters, polyanhydrides; polyaminoacids; polysaccharides;
polyphosphazenes; poly (ether-ester) copolymers, e.g., PEO-PLLA, or blends thereof. Nonabsorbable biocompatible polymers are also suitable candidates. Polymers such as polydimethylsiloxane; poly(ethylene-vinylacetate); acrylate based polymers or copolymers, e.g., poly(hydroxyethyl methylmethacrylate, polyvinyl pyrrolidinone; fluorinated polymers such as polytetrafluoroethylene; cellulose esters.

Bulking agents typically comprise inert materials. Suitable bulking agents are known to those skilled in the art. Polymers suitable to form a polymeric matrix of the sustained release composition of this invention are biocompatible polymers which can be either a biodegradable or non-biodegradable polymer, or blends or copolymers thereof.

Biodegradable, as defined herein, means the composition will degrade or erode in vivo to form smaller chemical species. Degradation can result, for example, by enzymatic, chemical and physical processes. Suitable biocompatible, biodegradable polymers include, for example, poly (lactides), poly(glycolides), poly(lactide-co-glycolides), poly(lactic acid)s, poly(glycolic acid)s, poly(lactic acid-coglycolic acid)s, poly caprolactone, polycarbonates, polyesteramides, polyanhydrides, poly(amino acids), polyorthoesters, polycyanoacrylates, poly (p-dioxanone), poly(alkylene oxalate)s, biodegradable polyurethanes, blends and copolymers thereof. Biocompatible, nonbiodegradable polymers suitable for the modulated release composition of this invention include non-biodegradable polymers selected from the group consisting of polyacrylates, polymers of ethylene-vinyl acetates and other acyl substituted cellulose acetates, non-degradable polyurethanes, polystyrenes, polyvinyl chloride, polyvinyl fluoride, poly(vinyl imidazole), chlorosulphonate polyolefins, polyethylene oxide, blends and copolymers thereof.

A polymer, or polymeric matrix, is biocompatible if the polymer, and any degradation products of the polymer, are non-toxic to the recipient and also present no significant deleterious or untoward effects on the recipient's body, such as an immunological reaction at the injection site. Further, the terminal functionalities of a polymer can be modified. For example, polyesters can be blocked, unblocked or a blend of blocked and unblocked polymers. A blocked polymer is as classically defined in the art, specifically having blocked carboxyl end groups. Generally, the blocking group is derived from the initiator of the polymerization and is typically an alkyl group.
An unblocked polymer is as classically defined in the art, specifically having free carboxyl end groups.

Acceptable molecular weights for polymers used in this invention can be determined by a person of ordinary skill in the art taking into consideration factors such as the desired polymer degradation rate, physical properties such as mechanical strength, and rate of dissolution of polymer in solvent. Typically, an acceptable range of molecular weights is of about 2,000 Daltons to about 2,000,000 Daltons. In a preferred embodiment, the polymer is a biodegradable polymer or copolymer. In a more preferred embodiment, the polymer is a poly(lactide-co-glycolide) (hereinafter "PLGA") with a lactide:glycolide ratio of about 1:1 and a molecular weight of about 5,000 Daltons to about 70,000 Daltons. In an even more preferred embodiment, the molecular weight of the PLGA used in the present invention has a molecular weight of about 10,000 Daltons.

Polymer/drug mixture is applied to the surfaces of the stent by either dip-coating, or spray coating, or brush coating or dip/spin coating or combinations thereof, and the solvent allowed to evaporate to leave a film with entrapped 3-\{(3R,4R)-4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidin-1-yl\}-3-oxo-propionitrile.

2. Experimental Stent Delivery Method-Delivery from Microporous Depots in Stern Through a Polymer Membrane Coating:

Stent, whose body has been modified to contain micropores or channels is dipped into a solution of 3-\{(3R,4R)-4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidin-1-yl\}-3-oxo-propionitrile, range 0.001 wt % to saturated, in organic solvent such as acetone or methylene chloride, for sufficient time to allow solution to permeate into the pores. (The dipping solution can also be compressed to improve the loading efficiency.) After solvent has been allowed to evaporate, the stent is dipped briefly in fresh solvent to remove excess surface bound drug. A solution of polymer, chosen from any identified in the first experimental method, is applied to the stent as detailed above. This outerlayer of polymer will act as diffusion-controller for release of drug.

3. Experimental Stent Delivery Method-Delivery Via Lysis of a Covalent Drug Tether
3-{(3R,4R)-4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperdin-1-yl}-3-oxo-propionitrile is modified to contain a hydrolytically or enzymatically labile covalent bond for attaching to the 65 surface of the stent which itself has been chemically derivatized to allow covalent immobilization. Covalent bonds such as ester, amides or anhydrides may be suitable for this.

4. Experimental Method-Pericardial Delivery

A: Polymeric Sheet 3-{(3R,4R)-4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperdin-1-yl}-3-oxo-propionitrile is combined at concentration range previously highlighted, with a degradable polymer such as poly(caprolactone-glycolide) or nondegradable polymer, e.g., polydimethylsiloxane, and mixture cast as a thin sheet, thickness range 10, u to 1000, u. The resulting sheet can be wrapped perivascularly on the target vessel. Preference would be for the absorbable polymer.

B: Conformal Coating: 3-{(3R,4R)-4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperdin-1-yl}-3-oxo-propionitrile is combined with a polymer that has a melting temperature just above 37°C, range 40°-45°C. Mixture is applied in a molten state to the external side of the target vessel. Upon cooling to body temperature the mixture solidifies conformally to the vessel wall. Both non-degradable and absorbable biocompatible polymers are suitable.

As seen in the figures it is also possible to modify currently manufactured stents in order to adequately provide the drug dosages such as 3-{(3R,4R)-4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperdin-1-yl}-3-oxo-propionitrile. As seen in FIGS. 1a, 2a and 3a, any stent strut 10, 20, 30 can be modified to have a certain reservoir or channel 11, 21, 31. Each of these reservoirs can be open or closed as desired. These reservoirs can hold the drug to be delivered. FIG. 4 shows a stent 40 with a reservoir 45 created at the apex of a flexible strut. Of course, this reservoir 45 is intended to be useful to deliver 3-{(3R,4R)-4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperdin-1-yl}-3-oxo-propionitrile or any other drug at a specific point of flexibility of the stent. Accordingly, this concept can be useful for "second generation" type stents.

In any of the foregoing devices, however, it is useful to have the drug dosage applied with enough specificity and enough concentration to provide an effective dosage in the lesion area. In this regard, the reservoir size in the stent struts must be
kept at a size of about 0.0005" to about 0.003". Then, it should be possible to adequately apply the drug dosage at the desired location and in the desired amount. These and other concepts will are disclosed herein. It would be apparent to the reader that modifications are possible to the stent or the drug dosage applied. In any event, however, the any obvious modifications should be perceived to fall within the scope of the invention which is to be realized from the attached claims and their equivalents.
What is claimed is:

1. A stent having a coating containing a compound of the formula

   \[ \text{R}^1 \text{N}^{(\text{CH}_2)_y} \text{R}^5 \]

   or the pharmaceutically acceptable salt thereof; wherein

   \[ \text{R}^1 \text{ is a group of the formula} \]

   \[ \text{wherein } y \text{ is 0, 1 or 2;} \]

   \[ \text{R}^4 \text{ is selected from the group consisting of hydrogen, (C}_{1-}{\text{C}}_{6}\text{)alkyl, (C}_{1-}{\text{C}}_{6}\text{)alkylsulfonyl, (C}_{2-}{\text{C}}_{6}\text{)alkenyl, (C}_{2-}{\text{C}}_{6}\text{)alkynyl wherein the alkyl, alkenyl and alkynyl} \]

   \[ \text{groups are optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C}_{1-}{\text{C}}_{4}\text{)alkoxy, (C}_{1-}{\text{C}}_{6}\text{)acyloxy, (C}_{1-}{\text{C}}_{6}\text{)alkylamino, ((C}_{1-}{\text{C}}_{6}\text{)alkyl})_2\text{amino, cyano, nitro, (C}_{2-}{\text{C}}_{6}\text{)alkenyl, (C}_{2-}{\text{C}}_{6}\text{)alkynyl or (C}_{1-}{\text{C}}_{6}\text{)acylamino; or R}^4 \text{ is (C}_{3-}{\text{C}}_{10}\text{)cycloalkyl wherein the cycloalkyl group is optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C}_{1-}{\text{C}}_{6}\text{)acyloxy, (C}_{1-}{\text{C}}_{6}\text{)acylamino, (C}_{1-}{\text{C}}_{6}\text{)alkylamino, ((C}_{1-}{\text{C}}_{6}\text{)alkyl})_2\text{amino, cyano, cyano(C}_{1-}{\text{C}}_{6}\text{)alkyl, trifluoromethyl(C}_{1-}{\text{C}}_{6}\text{)alkyl, nitro, nitro(C}_{1-}{\text{C}}_{6}\text{)alkyl or (C}_{1-}{\text{C}}_{6}\text{)acylamino;}} \]

   \[ \text{R}^5 \text{ is (C}_{2-}{\text{C}}_{6}\text{)heterocycloalkyl wherein the heterocycloalkyl groups must be substituted by one to five carboxy, cyano, amino, deuterium, hydroxy, (C}_{1-}{\text{C}}_{6}\text{)alkyl, (C}_{1-}{\text{C}}_{6}\text{)alkoxy, halo, (C}_{1-}{\text{C}}_{6}\text{)acyl, (C}_{1-}{\text{C}}_{6}\text{)alkylamino, amino(C}_{1-}{\text{C}}_{6}\text{)alkyl, (C}_{1-}{\text{C}}_{6}\text{)alkoxy-CO-NH, (C}_{1-}{\text{C}}_{6}\text{)alkylamino-CO-}, (C}_{1-}{\text{C}}_{6}\text{)alkenyl, (C}_{1-}{\text{C}}_{6}\text{)alkynyl, (C}_{1-}{\text{C}}_{6}\text{)alkylamino, amino(C}_{1-}{\text{C}}_{6}\text{)alkyl, hydroxy(C}_{1-}{\text{C}}_{6}\text{)alkyl, (C}_{1-}{\text{C}}_{6}\text{)alkoxy(C}_{1-}{\text{C}}_{6}\text{)alkyl, (C}_{1-}{\text{C}}_{6}\text{)acyloxy(C}_{1-}{\text{C}}_{6}\text{)alkyl, nitro, cyano(C}_{1-}{\text{C}}_{6}\text{)alkyl, halo(C}_{1-}{\text{C}}_{6}\text{)alkyl, nitro(C}_{1-}{\text{C}}_{6}\text{)alkyl, trifluoromethyl, trifluoromethyl(C}_{1-}{\text{C}}_{6}\text{)alkyl, (C}_{1-}{\text{C}}_{6}\text{)acylamino, (C}_{1-}{\text{C}}_{6}\text{)acylamino(C}_{1-}{\text{C}}_{6}\text{)alkyl, (C}_{1-}{\text{C}}_{6}\text{)alkoxy(C}_{1-}{\text{C}}_{6}\text{)acylamino, amino(C}_{1-}{\text{C}}_{6}\text{)acyl, amino(C}_{1-}{\text{C}}_{6}\text{)acyl(C}_{1-}{\text{C}}_{6}\text{)alkyl, (C}_{1-}{\text{C}}_{6}\text{)alkylamino(C}_{1-}{\text{C}}_{6}\text{)acyl, ((C}_{1-}{\text{C}}_{6}\text{)alkyl)_2\text{amino(C}_{1-}{\text{C}}_{6}\text{)acyl, R}^{15}\text{R}^{16}\text{N-CO-O, R}^{15}\text{R}^{16}\text{N-CO-(C}_{1-}{\text{C}}_{6}\text{)alkyl, (C}_{1-}{\text{C}}_{6}\text{)alkyl-S(O)}_{m}\text{, R}^{15}\text{R}^{16}\text{NS(O)}_{m}, \text{R}^{15}\text{R}^{16}\text{NS(O)}_{m} \text{(C}_{1-}{\text{C}}_{6}\text{)alkyl, R}^{15}\text{S(O)}_{m}, \text{R}^{15}\text{N, R}^{15}\text{S(O)}_{m} \text{R}^{16}\text{N(C}_{1-}{\text{C}}_{6})\text{)}}\]
C₉alkyl wherein m is 0, 1 or 2 and R¹⁵ and R¹⁶ are each independently selected from hydrogen or (C₇-C₉)alkyl; or a group of the formula

wherein a is 0, 1, 2, 3 or 4;

b, c, e, f and g are each independently 0 or 1;
d is 0, 1, 2, or 3;

X is S(O)ₙ wherein n is 0, 1 or 2; oxygen, carbonyl or =C(=N-cyano)-;

Y is S(O)ₙ wherein n is 0, 1 or 2; or carbonyl; and

Z is carbonyl, C(O)O-, C(O)NR- or S(O)ₙ wherein n is 0, 1 or 2;

R⁶, R⁷, R⁸, R⁹, R¹⁰ and R¹¹ are each independently selected from the group consisting of hydrogen or (C₁-C₆)alkyl optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C₁-C₆)acyloxy, (C₁-C₆)acylamino, (C₁-C₆)alkylamino, ((C₁-C₆)alkyl)₂amino, cyano, cyano(C₁-C₆)alkyl, trifluoromethyl(C₁-C₆)alkyl, nitro, nitro(C₁-C₆)alkyl or (C₁-C₆)acylamino;

R¹² is carboxy, cyano, amino, oxo, deuterium, hydroxy, trifluoromethyl, (C₁-C₆)alkyl, trifluoromethyl(C₁-C₆)alkyl, (C₁-C₆)alkoxy, halo, (C₁-C₆)acyl, (C₁-C₆)alkylamino, ((C₁-C₆)alkyl)₂amino, amino(C₁-C₆)alkyl, (C₁-C₆)alkoxy-CO-NH, (C₁-C₆)alkylamino-CO-, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-C₆)alkylamino, hydroxy(C₁-C₆)alkyl, (C₁-C₆)alkoxy(C₁-C₆)alkyl, (C₁-C₆)acyloxy(C₁-C₆)alkyl, nitro, cyano(C₁-C₆)alkyl, halo(C₁-C₆)alkyl, nitro(C₁-C₆)alkyl, trifluoromethyl, trifluoromethyl(C₁-C₆)alkyl, (C₁-C₆)acylamino, (C₁-C₆)acylamino(C₁-C₆)alkyl, (C₁-C₆)alkoxy(C₁-C₆)acylaminono, amino(C₁-C₆)acyl, amino(C₁-C₆)acyl(C₁-C₆)alkyl, (C₁-C₆)alkylamino(C₁-C₆)acyl, (C₁-C₆)alkylamino(C₁-C₆)acyl, R¹⁵R¹⁶N-CO-O-, R¹⁵R¹⁶N-CO-(C₁-C₆)alkyl, R¹⁵C(O)NH, R¹⁵OC(O)NH, R¹⁵NHC(O)NH, (C₁-C₆)alkyl-S(O)ₙm, (C₁-C₆)alkyl-S(O)ₙm(C₁-C₆)alkyl, R¹⁵R¹⁶NS(O)ₙm, R¹⁵R¹⁶NS(O)ₙm(C₁-C₆)alkyl, R¹⁵S(O)ₙmR¹⁶N, R¹⁵S(O)ₙmR¹⁶N(C₁-C₆)alkyl

wherein m is 0, 1 or 2 and R¹⁵ and R¹⁶ are each independently selected from hydrogen or (C₁-C₆)alkyl;
R² and R³ are each independently selected from the group consisting of hydrogen, deuterium, amino, halo, hydroxy, nitro, carboxy, (C₂₋C₆)alkenyl, (C₂₋C₆)alkynyl, trifluoromethyl, trifluoromethoxy, (C₁₋C₆)alkyl, (C₁₋C₆)alkoxy, (C₃₋C₁₀)cycloalkyl wherein the alkyl, alkoxy or cycloalkyl groups are optionally substituted by one to three groups selected from halo, hydroxy, carboxy, amino (C₁₋C₆)alkylthio, (C₁₋C₆)alkylamino, ((C₁₋C₆)alkyl)₂amino, (C₅₋C₆)heteroaryl, (C₂₋C₆)heterocycloalkyl, (C₃₋C₆)cycloalkyl or (C₅₋C₁₀)aryl; or R² and R³ are each independently (C₃₋C₁₀)cycloalkyl, (C₃₋C₁₀)cycloalkoxy, (C₁₋C₆)alkylamino, ((C₁₋C₆)alkyl)₂amino, (C₆₋C₁₀)arylamino, (C₁₋C₆)alkylthio, (C₆₋C₁₀)arylamino, (C₁₋C₆)alkylsulfinyl, (C₆₋C₁₀)arylsulfinyl, (C₁₋C₆)alkylsulfonyl, (C₆₋C₁₀)arylsulfonyl, (C₁₋C₆)acyl, (C₁₋C₆)alkoxy-CO-NH-, (C₁₋C₆)alkylamino-CO-, (C₅₋C₆)heteroaryl, (C₂₋C₆)heterocycloalkyl or (C₆₋C₁₀)aryl wherein the heteroaryl, heterocycloalkyl and aryl groups are optionally substituted by one to three halo, (C₁₋C₆)alkyl, (C₁₋C₆)alkyl-CO-NH-, (C₁₋C₆)alkoxy-CO-NH-, (C₁₋C₆)alkyl-CO-NH-(C₁₋C₆)alkyl, (C₁₋C₆)alkoxy-CO-NH-(C₁₋C₆)alkyl, (C₁₋C₆)alkoxy-CO-(C₁₋C₆)alkoxy, carboxy, carboxy(C₁₋C₆)alkyl, carboxy(C₁₋C₆)alkoxy, benzyloxy carbonyl(C₁₋C₆)alkoxy, (C₁₋C₆)alkoxy carbonyl(C₁₋C₆)alkoxy, (C₆₋C₁₀)aryl amino, amino(C₁₋C₆)alkyl, (C₁₋C₆)alkoxycarbonylamino, (C₆₋C₁₀)arylamino(C₁₋C₆)alkoxycarbonylamino, (C₁₋C₆)alkoxycarbonylamino, (C₁₋C₆)alkoxycarbonylamino, (C₁₋C₆)alkoxycarbonylamino, (C₆₋C₆)alkoxycarbonylamino(C₁₋C₆)alkyl, (C₆₋C₁₀)alkoxycarbonylamino(C₁₋C₆)alkyl, amino(C₁₋C₆)alkyl, carboxy, carboxy(C₁₋C₆)alkyl, (C₁₋C₆)alkoxycarbonyl, (C₁₋C₆)alkoxycarbonyl(C₁₋C₆)alkyl, (C₁₋C₆)alkoxycarbonyl-CO-NH-, (C₁₋C₆)alkyl-CO-NH-, cyano, (C₅₋C₆)heterocycloalkyl, amino-CO-NH-, (C₁₋C₆)alkylamino-CO-NH-, ((C₁₋C₆)alkyl)₂amino-CO-NH-, (C₁₋C₁₀)arylamino-CO-NH-, (C₅₋C₆)heteroarylamino-CO-NH-, (C₁₋C₆)alkylamino-CO-NH-(C₁₋C₆)alkyl, (C₁₋C₆)alkylamino-CO-NH-(C₆₋C₁₀)arylamino-CO-NH-(C₁₋C₆)alkyl, (C₁₋C₆)alkyl(C₅₋C₆)heteroarylaminocO-NH-(C₁₋C₆)alkyl, (C₁₋C₆)alkyl(C₆₋C₁₀)arylamino-CO-NH-(C₁₋C₆)alkyl, (C₁₋C₆)alkyl(C₅₋C₆)heteroarylaminocO-NH-(C₁₋C₆)alkyl, (C₆₋C₁₀)arylsulfonylamino, (C₁₋C₆)alkylsulfonylamino, (C₁₋C₆)alkylsulfonylamino(C₁₋C₆)alkyl, (C₆₋C₁₀)arylsulfonylamino, (C₁₋C₆)alkylsulfonylamino(C₁₋C₆)alkyl, (C₁₋C₆)alkylsulfonylamino, (C₁₋C₆)alkylsulfonylamino(C₁₋C₆)alkyl, (C₅₋C₆)heteroaryl or (C₂₋C₆)heterocycloalkyl,

said coating formed from a polymer mixed carrier containing the compound of Formula I; and said coating applied to said stent.

2. The stent of claim 1 wherein the stent is dip-coated.

3. The stent of claim 1 wherein the stent is sprayed with said coating.
4. A stent having a coating containing a compound of the formula

or the pharmaceutically acceptable salt thereof; wherein

R¹ is a group of the formula

wherein y is 0, 1 or 2;

R⁴ is selected from the group consisting of hydrogen, (C₁-C₆)alkyl, (C₁-C₆)alkylsulfonyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl wherein the alkyl, alkenyl and alkynyl groups are optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C₁-C₄)alkoxy, (C₁-C₆)acyloxy, (C₁-C₆)alkylamino, ((C₁-C₆)alkyl)₂amino, cyano, nitro, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl or (C₁-C₆)acylamino; or R⁴ is (C₅-C₁₀)cycloalkyl wherein the cycloalkyl group is optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C₁-C₆)acyloxy, (C₁-C₆)acylamino, (C₁-C₆)alkylamino, ((C₁-C₆)alkyl)₂amino, cyano, cyano(C₁-C₆)alkyl, trifluoromethyl(C₁-C₆)alkyl, nitro, nitro(C₁-C₆)alkyl or (C₁-C₆)acylamino;

R⁵ is (C₂-C₆)heterocycloalkyl wherein the heterocycloalkyl groups must be substituted by one to five carboxy, cyano, amino, deuterium, hydroxy, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, halo, (C₁-C₆)acyl, (C₁-C₆)alkylamino, amino(C₁-C₆)alkyl, (C₁-C₆)alkoxy-CO-NH, (C₁-C₆)alkylamino-CO-, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₂-C₆)alkylamino, amino(C₁-C₆)alkyl, hydroxy(C₁-C₆)alkyl, (C₁-C₆)alkoxy(C₁-C₆)alkyl, (C₁-C₆)acyloxy(C₁-C₆)alkyl, nitro, cyano(C₁-C₆)alkyl, halo(C₁-C₆)alkyl, nitro(C₁-C₆)alkyl, trifluoromethyl, trifluoromethyl(C₁-C₆)alkyl, (C₁-C₆)acylamino, (C₁-C₆)acylamino(C₁-C₆)alkyl, (C₁-C₆)alkoxy(C₁-C₆)acylamino, amino(C₁-C₆)acyl, amino(C₁-C₆)acyl(C₁-C₆)alkyl, (C₁-C₆)alkylamino(C₁-C₆)acyl, ((C₁-C₆)alkyl)₂amino(C₁-C₆)acyl, R¹⁶R¹⁶N-CO-O-, R¹⁵R¹⁶N-CO-(C₁-C₆)alkyl, (C₁-C₆)alkyl-S(O)ₘ, R¹⁵R¹⁶NS(O)ₘ, R¹⁵R¹⁶NS(O)ₘ(C₁-C₆)alkyl, R¹⁶S(O)ₘ, R¹⁶N, R¹⁵S(O)ₘR¹⁶N(C₁-C₆)alkyl.
C₆alkyl wherein m is 0, 1 or 2 and R¹⁵ and R¹⁶ are each independently selected from hydrogen or (C₁₋C₆)alkyl; or a group of the formula

wherein a is 0, 1, 2, 3 or 4;

b, c, e, f and g are each independently 0 or 1;
d is 0, 1, 2, or 3;
X is S(O)ₙ wherein n is 0, 1 or 2; oxygen, carbonyl or −C(=N-cyano)−;
Y is S(O)ₙ wherein n is 0, 1 or 2; or carbonyl; and
Z is carbonyl, C(O)O−, C(O)NR− or S(O)ₙ wherein n is 0, 1 or 2;

R⁶, R⁷, R⁸, R⁹, R¹⁰ and R¹¹ are each independently selected from the group consisting of hydrogen or (C₁₋C₆)alkyl optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C₁₋C₆)acyloxy, (C₁₋C₆)acylamino, (C₁₋C₆)alkylamino, ((C₁₋C₆)alkyl)₂amino, cyano, cyano(C₁₋C₆)alkyl, trifluoromethyl(C₁₋C₆)alkyl, nitro, nitro(C₁₋C₆)alkyl or (C₁₋C₆)acylamino;

R¹² is carboxy, cyano, amino, oxo, deuterium, hydroxy, trifluoromethyl, (C₁₋C₆)alkyl, trifluoromethyl(C₁₋C₆)alkyl, (C₁₋C₆)alkoxy, halo, (C₁₋C₆)acyl, (C₁₋C₆)alkylamino, (C₁₋C₆)alkyl, amino(C₁₋C₆)alkyl, (C₁₋C₆)alkoxy-CO-NH, (C₁₋C₆)alkylamino-CO−, (C₂₋C₆)alkenyl, (C₂₋C₆)alkynyl, (C₁₋C₆)alkylamino, hydroxy(C₁₋C₆)alkyl, (C₁₋C₆)alkoxy(C₁₋C₆)alkyl, (C₁₋C₆)alkoxy(C₁₋C₆)alkyl, nitro, cyano(C₁₋C₆)alkyl, halo(C₁₋C₆)alkyl, nitro(C₁₋C₆)alkyl, trifluoromethyl, trifluoromethyl(C₁₋C₆)alkyl, (C₁₋C₆)acylamino, (C₁₋C₆)acylamino(C₁₋C₆)alkyl, (C₁₋C₆)alkoxy(C₁₋C₆)acylamino, amino(C₁₋C₆)acyl, amino(C₁₋C₆)acyl(C₁₋C₆)alkyl, (C₁₋C₆)alkylamino(C₁₋C₆)alkyl, (C₁₋C₆)alkylamino(C₁₋C₆)alkyl, R¹⁵R¹⁶N-CO-O−, R¹⁵R¹⁶N-CO-(C₁₋C₆)alkyl, R¹⁵C(O)NH, R¹⁵OC(O)NH, R¹⁵NHC(O)NH, (C₁₋C₆)alkyl-S(O)ₙm, (C₁₋C₆)alkyl-S(O)ₙm-(C₁₋C₆)alkyl, R¹⁵R¹⁶NS(O)ₙm, R¹⁵R¹⁶NS(O)ₙm-(C₁₋C₆)alkyl, R¹⁵S(O)ₙmR¹⁶N, R¹⁵S(O)ₙmR¹⁶N(C₁₋C₆)alkyl

wherein m is 0, 1 or 2 and R¹⁵ and R¹⁶ are each independently selected from hydrogen or (C₁₋C₆)alkyl;
$R^2$ and $R^3$ are each independently selected from the group consisting of hydrogen, deuterium, amino, halo, hydroxy, nitro, carboxy, (C$_2$-C$_6$)alkenyl, (C$_2$-C$_6$)alkynyl, trifluoromethyl, trifluoromethoxy, (C$_1$-C$_6$)alkyl, (C$_1$-C$_6$)alkoxy, (C$_3$-C$_{10}$)cycloalkyl wherein the alkyl, alkoxy or cycloalkyl groups are optionally substituted by one to three groups selected from halo, hydroxy, carboxy, amino (C$_1$-C$_6$)alkylthio, (C$_1$-C$_6$)alkylamino, ((C$_1$-C$_6$)alkyl)$_2$amino, (C$_2$-C$_6$)heteroaryl, (C$_2$-C$_6$)heterocycloalkyl, (C$_3$-C$_9$)cycloalkyl or (C$_5$-C$_{10}$)aryl; or $R^2$ and $R^3$ are each independently (C$_3$-C$_{10}$)cycloalkyl, (C$_9$-C$_{10}$)cycloalkoxy, (C$_1$-C$_6$)alkylamino, ((C$_1$-C$_6$)alkyl)$_2$amino, (C$_6$-C$_{10}$)arylamino, (C$_1$-C$_6$)alkylthio, (C$_6$-C$_{10}$)arylsulfonyl, (C$_6$-C$_{10}$)arylsulfinyl, (C$_6$-C$_{10}$)arylsulfonylamino, (C$_6$-C$_{10}$)arylamidino, (C$_1$-C$_6$)alkoxy- CO-NH-; (C$_1$-C$_6$)alkyamino-CO-, (C$_2$-C$_6$)heteroaryl, (C$_2$-C$_6$)heterocycloalkyl or (C$_6$-C$_{10}$)aryl wherein the heteroaryl, heterocycloalkyl and aryl groups are optionally substituted by one to three halo, (C$_1$-C$_6$)alkyl, (C$_1$-C$_6$)alkyl- CO-NH-, (C$_1$-C$_6$)alkoxy- CO-NH-, (C$_1$-C$_6$)alkyl-CO-NH-(C$_1$-C$_6$)alkyl, (C$_1$-C$_6$)alkoxy-CO-NH-(C$_1$-C$_6$)alkyl, (C$_1$-C$_6$)alkoxy-CO-NH-(C$_1$- C$_6$)alkyl, carboxy, carboxy(C$_1$-C$_6$)alkyl, carboxy(C$_1$-C$_6$)alkoxy, benzoylcarboxy(C$_1$-C$_6$)alkoxy, (C$_1$-C$_6$)alkoxybenzoylcarboxy(C$_1$-C$_6$)alkoxy, (C$_6$-C$_{10}$)aryl, amino, amine(C$_1$-C$_6$)alkyl, (C$_1$-C$_6$)alkoxyaminocarbonylamino, (C$_6$-C$_{10}$)aryl(C$_1$- C$_6$)alkoxyaminocarbonylamino, (C$_1$-C$_6$)alkylaminocarbonylamino, ((C$_1$-C$_6$)alkyl)$_2$amino, (C$_1$- C$_6$)alkylaminocarbonylamino, ((C$_1$-C$_6$)alkyl)$_2$amino(C$_1$-C$_6$)alkyl, hydroxy, (C$_1$-C$_6$)alkoxy, carboxy, carboxy(C$_1$-C$_6$)alkyl, (C$_1$-C$_6$)alkoxyaminocarbonyl, (C$_1$-C$_6$)alkoxyaminocarbonyl(C$_1$- C$_6$)alkyl, (C$_1$-C$_6$)alkoxy-CO-NH-, (C$_1$-C$_6$)alkyl-CO-NH-, cyano, (C$_5$-C$_6$)heterocycloalkyl, amino-CO-NH-, (C$_1$-C$_6$)alkylaminocarbonyl-CO-NH-, ((C$_1$-C$_6$)alkyl)$_2$amino-CO-NH-, (C$_6$- C$_{10}$)arylaminocarbonyl-CO-NH-, (C$_5$-C$_6$)heteroarylamino-CO-NH-, (C$_1$-C$_6$)alkylaminocarbonyl-CO-NH-(C$_1$-C$_6$)alkyl, ((C$_1$-C$_6$)alkyl)$_2$amino-CO-NH-(C$_1$-C$_6$)alkyl, (C$_6$-C$_{10}$)arylaminocarbonyl-CO-NH-(C$_1$-C$_6$)alkyl, (C$_1$- C$_6$)alkyl, (C$_5$-C$_6$)heteroarylamino-CO-NH-(C$_1$-C$_6$)alkyl, (C$_1$-C$_6$)alkylsulfonylamino, (C$_1$- C$_6$)alkylsulfonylamino(C$_1$-C$_6$)alkyl, (C$_6$-C$_{10}$)arylaminocarbonyl, (C$_6$-C$_{10}$)arylaminocarbonyl(C$_1$-C$_6$)alkyl, (C$_1$-C$_6$)alkylsulfonylamino, (C$_1$-C$_6$)alkylsulfonylamino(C$_1$-C$_6$)alkyl, (C$_5$-C$_6$)heteroaryl or (C$_2$-C$_6$)heterocycloalkyl, wherein said compound of Formula are contained in the coating at a weight percentage of 0.0001% to 30%.

5. The stent of claim 4 wherein a polymer is mixed to the compound of Formula I.
6. The stent of claim 4 wherein a polymer is bound to the compound of Formula I.

7. The stent of claim 4 wherein the compound of Formula I is entrapped on the surface of the stent by a polymer.

8. A stent having a coating containing a compound of the formula

   \[
   \begin{array}{c}
   \text{R}^1 \text{R}^2 \text{R}^3 \\
   \text{N} \text{(CH}_2\text{)}_y
   \end{array}
   \]

or the pharmaceutically acceptable salt thereof; wherein

   \( \text{R}^1 \) is a group of the formula

   \[
   \text{R}^4 \text{N}(\text{CH}_2\text{)}_y
   \]

   wherein \( y \) is 0, 1 or 2;

   \( \text{R}^4 \) is selected from the group consisting of hydrogen, (C\(_1\)-C\(_6\))alkyl, (C\(_1\)-C\(_6\))alkylsulfonfonyl, (C\(_2\)-C\(_6\))alkenyl, (C\(_2\)-C\(_6\))alkynyl wherein the alkyl, alkenyl and alkynyl groups are optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C\(_1\)-C\(_4\))alkoxy, (C\(_1\)-C\(_6\))acyloxy, (C\(_1\)-C\(_6\))alkylamino, ((C\(_1\)-C\(_6\))alkyl)_2 amino, cyano, nitro, (C\(_2\)-C\(_6\))alkenyl, (C\(_2\)-C\(_6\))alkynyl or (C\(_1\)-C\(_6\))acylamino; or \( \text{R}^4 \) is (C\(_3\)-C\(_10\))cycloalkyl wherein the cycloalkyl group is optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C\(_1\)-C\(_6\))acyloxy, (C\(_1\)-C\(_6\))acylamino, (C\(_1\)-C\(_6\))alkylamino, ((C\(_1\)-C\(_6\))alkyl)_2 amino, cyano, cyano(C\(_1\)-C\(_6\))alkyl, trifluoromethyl(C\(_1\)-C\(_6\))alkyl, nitro, nitro(C\(_1\)-C\(_6\))alkyl or (C\(_1\)-C\(_6\))acylamino;

   \( \text{R}^5 \) is (C\(_2\)-C\(_6\))heterocycloalkyl wherein the heterocycloalkyl groups must be substituted by one to five carboxy, cyano, amino, deuterium, hydroxy, (C\(_1\)-C\(_6\))alkyl, (C\(_1\)-C\(_6\))alkoxy, halo, (C\(_1\)-C\(_6\))acyl, (C\(_1\)-C\(_6\))alkylamino, amino(C\(_1\)-C\(_6\))alkyl, (C\(_1\)-C\(_6\))alkoxy-CO-NH, (C\(_1\)-C\(_6\))alkylamino-CO-, (C\(_2\)-C\(_6\))alkenyl, (C\(_2\)-C\(_6\))alkynyl, (C\(_1\)-C\(_6\))alkylamino, amino(C\(_1\)-C\(_6\))alkyl, hydroxy(C\(_1\)-C\(_6\))alkyl, (C\(_1\)-C\(_6\))alkoxy(C\(_1\)-C\(_6\))alkyl, (C\(_1\)-C\(_6\))acyloxy(C\(_1\)-C\(_6\))alkyl, nitro, cyano(C\(_1\)-C\(_6\))alkyl, halo(C\(_1\)-C\(_6\))alkyl, nitro(C\(_1\)-C\(_6\))alkyl, trifluoromethyl, trifluoromethyl(C\(_1\)-C\(_6\))alkyl, (C\(_1\)-C\(_6\))acylamino, (C\(_1\)-C\(_6\))acylamino(C\(_1\)-C\(_6\))alkyl, (C\(_1\)-C\(_6\))alkoxy(C\(_1\)-C\(_6\))acylamino, amino(C\(_1\)-C\(_6\))acyl,
amino(C₁-C₆)acyl(C₁-C₆)alkyl, (C₁-C₆)alkylamino(C₁-C₆)acyl, ((C₁-C₆)alkyl)₂amino(C₁-C₆)acyl, R¹⁵R¹⁶N-CO-O-, R¹⁵R¹⁶N-CO-(C₁-C₆)alkyl, (C₁-C₆)alkyl-S(O)ₘ, R¹⁵R¹⁶NS(O)ₘ, R¹¹R¹⁶NS(O)ₘ(C₁-C₆)alkyl, R¹⁵S(O)ₘ, R¹⁶N, R¹⁵S(O)ₘR¹⁶N(C₁-C₆)alkyl wherein m is 0, 1 or 2 and R¹⁵ and R¹⁶ are each independently selected from hydrogen or (C₁-C₆)alkyl; or a group of the formula

\[
\text{II}
\]

wherein a is 0, 1, 2, 3 or 4;
b, c, e, f and g are each independently 0 or 1;
d is 0, 1, 2, or 3;
x is S(O)ₙ wherein n is 0, 1 or 2; oxygen, carbonyl or –C(=N-cyano)–;
y is S(O)ₙ wherein n is 0, 1 or 2; or carbonyl; and
z is carbonyl, C(O)O-, C(O)NR- or S(O)ₙ wherein n is 0, 1 or 2;
R⁶, R⁷, R⁸, R⁹, R¹⁰ and R¹¹ are each independently selected from the group consisting of hydrogen or (C₁-C₆)alkyl optionally substituted by deuterium, hydroxy,
amino, trifluoromethyl, (C₁-C₆)acyloxy, (C₁-C₆)acylamino, (C₁-C₆)alkylamino, ((C₁-C₆)alkyl)₂amino, cyano, cyano(C₁-C₆)alkyl, trifluoromethyl(C₁-C₆)alkyl, nitro,
nitro(C₁-C₆)alkyl or (C₁-C₆)acylamino;
R¹² is carboxy, cyano, amino, oxo, deuterium, hydroxy, trifluoromethyl, (C₁-C₆)alkyl, trifluoromethyl(C₁-C₆)alkyl, (C₁-C₆)alkoxy, halo, (C₁-C₆)acyl, (C₁-C₆)alkylamino, (C₁-C₆)alkylamino, (C₁-C₆)alkylamino, (C₁-C₆)alkyl, amino(C₁-C₆)alkyl, (C₁-C₆)alkylamino(C₁-C₆)acyl, ((C₁-C₆)alkyl)₂amino(C₁-C₆)acyl, R¹⁵R¹⁶N-CO-O-, R¹⁵R¹⁶N-CO-(C₁-C₆)alkyl, R¹⁵C(O)NH, R¹⁵C(O)NH, R¹⁵NHC(O)NH, (C₁-C₆)alkyl-S(O)ₘ, (C₁-C₆)alkyl-S(O)ₘ(C₁-C₆)alkyl, R¹⁵R¹⁶NS(O)ₘ, R¹⁵R¹⁶NS(O)ₘ(C₁-C₆)alkyl, R¹⁵S(O)ₘR¹⁶N, R¹⁵S(O)ₘR¹⁶N(C₁-C₆)alkyl
wherein m is 0, 1 or 2 and R^15 and R^16 are each independently selected from hydrogen or (C_1-C_6)alkyl;

R^2 and R^3 are each independently selected from the group consisting of hydrogen, deuterium, amino, halo, hydroxy, nitro, carboxy, (C_2-C_6)alkeny1, (C_2-C_6)alkynyl, trifluoromethyl, trifluoromethoxy, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_3-C_10)cycloalkyl wherein the alkyl, alkoxy or cycloalkyl groups are optionally substituted by one to three groups selected from halo, hydroxy, carboxy, amino (C_1-C_6)alkylthio, (C_1-C_6)alkylamino, ((C_1-C_6)alkyl)amino, (C_5-C_9)heteroaryl, (C_2-C_9)heterocycloalkyl, (C_3-C_9)cycloalkyl or (C_5-C_10)ary1; or R^2 and R^3 are each independently (C_3-C_10)acy1, (C_2-C_10)cycloalkoxy, (C_1-C_6)alkylamino, ((C_1-C_6)alkyl)amino, (C_6-C_10)arylamino, (C_1-C_6)alkylthio, (C_6-C_10)arylsulfonyl, (C_6-C_10)arylsulfonyl, (C_1-C_6)alkylsulfonyl, (C_6-C_10)arylsulfonyl, (C_1-C_6)alkoxy-CO-NO_2, (C_1-C_6)alkylamino-NO_2, (C_2-C_9)heteroaryl, (C_2-C_9)heterocycloalkyl or (C_6-C_10)aryl wherein the heteroaryl, heterocycloalkyl and aryl groups are optionally substituted by one to three halo, (C_2-C_6)alkyl, (C_1-C_6)alkyl-CO-NH-, (C_1-C_6)alkoxy-CO-NH-, (C_1-C_6)alkoxy-CO-NO_2, (C_2-C_6)alkyl-CO-NH-(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-NO_2-(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-NO_2-(C_1-C_6)alkoxy, carboxy, carboxy(C_1-C_6)alkyl, carboxy(C_1-C_6)alkoxy, benzylxycarbonyl(C_1-C_6)alkoxy, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkoxy, (C_6-C_10)ary1, amino, amino(C_1-C_6)alkyl, (C_1-C_6)alkoxy carbamoylamino, (C_6-C_10)ary1(C_1-C_6)alkoxy carbamoylamino, (C_1-C_6)alkylamino, ((C_1-C_6)alkyl)amino, (C_1-C_6)alkylamino(C_1-C_6)alkyl, ((C_1-C_6)alkyl)amino(C_1-C_6)alkyl, hydroxy, (C_1-C_6)alkoxy, carboxy, carboxy(C_1-C_6)alkyl, (C_1-C_6)alkoxycarbonyl, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkyl, (C_1-C_6)alkoxy-CO-NO_2-(C_1-C_6)alkyl, (C_6-C_10)alkyl-NO_2, cyan0, (C_6-C_9)heterocycloalkyl, amino-CO-NH-, (C_1-C_6)alkylamino-CO-NO_2-, ((C_1-C_6)alkyl)amino-CO-NO_2-, (C_1-C_6)alkylamino-CO-NO_2-, (C_2-C_9)heteroaryl or (C_2-C_9)heterocycloalkyl,

said coating formed from a polymer mixed carrier containing the compound of Formula I; and said coating applied to said stent; wherein the polymer is biocompatible and degradable; and
wherein the polymer is chosen from: lactone-based polyesters, lactone-based copolyesters; polyanhydrides; polyaminoacids; polysaccharides; polyphosphazenes; poly(ether-ester) copolymers, and blends of such polymers.

9. A stent having a coating containing a compound of the formula

![Chemical Structure](image)

or the pharmaceutically acceptable salt thereof; wherein

R^1 is a group of the formula

![Chemical Structure](image)

wherein y is 0, 1 or 2;

R^4 is selected from the group consisting of hydrogen, (C_1-C_8)alkyl, (C_1-C_8)alkylsulfonyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl wherein the alkyl, alkenyl and alkynyl groups are optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C_1-C_4)alkoxy, (C_1-C_6)acyloxy, (C_1-C_6)alkylamino, ((C_1-C_6)alkyl)amino, cyano, nitro, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl or (C_1-C_6)acylamino; or R^4 is (C_3-C_10)cycloalkyl wherein the cycloalkyl group is optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C_1-C_6)acyloxy, (C_1-C_6)acylamino, (C_1-C_8)alkylamino, ((C_1-C_8)alkyl)amino, cyano, cyano(C_1-C_6)alkyl, trifluoromethyl(C_1-C_6)alkyl, nitro, nitro(C_1-C_6)alkyl or (C_1-C_6)acylamino;

R^5 is (C_2-C_9)heterocycloalkyl wherein the heterocycloalkyl groups must be substituted by one to five carboxy, cyano, amino, deuterium, hydroxy, (C_1-C_8)alkyl, (C_1-C_8)alkoxy, halo, (C_1-C_8)acyl, (C_1-C_8)alkylamino, amino(C_1-C_8)alkyl, (C_1-C_8)alkoxy-CO-NH, (C_1-C_6)alkylamino-CO-, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, (C_1-C_8)alkylamino, amino(C_1-C_8)alkyl, hydroxy(C_1-C_8)alkyl, (C_1-C_8)alkoxy(C_1-C_8)alkyl, (C_1-C_8)acyloxy(C_1-C_8)alkyl, nitro, cyano(C_1-C_8)alkyl, halo(C_1-C_8)alkyl, nitro(C_1-C_8)alkyl, trifluoromethyl, trifluoromethyl(C_1-C_8)alkyl, (C_1-C_8)acylamino, (C_1-C_8)acylamino(C_1-C_8)alkyl, (C_1-C_8)alkoxy(C_1-C_8)acylamino, amino(C_1-C_8)acyl, amino(C_1-C_8)acyl(C_1-C_8)alkyl, (C_1-C_8)alkylamino(C_1-C_8)acyl, ((C_1-
C₆alkyln(₃₆₋₇₆)acyl, R¹⁵R¹⁶N-CO-O-, R¹⁵R¹⁶N-CO-(C₁₋₇₆)alkyl, (C₁₋₇₆)alkyl-S(O)ₐₙ, R¹⁵R¹⁶NS(S)Oₐₙ, R¹⁵R¹⁶N-S(S)Oₐₙ(C₁₋₇₆)alkyl, R¹⁵S(O)ₐₙR¹⁶N(C₁₋₇₆)alkyl wherein m is 0, 1 or 2 and R¹⁵ and R¹⁶ are each independently selected from hydrogen or (C₁₋₇₆)alkyl; or a group of the formula

wherein a is 0, 1, 2, 3 or 4;

b, c, e, f and g are each independently 0 or 1;

d is 0, 1, 2, or 3;

X is S(O)ₐₙ wherein n is 0, 1 or 2; oxygen, carbonyl or –C(=N-cyano)–;

Y is S(O)ₐₙ wherein n is 0, 1 or 2; or carbonyl; and

Z is carbonyl, C(O)O-, C(O)NR- or S(O)ₐₙ wherein n is 0, 1 or 2;

R⁶, R⁷, R⁸, R⁹, R¹⁰ and R¹¹ are each independently selected from the group consisting of hydrogen or (C₁₋₇₆)alkyl optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C₁₋₇₆)acyloxy, (C₁₋₇₆)acylamino, (C₁₋₇₆)alkylamino, (C₁₋₇₆)alkylamino, cyano, cyano(C₁₋₇₆)alkyl, trifluoromethyl(C₁₋₇₆)alkyl, nitro, nitro(C₁₋₇₆)alkyl or (C₁₋₇₆)acylamino;

R¹² is carboxy, cyano, amino, oxo, deuterium, hydroxy, trifluoromethyl, (C₁₋₇₆)alkyl, trifluoromethyl(C₁₋₇₆)alkyl, (C₁₋₇₆)alkoxy, halo, (C₁₋₇₆)acyl, (C₁₋₇₆)alkylamino, (C₁₋₇₆)alkylamino, amino(C₁₋₇₆)alkyl, (C₁₋₇₆)alkoxy-CO-NH, (C₁₋₇₆)alkylamino-CO-, (C₂₋₇₆)alkenyl, (C₂₋₇₆)alkynyl, (C₁₋₇₆)alkylamino, hydroxy(C₁₋₇₆)alkyl, (C₁₋₇₆)alkoxy(C₁₋₇₆)alkyl, (C₁₋₇₆)acyloxy(C₁₋₇₆)alkyl, nitro, cyano(C₁₋₇₆)alkyl, halo(C₁₋₇₆)alkyl, nitro(C₁₋₇₆)alkyl, trifluoromethyl, trifluoromethyl(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acyloxy(C₁₋₇₆)alkyl, amino(C₁₋₇₆)acyl, amino(C₁₋₇₆)acyl(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁₋₇₆)alkyl, (C₁₋₇₆)acylamino(C₁-_
wherein \( m \) is 0, 1 or 2 and \( R^{15} \) and \( R^{16} \) are each independently selected from hydrogen or \((C_1-C_6)\)alkyl;

\( R^2 \) and \( R^3 \) are each independently selected from the group consisting of hydrogen, deuterium, amino, halo, hydroxy, nitro, carboxy, \((C_2-C_6)\)alkenyl, \((C_2-C_6)\)alkyl, trifluoromethyl, trifluoromethoxy, \((C_1-C_6)\)alkyl, \((C_1-C_6)\)alkoxy, \((C_3-C_9)\)cycloalkyl wherein the alkyl, alkoxy or cycloalkyl groups are optionally substituted by one to three groups selected from halo, hydroxy, carboxy, amino \((C_1-C_6)\)alkylthio, \((C_1-C_6)\)alkylamino, \((C_1-C_6)\)alkylsulfanyl, \((C_3-C_9)\)heterocycloalkyl, \((C_2-C_9)\)heteroaryl, or \((C_3-C_9)\)aryl or \((C_3-C_9)\)aryloxy; or \( R^2 \) and \( R^3 \) are each independently \((C_3-C_9)\)cycloalkyl, \((C_3-C_9)\)cycloalkoxy, \((C_1-C_6)\)alkylamino, \((C_1-C_6)\)alkylsulfanyl, \((C_6-C_{10})\)arylsulfanyl, \((C_6-C_{10})\)cyano, \((C_5-C_9)\)heterocycloalkyl, \((C_2-C_9)\)heterocycloalkyl or \((C_6-C_{10})\)arylsulfanyl, \((C_6-C_{10})\)cyano, \((C_5-C_9)\)heterocycloalkyl; or \( R^2 \) and \( R^3 \) are each independently \((C_3-C_9)\)cycloalkyl and \((C_1-C_6)\)alkylthio, \((C_1-C_6)\)alkylsulfanyl, \((C_6-C_{10})\)arylsulfanyl, \((C_6-C_{10})\)cyano, \((C_5-C_9)\)heterocycloalkyl.

Substituted halogen or \((C_1-C_6)\)alkyl, \((C_1-C_6)\)alkylsulfanyl, \((C_1-C_6)\)cyano, \((C_5-C_9)\)heterocycloalkyl, \((C_2-C_9)\)heteroaryl, or \((C_3-C_9)\)aryl or \((C_3-C_9)\)aryloxy; or \( R^2 \) and \( R^3 \) are each independently \((C_3-C_9)\)cycloalkyl and \((C_1-C_6)\)alkylthio, \((C_1-C_6)\)alkylsulfanyl, \((C_6-C_{10})\)arylsulfanyl, \((C_6-C_{10})\)cyano, \((C_5-C_9)\)heterocycloalkyl, \((C_2-C_9)\)heteroaryl, or \((C_3-C_9)\)aryl or \((C_3-C_9)\)aryloxy; or \( R^2 \) and \( R^3 \) are each independently \((C_3-C_9)\)cycloalkyl and \((C_1-C_6)\)alkylthio, \((C_1-C_6)\)alkylsulfanyl, \((C_6-C_{10})\)arylsulfanyl, \((C_6-C_{10})\)cyano, \((C_5-C_9)\)heterocycloalkyl, \((C_2-C_9)\)heteroaryl, or \((C_3-C_9)\)aryl or \((C_3-C_9)\)aryloxy.

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said coating formed from a polymer mixed carrier containing the compound of

Formula I; and said coating applied to said stent; and

wherein the polymer is chosen from: lactone-based polyesters, lactone-based
copolymers; polyanhydrides; polyaminoacids; polysaccharides; polyphosphazenes; poly(ether-ester) copolymers, and blends of such polymers.

10. A stent having a coating containing a compound of the formula

5 or the pharmaceutically acceptable salt thereof; wherein

\[ R^1 \text{ is a group of the formula } \]

\[ R^4 \text{ is selected from the group consisting of hydrogen, (C}_1\text{C}_6\text{)alkyl, (C}_1\text{C}_6\text{)alkylsulfonyl, (C}_2\text{C}_6\text{)alkenyl, (C}_2\text{C}_6\text{)alkynyl wherein the alkyl, alkenyl and alkynyl groups are optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C}_1\text{C}_4\text{)alkoxy, (C}_1\text{C}_6\text{)acyloxy, (C}_1\text{C}_6\text{)alkylamino, ((C}_1\text{C}_6\text{)alkyl})_2\text{amino, cyano, nitro, (C}_2\text{C}_6\text{)alkenyl, (C}_2\text{C}_6\text{)alkynyl or (C}_1\text{C}_6\text{)acylamino; or } R^4 \text{ is (C}_3\text{C}_10\text{)cycloalkyl wherein the cycloalkyl group is optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C}_1\text{C}_6\text{)acyloxy, (C}_1\text{C}_6\text{)acylamino, (C}_1\text{C}_6\text{)alkylamino, ((C}_1\text{C}_6\text{)alkyl})_2\text{amino, cyano, cyano(C}_1\text{C}_6\text{)alkyl, trifluoromethyl(C}_1\text{C}_6\text{)alkyl, nitro, nitro(C}_1\text{C}_6\text{)alkyl or (C}_1\text{C}_6\text{)acylamino;}} \]

\[ R^5 \text{ is (C}_2\text{C}_6\text{)heterocycloalkyl wherein the heterocycloalkyl groups must be substituted by one to five carboxy, cyano, amino, deuterium, hydroxy, (C}_1\text{C}_6\text{)alkyl, (C}_1\text{C}_6\text{)alkoxy, halo, (C}_1\text{C}_6\text{)acyl, (C}_1\text{C}_6\text{)alkylamino, amino(C}_1\text{C}_6\text{)alkyl, (C}_1\text{C}_6\text{)alkoxy-CO-NH, (C}_1\text{C}_6\text{)alkylamino-CO-, (C}_2\text{C}_6\text{)alkenyl, (C}_2\text{C}_6\text{)alkynyl, (C}_1\text{C}_6\text{)alkylamino, amino(C}_1\text{C}_6\text{)alkyl, hydroxy(C}_1\text{C}_6\text{)alkyl, (C}_1\text{C}_6\text{)alkoxy(C}_1\text{C}_6\text{)alkyl, (C}_1\text{C}_6\text{)acyloxy(C}_1\text{C}_6\text{)alkyl, nitro, cyano(C}_1\text{C}_6\text{)alkyl, halo(C}_1\text{C}_6\text{)alkyl, nitro(C}_1\text{C}_6\text{)alkyl, trifluoromethyl((C}_1\text{C}_6\text{)alkyl, (C}_1\text{C}_6\text{)acylamino, (C}_1\text{C}_6\text{)acylamino(C}_1\text{C}_6\text{)alkyl, (C}_1\text{C}_6\text{)alkoxy(C}_1\text{C}_6\text{)acylamino, amino(C}_1\text{C}_6\text{)acyl, amino(C}_1\text{C}_6\text{)acyl(C}_1\text{C}_6\text{)alkyl, (C}_1\text{C}_6\text{)alkylamino(C}_1\text{C}_6\text{)acyl, ((C}_1\text{C}_6\text{)alkyl})_2\text{amino(C}_1\text{C}_6\text{)acyl, } R^{15}R^{16}\text{N-CO-O-, } R^{15}R^{16}\text{N-CO-(C}_1\text{C}_6\text{)alkyl, (C}_1\text{C}_6\text{)alkyl-} \]
S(O)ₘ, R¹⁵R¹⁶NS(O)ₘ, R¹⁵R¹⁶NS(O)ₘ(C₁–C₆)alkyl, R¹⁵S(O)ₘR¹⁶N, R¹⁵S(O)ₘR¹⁶N(C₁–
C₆)alkyl wherein m is 0, 1 or 2 and R¹⁵ and R¹⁶ are each independently selected
from hydrogen or (C₁–C₆)alkyl; or a group of the formula

\[
\begin{align*}
&\text{R}^a \quad \text{R}^b \quad \text{R}^c \quad \text{R}^d \quad \text{R}^e \quad \text{R}^f \quad \text{R}^g \\
&\text{X} \quad \text{Y} \quad \text{Z} \\
&\text{R}^8 \\
&\text{R}^9 \\
&\text{R}^{10} \\
&\text{R}^{11} \\
&\text{R}^{12} \\
&\text{II}
\end{align*}
\]

wherein a is 0, 1, 2, 3 or 4;

b, c, e, f and g are each independently 0 or 1;

d is 0, 1, 2, or 3;

X is S(O)ₙ wherein n is 0, 1 or 2; oxygen, carbonyl or –C(=N-cyano)–;

Y is S(O)ₙ wherein n is 0, 1 or 2; or carbonyl; and

Z is carbonyl, C(O)O–, C(O)NR– or S(O)ₙ wherein n is 0, 1 or 2;

\[
\begin{align*}
&\text{R}^6, \text{R}^7, \text{R}^8, \text{R}^9, \text{R}^{10} \text{ and } \text{R}^{11} \text{ are each independently selected from the group}
\end{align*}
\]

consisting of hydrogen or (C₁–C₆)alkyl optionally substituted by deuterium, hydroxy,

amino, trifluoromethyl, (C₁–C₆)acyloxy, (C₁–C₆)acylamino, (C₁–C₆)alkylamino, ((C₁–
C₆)alkyl)ₙ amino, cyano, cyano(C₁–C₆)alkyl, trifluoromethyl(C₁–C₆)alkyl, nitro,

nitro(C₁–C₆)alkyl or (C₁–C₆)acylamino;

\[
\begin{align*}
&\text{R}^{12} \text{ is carboxy, cyano, amino, oxo, deuterium, hydroxy, trifluoromethyl, (C₁–}
\end{align*}
\]

C₆)alkyl, trifluoromethyl(C₁–C₆)alkyl, (C₁–C₆)alkoxy, halo, (C₁–C₆)acyl, (C₁–
C₆)alkylamino, (C₁–C₆)alkyl)ₙ amino, amino(C₁–C₆)alkyl, (C₁–C₆)alkoxy-CO-NH, (C₁–
C₆)alkylamino-CO₂–, (C₂–C₆)alkeny1, (C₂–C₆)alkynyl, (C₁–C₆)alkylamino, hydroxy(C₁–
C₆)alkyl, (C₁–C₆)alkoxy(C₁–C₆)alkyl, (C₁–C₆)acyloxy(C₁–C₆)alkyl, nitro, cyano(C₁–
C₆)alkyl, halo(C₁–C₆)alkyl, nitro(C₁–C₆)alkyl, trifluoromethyl, trifluoromethyl(C₁–C₆)alkyl,

(C₁–C₆)acylamino, (C₁–C₆)acrylamino(C₁–C₆)alkyl, (C₁–C₆)acrylamino(C₁–C₆)alkyl, (C₁–C₆)acryloxy(C₁–C₆)acylamino,

amino(C₁–C₆)acyl, amino(C₁–C₆)acyl(C₁–C₆)alkyl, (C₁–C₆)alkylamino(C₁–C₆)acyl, ((C₁–
C₆)alkyl)ₙ amino(C₁–C₆)acyl, R¹⁵R¹⁶N-CO-O–, R¹⁵R¹⁶N-CO-(C₁–C₆)alkyl, R¹⁵C(O)NH,

R¹⁵OC(O)NH, R¹⁵NHC(O)NH, (C₁–C₆)alkyl-S(O)ₘ, (C₁–C₆)alkyl-S(O)ₘ(C₁–C₆)alkyl,

R¹⁵R¹⁶NS(O)ₘ, R¹⁵R¹⁶NS(O)ₘ(C₁–C₆)alkyl, R¹⁵S(O)ₘR¹⁶N, R¹⁵S(O)ₘR¹⁶N(C₁–C₆)alkyl

wherein m is 0, 1 or 2 and R¹⁵ and R¹⁶ are each independently selected from

hydrogen or (C₁–C₆)alkyl;
R² and R³ are each independently selected from the group consisting of hydrogen, deuterium, amino, halo, hydroxy, nitro, carboxy, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, trifluoromethyl, trifluoromethoxy, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, (C₃-C₁₀)cycloalkyl wherein the alkyl, alkoxy or cycloalkyl groups are optionally substituted by one to three groups selected from halo, hydroxy, carboxy, amino (C₁-C₆)alkylthio, (C₁-C₆)alkylamino, ((C₁-C₆)alkyl)₂amino, (C₆-C₁₀)heteroaryl, (C₂-C₉)heterocycloalkyl, (C₃-C₉)cycloalkyl or (C₆-C₁₀)aryl; or R² and R³ are each independently (C₃-C₁₀)cycloalkyl, (C₃-C₁₀)cycloalkoxy, (C₁-C₆)alkylamino, ((C₁-C₆)alkyl)₂amino, (C₆-C₁₀)arylamino, (C₁-C₆)alkylthio, (C₆-C₁₀)arythio, (C₁-C₆)alkylsulfanyl, (C₆-C₁₀)arylsulfanyl, (C₁-C₆)acetylenic, (C₁-C₆)alkoxy- CO-NH, (C₁-C₆)alkyamino-CO-, (C₂-C₉)heteroaryl, (C₂-C₉)heterocycloalkyl or (C₆-C₁₀)aryl wherein the heteroaryl, heterocycloalkyl and aryl groups are optionally substituted by one to three halo, (C₁-C₆)alkyl, (C₁-C₆)alkyl-CO-NH, (C₁-C₆)alkoxy-CO-NH, (C₁-C₆)alkyl-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkoxy-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkoxy-CO-NH-(C₁-C₆)alkyl, carboxy, carboxy(C₁-C₆)alkyl, carboxy(C₁-C₆)alkoxy, benzylxycarbonyl(C₁-C₆)alkoxy, (C₁-C₆)alkoxy-carbonyl(C₁-C₆)alkoxy, (C₆-C₁₀)aryl, amino, amino(C₁-C₆)alkyl, (C₁-C₆)alkoxycarbonylamino, (C₆-C₁₀)aryl(C₁-C₆)alkoxycarbonylamino, (C₁-C₆)alkyamino, (C₁-C₆)alkylamino, (C₁-C₆)alkylamino, ((C₁-C₆)alkyl)₂amino, hydroxy, (C₁-C₆)alkoxy, carboxy, carboxy(C₁-C₆)alkyl, (C₁-C₆)alkoxycarbonyl, (C₁-C₆)alkoxycarbonyl(C₁-C₆)alkyl, (C₁-C₆)alkoxy-CO-NH, (C₁-C₆)alkyl-CO-NH, cyano, (C₆-C₁₀)heterocycloalkyl, amino-CO-NH, (C₁-C₆)alkylamino-CO-NH, ((C₁-C₆)alkyl)₂amino-CO-NH, (C₆-C₁₀)arylamino-CO-NH, (C₆-C₁₀)arylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, (C₁-C₆)alkylamino-CO-NH-(C₁-C₆)alkyl, said coating formed from a polymer mixed carrier containing the compound of Formula I; and said coating applied to said stent; wherein the polymer is nonabsorbable; and wherein the polymer is chosen from: polydimethylsiloxane; poly(ethylene)vinyl
acetate; poly(hydroxy) ethylmethacrylate, polyvinyl pyrrolidone; polytetrafluoroethylene; and cellulose esters.

11. A stent having a coating containing a compound of the formula

\[ \text{R}^1 \text{R}^2 \overset{\text{N}}{\text{R}^3} \]

or the pharmaceutically acceptable salt thereof; wherein

\( \text{R}^1 \) is a group of the formula

\[ \text{R}^4 \overset{\text{N}}{(\text{CH}_2)^y} \text{R}^5 \]

wherein \( y \) is 0, 1 or 2;

\( \text{R}^4 \) is selected from the group consisting of hydrogen, \((\text{C}_1-\text{C}_6)\)alkyl, \((\text{C}_1-\text{C}_6)\)alkylsulfonyl, \((\text{C}_2-\text{C}_6)\)alkenyl, \((\text{C}_2-\text{C}_6)\)alkynyl wherein the alkyl, alkenyl and alkynyl groups are optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, \((\text{C}_1-\text{C}_4)\)alkoxy, \((\text{C}_1-\text{C}_6)\)acyloxy, \((\text{C}_1-\text{C}_6)\)alkylamino, \((\text{C}_1-\text{C}_6)\)alkylamino, cyano, nitro, \((\text{C}_2-\text{C}_6)\)alkenyl, \((\text{C}_2-\text{C}_6)\)alkynyl or \((\text{C}_1-\text{C}_6)\)acylamino; or \( \text{R}^4 \) is \((\text{C}_2-\text{C}_{10})\)cycloalkyl wherein the cycloalkyl group is optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, \((\text{C}_1-\text{C}_6)\)acyloxy, \((\text{C}_1-\text{C}_6)\)acylamino, \((\text{C}_1-\text{C}_6)\)alkylamino, \((\text{C}_1-\text{C}_6)\)alkylamino, cyano, cyano(\((\text{C}_1-\text{C}_6)\)alkyl, trifluoromethyl(\((\text{C}_1-\text{C}_6)\)alkyl, nitro, nitro(\((\text{C}_1-\text{C}_6)\)alkyl or \((\text{C}_1-\text{C}_6)\)acylamino;

\( \text{R}^5 \) is \((\text{C}_2-\text{C}_9)\)heterocycloalkyl wherein the heterocycloalkyl groups must be substituted by one to five carboxy, cyano, amino, deuterium, hydroxy, \((\text{C}_1-\text{C}_6)\)alkyl, \((\text{C}_1-\text{C}_6)\)alkoxy, halo, \((\text{C}_1-\text{C}_6)\)acyl, \((\text{C}_1-\text{C}_6)\)alkylamino, amino(\((\text{C}_1-\text{C}_6)\)alkyl, \((\text{C}_1-\text{C}_6)\)alkoxy-\text{CO-NH}, \((\text{C}_1-\text{C}_6)\)alkylamino-\text{CO-}, \((\text{C}_2-\text{C}_6)\)alkenyl, \((\text{C}_2-\text{C}_6)\)alkynyl, \((\text{C}_1-\text{C}_6)\)alkylamino, amino(\((\text{C}_1-\text{C}_6)\)alkyl, hydroxy(\((\text{C}_1-\text{C}_6)\)alkyl, \((\text{C}_1-\text{C}_6)\)alkoxy(\((\text{C}_1-\text{C}_6)\)alkyl, (\((\text{C}_1-\text{C}_6)\)acyloxy(\((\text{C}_1-\text{C}_6)\)alkyl, nitro, cyano(\((\text{C}_1-\text{C}_6)\)alkyl, halo(\((\text{C}_1-\text{C}_6)\)alkyl, nitro(\((\text{C}_1-\text{C}_6)\)alkyl, trifluoromethyl, trifluoromethyl(\((\text{C}_1-\text{C}_6)\)alkyl, \((\text{C}_1-\text{C}_6)\)acylamino, \((\text{C}_1-\text{C}_6)\)acylamino(\((\text{C}_1-\text{C}_6)\)alkyl, \((\text{C}_1-\text{C}_6)\)alkoxy(\((\text{C}_1-\text{C}_6)\)acylamino, amino(\((\text{C}_1-\text{C}_6)\)acyl, amino(\((\text{C}_1-\text{C}_6)\)acy(\((\text{C}_1-\text{C}_6)\)alkyl, (\((\text{C}_1-\text{C}_6)\)alkylamino(\((\text{C}_1-\text{C}_6)\)acyl,
C₆alkyl₂amino(C₁-C₆)acyl, R¹⁵R¹⁶N-CO-O-, R¹⁵R¹⁶N-CO-(C₁-C₆)alkyl, (C₁-C₆)alkyl-S(O)ₓm, R¹⁵R¹⁶NS(O)ₓm, R¹⁵R¹⁶NS(O)ₓm (C₁-C₆)alkyl, R¹⁵S(O)ₓm, R¹⁵N, R¹⁵S(O)ₓm R¹⁶N(C₁-C₆)alkyl where m is 0, 1 or 2 and R¹⁵ and R¹⁶ are each independently selected from hydrogen or (C₁-C₆)alkyl; or a group of the formula

wherein a is 0, 1, 2, 3 or 4;
b, c, e, f and g are each independently 0 or 1;
d is 0, 1, 2, or 3;
X is S(O)ₓn wherein n is 0, 1 or 2; oxygen, carbonyl or –C(=N-cyano)–;
Y is S(O)ₓn wherein n is 0, 1 or 2; or carbonyl; and
Z is carbonyl, C(O)O-, C(O)NR- or S(O)ₓn wherein n is 0, 1 or 2;
R⁶, R⁷, R⁸, R⁹, R¹⁰ and R¹¹ are each independently selected from the group consisting of hydrogen or (C₁-C₆)alkyl optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C₁-C₆)acyloxy, (C₁-C₆)acylamino, (C₁-C₆)alkylamino, ((C₁-C₆)alkyl)₂amino, cyano, cyano(C₁-C₆)alkyl, trifluoromethyl(C₁-C₆)alkyl, nitro, nitro(C₁-C₆)alkyl or (C₁-C₆)acylamino;
R¹² is carboxy, cyano, amino, oxo, deuterium, hydroxy, trifluoromethyl, (C₁-C₆)alkyl, trifluoromethyl(C₁-C₆)alkyl, (C₁-C₆)alkoxy, halo, (C₁-C₆)acyl, (C₁-C₆)alkylamino, ((C₁-C₆)alkyl)₂amino, amino(C₁-C₆)alkyl, (C₁-C₆)alkoxy-CO-NH, (C₁-C₆)alkylamino-CO-, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-C₆)alkylamino, hydroxy(C₁-C₆)alkyl, (C₁-C₆)alkoxy(C₁-C₆)alkyl, (C₁-C₆)acyloxy(C₁-C₆)alkyl, nitro, cyano(C₁-C₆)alkyl, halo(C₁-C₆)alkyl, nitro(C₁-C₆)alkyl, trifluoromethyl, trifluoromethyl(C₁-C₆)alkyl, (C₁-C₆)acylamino, (C₁-C₆)acylamino(C₁-C₆)alkyl, (C₁-C₆)alkoxy(C₁-C₆)acylamino, amino(C₁-C₆)acyl, amino(C₁-C₆)acyl(C₁-C₆)alkyl, (C₁-C₆)alkylamino(C₁-C₆)acyl, ((C₁-C₆)alkyl)₂amino(C₁-C₆)acyl, R¹⁵R¹⁶N-CO-O-, R¹⁵R¹⁶N-CO-(C₁-C₆)alkyl, R¹⁵C(O)NH, R¹⁵OC(O)NH, R¹⁵NHC(O)NH, (C₁-C₆)alkyl-S(O)ₓm, (C₁-C₆)alkyl-S(O)ₓm-(C₁-C₆)alkyl, R¹⁵R¹⁶NS(O)ₓm, R¹⁵R¹⁶NS(O)ₓm(C₁-C₆)alkyl, R¹⁵S(O)ₓm, R¹⁶N, R¹⁵S(O)ₓmR¹⁶N(C₁-C₆)alkyl
wherein m is 0, 1 or 2 and R^{15} and R^{16} are each independently selected from hydrogen or (C_{1}-C_{6})alkyl;

R^2 and R^3 are each independently selected from the group consisting of hydrogen, deuterium, amino, halo, hydroxy, nitro, carboxy, (C_{2}-C_{6})alkenyl, (C_{2}-C_{6})alkynyl, trifluoromethyl, trifluoromethoxy, (C_{1}-C_{6})alkyl, (C_{1}-C_{6})alkoxy, (C_{3}-C_{10})cycloalkyl wherein the alkyl, alkoxy or cycloalkyl groups are optionally substituted by one to three groups selected from halo, hydroxy, carboxy, amino (C_{1}-C_{6})alkylthio, (C_{1}-C_{6})alkylamino, ((C_{1}-C_{6})alkyl)_{2}amino, (C_{2}-C_{9})heteroaryl, (C_{2}-C_{9})heterocycloalkyl, (C_{3}-C_{9})cycloalkyl or (C_{6}-C_{10})ary; or R^2 and R^3 are each independently (C_{1}-C_{6})cycloalkyl, (C_{3}-C_{10})cycloalkoxy, (C_{1}-C_{6})alkylamino, ((C_{1}-C_{6})alkyl)_{2}amino, (C_{6}-C_{10})arylamino, (C_{1}-C_{6})alkylthio, (C_{6}-C_{10})arylsulfanyl, (C_{6}-C_{10})arylsulfanyl, (C_{1}-C_{6})acyl, (C_{1}-C_{6})alkoxyCO-NH-, (C_{1}-C_{6})alkylamino-CO-, (C_{2}-C_{9})heteroaryl, (C_{2}-C_{9})heterocycloalkyl or (C_{6}-C_{10})aryl wherein the heteroaryl, heterocycloalkyl and aryl groups are optionally substituted by one to three halo, (C_{1}-C_{6})alkyl, (C_{1}-C_{6})alkyl-CO-NH-, (C_{1}-C_{6})alkoxy-CO-NH-, (C_{1}-C_{6})alkoxy-CO-NH-(C_{1}-C_{6})alkyl, (C_{1}-C_{6})alkoxy-CO-NH-(C_{1}-C_{6})alkoxy, carboxy, carboxy(C_{1}-C_{6})alkyl, carboxy(C_{1}-C_{6})alkoxy, benzyloxycarbonyl(C_{1}-C_{6})alkoxy, (C_{1}-C_{6})alkoxycarbonyl(C_{1}-C_{6})alkoxy, (C_{6}-C_{10})ary, amino, amino(C_{1}-C_{6})alkyl, (C_{1}-C_{6})alkoxycarbonylamino, (C_{6}-C_{10})ary(C_{1}-C_{6})alkylamino, ((C_{1}-C_{6})alkyl)_{2}amino, (C_{1}-C_{6})alkylamino(C_{1}-C_{6})alkyl, ((C_{1}-C_{6})alkyl)_{2}amino(C_{1}-C_{6})alkyl, hydroxy, (C_{1}-C_{6})alkoxy, carboxy, carboxy(C_{1}-C_{6})alkyl, (C_{1}-C_{6})alkoxycarbonyl(C_{1}-C_{6})alkyl, (C_{1}-C_{6})alkoxycarbonyl(C_{1}-C_{6})alkyl, (C_{1}-C_{6})alkylamino-CO-NH-, (C_{1}-C_{6})alkyl-CO-NH-, cyano, (C_{5}-C_{9})heterocycloalkyl, amino-CO-NH-, (C_{1}-C_{6})alkylamino-CO-NH-, ((C_{1}-C_{6})alkyl)_{2}amino-CO-NH-, (C_{6}-C_{10})arylamino-CO-NH-, (C_{5}-C_{9})heteroarylamino-CO-NH-, (C_{1}-C_{6})alkylamino-CO-NH-(C_{1}-C_{6})alkyl, ((C_{1}-C_{6})alkyl)_{2}amino-CO-NH-(C_{1}-C_{6})alkyl, (C_{6}-C_{10})arylamino-CO-NH-(C_{1}-C_{6})alkyl, (C_{1}-C_{6})alkylsulfanyl, (C_{1}-C_{6})alkylsulfonamyl, (C_{1}-C_{6})alkylsulfonamylamino(C_{1}-C_{6})alkyl, (C_{6}-C_{10})arylsulfonamyl, (C_{6}-C_{10})arylsulfonamylamino(C_{1}-C_{6})alkyl, (C_{1}-C_{6})alkylsulfonamylamino(C_{1}-C_{6})alkyl, (C_{5}-C_{9})heteroaryl or (C_{2}-C_{9})heterocycloalkyl,

said coating formed from a polymer mixed carrier containing the compound of Formula I; and said coating applied to said stent; and wherein the polymer is chosen from: polydimethylsiloxane; poly(ethylene)vinylacetate; poly(hydroxy)
ethylmethylmethacrylate, polyvinyl pyrrolidone; polytetrafluoroethylene; and cellulose esters.

12. A stent having a coating containing a compound of the formula

\[
\begin{array}{c}
\text{R}^1 \quad \text{R}^2 \\
\text{R}^3 \\

\end{array}
\]

or the pharmaceutically acceptable salt thereof; wherein

R\(^1\) is a group of the formula

\[
\begin{array}{c}
\text{R}^4 \\
\text{N} \\
\text{R}^5 \\
(\text{CH}_2)_y \\

\end{array}
\]

wherein y is 0, 1 or 2;

R\(^4\) is selected from the group consisting of hydrogen, (C\(_1\)-C\(_6\))alkyl, (C\(_1\)-C\(_6\))alkylsulfonyl, (C\(_2\)-C\(_6\))alkenyl, (C\(_2\)-C\(_6\))alkynyl wherein the alkyl, alkenyl and alkynyl groups are optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C\(_1\)-C\(_4\))alkoxy, (C\(_1\)-C\(_8\))acycloxy, (C\(_1\)-C\(_8\))alkylamino, ((C\(_1\)-C\(_8\))alkyl)\(^2\)amino, cyano, nitro, (C\(_2\)-C\(_6\))alkenyl, (C\(_2\)-C\(_6\))alkynyl or (C\(_1\)-C\(_8\))acylamino; or R\(^4\) is (C\(_3\)-C\(_10\))cycloalkyl wherein the cycloalkyl group is optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C\(_1\)-C\(_6\))acycloxy, (C\(_1\)-C\(_8\))acylamino, (C\(_1\)-C\(_8\))alkylamino, ((C\(_1\)-C\(_6\))alkyl)\(^2\)amino, cyano, cyano(C\(_1\)-C\(_8\))alkyl, trifluoromethyl(C\(_1\)-C\(_6\))alkyl, nitro, nitro(C\(_1\)-C\(_8\))alkyl or (C\(_1\)-C\(_8\))acylamino;

R\(^5\) is (C\(_2\)-C\(_8\))heterocycloalkyl wherein the heterocycloalkyl groups must be substituted by one to five carboxy, cyano, amino, deuterium, hydroxy, (C\(_1\)-C\(_8\))alkyl, (C\(_1\)-C\(_8\))alkoxy, halo, (C\(_1\)-C\(_8\))acyl, (C\(_1\)-C\(_8\))alkylamino, amino(C\(_1\)-C\(_8\))alkyl, (C\(_1\)-C\(_8\))alkoxy-CO-NH, (C\(_1\)-C\(_8\))alkylamino-CO-, (C\(_2\)-C\(_8\))alkenyl, (C\(_2\)-C\(_8\))alkynyl, (C\(_1\)-C\(_8\))alkylamino, amino(C\(_1\)-C\(_8\))alkyl, hydroxy(C\(_1\)-C\(_8\))alkyl, (C\(_1\)-C\(_8\))alkoxy(C\(_1\)-C\(_8\))alkyl, (C\(_1\)-C\(_8\))acycloxy(C\(_1\)-C\(_8\))alkyl, nitro, cyano(C\(_1\)-C\(_8\))alkyl, halo(C\(_1\)-C\(_8\))alkyl, nitro(C\(_1\)-C\(_8\))alkyl, trifluoromethyl(C\(_1\)-C\(_8\))alkyl, (C\(_1\)-C\(_8\))acylamino, (C\(_1\)-C\(_8\))acylaminocarboxy(C\(_1\)-C\(_8\))alkyl, (C\(_1\)-C\(_8\))alkoxy(C\(_1\)-C\(_8\))acylamino, amino(C\(_1\)-C\(_8\))acyl, amino(C\(_1\)-C\(_8\))acyl (C\(_1\)-C\(_8\))alkylamino(C\(_1\)-C\(_8\))acyl, ((C\(_1\)-C\(_8\))alkyl)\(^2\)amino(C\(_1\)-C\(_8\))acyl, R\(^{15}\)R\(^{16}\)N-CO-O-, R\(^{15}\)R\(^{16}\)N-CO-(C\(_1\)-C\(_8\))alkyl, (C\(_1\)-C\(_8\))alkyl-
S(O)_m, R^{15}R^{16}NS(O)_m, R^{15}R^{16}NS(O)_m(C_1-C_6)alkyl, R^{15}S(O)_m, R^{16}N, R^{15}S(O)_mR^{16}N(C_1-C_6)alkyl wherein m is 0, 1 or 2 and R^{15} and R^{16} are each independently selected from hydrogen or (C_1-C_6)alkyl; or a group of the formula

wherein a is 0, 1, 2, 3 or 4;
b, c, e, f and g are each independently 0 or 1;
d is 0, 1, 2, or 3;
X is S(O)_n wherein n is 0, 1 or 2; oxygen, carbonyl or –C(=N-cyano)-;
Y is S(O)_n wherein n is 0, 1 or 2; or carbonyl; and
Z is carbonyl, C(O)O-, C(O)NR- or S(O)_n wherein n is 0, 1 or 2;
R^6, R^7, R^8, R^9, R^{10} and R^{11} are each independently selected from the group consisting of hydrogen or (C_1-C_6)alkyl optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C_1-C_6)acyloxy, (C_1-C_6)acylamino, (C_1-C_6)alkylamino, ((C_1-C_6)alkyl)amino, cyan, cyan(C_1-C_6)alkyl, trifluoromethyl(C_1-C_6)alkyl, nitro,
nitro(C_1-C_6)alkyl or (C_1-C_6)acylamino;
R^{12} is carboxy, cyano, amino, oxo, deuterium, hydroxy, trifluoromethyl, (C_1-C_6)alkyl, trifluoromethyl(C_1-C_6)alkyl, (C_1-C_6)alkoxy, halo, (C_1-C_6)acyl, (C_1-C_6)alkylamino, ((C_1-C_6)alkyl)aminoc, (C_1-C_6)alkoxy-CN-H, (C_1-C_6)alkylamino-CN-O-, (C_1-C_6)alkynyl, (C_1-C_6)alkylamino, hydroxy(C_1-C_6)
C_6)alkyl, (C_1-C_6)alkoxy(C_1-C_6)alkyl, (C_1-C_6)acyloxy(C_1-C_6)alkyl, nitro, cyano(C_1-C_6)alkyl, halo(C_1-C_6)alkyl, nitro(C_1-C_6)alkyl, trifluoromethyl, trifluoromethyl(C_1-C_6)alkyl, (C_1-C_6)acylamino, (C_1-C_6)acylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxy(C_1-C_6)acylamino, amino(C_1-C_6)acyl, amino(C_1-C_6)acyl(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)acyl, ((C_1-C_6)alkyl)aminoc,C_6)alkyl, amino(C_1-C_6)acyl, R^{15}R^{16}N-CO-O-, R^{15}R^{16}N-CO-(C_1-C_6)alkyl, R^{15}C(O)NH,
R^{15}OC(O)NH, R^{15}NHC(O)NH, (C_1-C_6)alkyl-S(O)_m, (C_1-C_6)alkyl-S(O)_m(C_1-C_6)alkyl, R^{15}R^{16}NS(O)_m, R^{15}R^{16}NS(O)_m(C_1-C_6)alkyl, R^{15}S(O)_m, R^{16}N, R^{15}S(O)_mR^{16}N(C_1-C_6)alkyl wherein m is 0, 1 or 2 and R^{15} and R^{16} are each independently selected from hydrogen or (C_1-C_6)alkyl;
\[ R^2 \text{ and } R^3 \text{ are each independently selected from the group consisting of} 
\text{hydrogen, deuterium, amino, halo, hydoxy, nitro, carboxy, (C}_2\text{-C}_6\text{)alkenyl, (C}_2\text{-} 
\text{C}_6\text{)alkynyl, trifluoromethyl, trifluoromethoxy, (C}_1\text{-C}_6\text{)alkyl, (C}_1\text{-C}_6\text{)alkoxy, (C}_3\text{-} 
\text{C}_{10}\text{)cycloalkyl wherein the alkyl, alkoxy or cycloalkyl groups are optionally} 
\text{substituted by one to three groups selected from halo, hydroxy, carboxy, amino} 
\text{(C}_1\text{-C}_6\text{)alkylthio, (C}_1\text{-C}_6\text{)alkylamino, ((C}_1\text{-C}_6\text{)alkyl)coamin, (C}_2\text{-C}_6\text{)heteroaryl, (C}_2\text{-} 
\text{C}_6\text{)heterocycloalkyl, (C}_3\text{-C}_9\text{)cycloalkyl or (C}_6\text{-C}_{10}\text{)aryl; or } R^2 \text{ and } R^3 \text{ are each} 
\text{independently (C}_3\text{-C}_{10}\text{)cycloalkyl, (C}_3\text{-C}_{10}\text{)cycloalkoxy, (C}_1\text{-C}_6\text{)alkylamino, ((C}_1\text{-} 
\text{C}_6\text{)alkyl)coamin, (C}_6\text{-C}_{10}\text{)arylamino, (C}_1\text{-C}_6\text{)alkylthio, (C}_6\text{-C}_{10}\text{)arylamino, (C}_1\text{-} 
\text{C}_6\text{)alkylsulfanyl, (C}_6\text{-C}_{10}\text{)arylsulfanyl, (C}_1\text{-C}_6\text{)acyl, (C}_1\text{-C}_6\text{)alkoxy-} 
\text{CO-NH-, (C}_1\text{-C}_6\text{)alkylamino-CO-, (C}_2\text{-C}_6\text{)heteroaryl, (C}_2\text{-} 
\text{C}_6\text{)heterocycloalkyl or (C}_6\text{-C}_{10}\text{)aryl wherein the heteroaryl, heterocycloalkyl and} 
\text{aryl groups are optionally substituted by one to three halo, (C}_1\text{-C}_6\text{)alkyl, (C}_1\text{-} 
\text{C}_6\text{)alkyl-CO-NH-, (C}_1\text{-C}_6\text{)alkyl-CO-NH-, (C}_1\text{-C}_6\text{)alkyl-CO-NH-(C}_1\text{-C}_6\text{)alkyl, (C}_1\text{-} 
\text{C}_6\text{)alkoxy-CO-NH-(C}_1\text{-C}_6\text{)alkyl, (C}_1\text{-C}_6\text{)alkoxy-CO-NH-(C}_1\text{-C}_6\text{)alkoxy, carboxy} 
\text{carboxy(C}_1\text{-C}_6\text{)alkyl, carboxy(C}_1\text{-C}_6\text{)alkoxy, benzoxycarbonyl(C}_1\text{-C}_6\text{)alkoxy, (C}_1\text{-} 
\text{C}_6\text{)alkoxycarbonyl(C}_1\text{-C}_6\text{)alkoxy, (C}_6\text{-C}_{10}\text{)arylamino, amino, amino(C}_1\text{-C}_6\text{)alkyl, (C}_1\text{-} 
\text{C}_6\text{)alkoxycarbonylamino, (C}_6\text{-C}_{10}\text{)arylamino(C}_1\text{-C}_6\text{)alkoxycarbonylamino}, (C}_1\text{-} 
\text{C}_6\text{)alkylamino, ((C}_1\text{-C}_6\text{)alkyl)coamin, (C}_1\text{-C}_6\text{)alkylamino(C}_1\text{-C}_6\text{)alkyl, ((C}_1\text{-} 
\text{C}_6\text{)alkyl)coamin(C}_1\text{-C}_6\text{)alkyl, hydroxy, (C}_1\text{-C}_6\text{)alkoxy, carboxy, carboxy(C}_1\text{-C}_6\text{)alkyl,} 
\text{(C}_1\text{-C}_6\text{)alkoxycarbonyl, (C}_1\text{-C}_6\text{)alkoxycarbonyl(C}_1\text{-C}_6\text{)alkyl, (C}_1\text{-C}_6\text{)alkoxy-CO-NH-,} 
\text{(C}_1\text{-C}_6\text{)alkyl-CO-NH-, cyano, (C}_5\text{-C}_9\text{)heterocycloalkyl, amino-CO-NH-, (C}_1\text{-} 
\text{C}_6\text{)alkylamino-CO-NH-, ((C}_1\text{-C}_6\text{)alkyl)coamin-CO-NH-, (C}_6\text{-C}_{10}\text{)arylamino-CO-NH-,} 
\text{(C}_2\text{-C}_6\text{)heteroarylamino-CO-NH-, (C}_1\text{-C}_6\text{)alkylamino-CO-NH-(C}_1\text{-C}_6\text{)alkyl, ((C}_1\text{-} 
\text{C}_6\text{)alkyl)coamin-CO-NH-(C}_1\text{-C}_6\text{)alkyl, (C}_6\text{-C}_{10}\text{)arylamino-CO-NH-(C}_1\text{-C}_6\text{)alkyl, (C}_1\text{-} 
\text{C}_6\text{)alkoxycarbonyl, (C}_1\text{-C}_6\text{)alkoxycarbonyl(C}_1\text{-C}_6\text{)alkyl, (C}_1\text{-C}_6\text{)alkylsulfanyl, (C}_1\text{-} 
\text{C}_6\text{)alkylsulfonylamino, (C}_1\text{-C}_6\text{)alkylsulfonylamino(C}_1\text{-C}_6\text{)alkyl, (C}_6\text{-C}_{10}\text{)arylsulfonylamino,} 
\text{(C}_1\text{-C}_6\text{)arylsulfonylamino(C}_1\text{-C}_6\text{)alkyl, (C}_1\text{-C}_6\text{)arylsulfonylamino(C}_1\text{-C}_6\text{)alkyl, (C}_5\text{-C}_9\text{)heteroarylor} 
\text{said coating formed from a polymer mixed carrier containing the compound of} 
\text{Formula I; and said coating applied to said stent; and further comprising:} 
\text{a generally thin walled cylinder, said cylinder containing a plurality of generally} 
\text{solid struts, said applied to said strut, and a channel formed in at least one of said} 
\text{cylinder.}}
\]
struts, said channel having a closed perimeter on all sides and an open top, and said channel smaller in all dimensions than said strut, said channel containing a reservoir of said compound of Formula I coating applied therein.

13. A stent having a coating containing a compound of the formula

![Chemical Structure](image)

or the pharmaceutically acceptable salt thereof; wherein

R\(^1\) is a group of the formula

![Chemical Structure](image)

wherein y is 0, 1 or 2;

R\(^4\) is selected from the group consisting of hydrogen, (C\(_1\)-C\(_6\))alkyl, (C\(_1\)-C\(_6\))alkylsulfonyl, (C\(_2\)-C\(_6\))alkenyl, (C\(_2\)-C\(_6\))alkynyl wherein the alkyl, alkenyl and alkynyl groups are optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C\(_1\)-C\(_4\))alkoxy, (C\(_1\)-C\(_6\))acyloxy, (C\(_1\)-C\(_6\))alkylamino, ((C\(_1\)-C\(_6\))alkyl)\(_2\)amino, cyano, nitro, (C\(_2\)-C\(_6\))alkenyl, (C\(_2\)-C\(_6\))alkynyl or (C\(_1\)-C\(_6\))acylamino; or R\(^4\) is (C\(_3\)-C\(_10\))cycloalkyl wherein the cycloalkyl group is optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C\(_1\)-C\(_6\))acyloxy, (C\(_1\)-C\(_6\))acylamino, (C\(_1\)-C\(_6\))alkylamino, ((C\(_1\)-C\(_6\))alkyl)\(_2\)amino, cyano, cyano(C\(_1\)-C\(_6\))alkyl, trifluoromethyl(C\(_1\)-C\(_6\))alkyl, nitro, nitro(C\(_1\)-C\(_6\))alkyl or (C\(_1\)-C\(_6\))acylamino;

R\(^5\) is (C\(_2\)-C\(_6\))heterocycloalkyl wherein the heterocycloalkyl groups must be substituted by one to five carboxy, cyano, amino, deuterium, hydroxy, (C\(_1\)-C\(_6\))alkyl, (C\(_1\)-C\(_6\))alkoxy, halo, (C\(_1\)-C\(_6\))acyl, (C\(_1\)-C\(_6\))alkylamino, amino(C\(_1\)-C\(_6\))alkyl, (C\(_1\)-C\(_6\))alkoxy-CO-NH, (C\(_1\)-C\(_6\))alkylamino-CO-NH, (C\(_2\)-C\(_6\))alkenyl, (C\(_2\)-C\(_6\))alkynyl, (C\(_1\)-C\(_6\))alkylamino, amino(C\(_1\)-C\(_6\))alkyl, hydroxy(C\(_1\)-C\(_6\))alkyl, (C\(_1\)-C\(_6\))alkoxy(C\(_1\)-C\(_6\))alkyl, (C\(_1\)-C\(_6\))acyloxy(C\(_1\)-C\(_6\))alkyl, nitro, cyano(C\(_1\)-C\(_6\))alkyl, halo(C\(_1\)-C\(_6\))alkyl, nitro(C\(_1\)-C\(_6\))alkyl, trifluoromethyl, trifluoromethyl(C\(_1\)-C\(_6\))alkyl, (C\(_1\)-C\(_6\))acylamino, (C\(_1\)-C\(_6\))acylamino(C\(_1\)-C\(_6\))alkyl, (C\(_1\)-C\(_6\))alkoxy(C\(_1\)-C\(_6\))acylamino, amino(C\(_1\)-C\(_6\))acyl, amino(C\(_1\)-C\(_6\))acyl(C\(_1\)-C\(_6\))alkyl, (C\(_1\)-C\(_6\))alkylamino(C\(_1\)-C\(_6\))acyl, ((C\(_1\)-
C₆alkyl₂amino(C₆-C₆)acyl, R¹⁵⁺R¹⁶-N-CO-O⁻, R¹⁵⁺R¹⁶-N-CO-(C₁-C₆)alkyl, (C₁-C₆)alkyl-S(O)ₘ, R¹⁵⁺R¹⁶NS(O)ₙ, R¹⁵⁺R¹⁶NS(O)ₙ(C₁-C₆)alkyl, R¹⁵⁺S(O)ₘR¹⁶N, R¹⁵⁺S(O)ₙR¹⁶N(C₁-C₆)alkyl wherein m is 0, 1 or 2 and R¹⁵⁺ and R¹⁶⁺ are each independently selected from hydrogen or (C₁-C₆)alkyl; or a group of the formula

\[
\begin{align*}
\text{R}^6 & \text{R}^7, \text{R}^8, \text{R}^9, \text{R}^{10} \text{ and R}^{11} \text{ are each independently selected from the group} \\
\text{consisting of hydrogen or (C₁-C₆)alkyl optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C₁-C₆)acyloxy, (C₁-C₆)acylamino, (C₁-C₆)alkylamino, ((C₁-C₆)alkyl)₂amino, cyano, cyano(C₁-C₆)alkyl, trifluoromethyl(C₁-C₆)alkyl, nitro, nitro(C₁-C₆)alkyl or (C₁-C₆)acylamino;}
\end{align*}
\]

\[
\begin{align*}
\text{R}^{12} \text{ is carboxy, cyano, amino, oxo, deuterium, hydroxy, trifluoromethyl, (C₁-C₆)alkyl, trifluoromethyl(C₁-C₆)alkyl, (C₁-C₆)alkoxy, halo, (C₁-C₆)acyl, (C₁-C₆)alkylamino, ((C₁-C₆)alkyl)₂amino, amino(C₁-C₆)alkyl, (C₁-C₆)alkoxy-CO-NH, (C₁-C₆)alkylamino-CO⁻, (C₁-C₆)alkenyl, (C₁-C₆)alkynyl, (C₁-C₆)alkylamino, hydroxy(C₁-C₆)alkyl, (C₁-C₆)alkoxy(C₁-C₆)alkyl, (C₁-C₆)acyloxy(C₁-C₆)alkyl, nitro, cyano(C₁-C₆)alkyl, halo(C₁-C₆)alkyl, nitro(C₁-C₆)alkyl, trifluoromethyl, trifluoromethyl(C₁-C₆)alkyl, (C₁-C₆)acrylamino, (C₁-C₆)acylamino(C₁-C₆)alkyl, (C₁-C₆)alkoxy(C₁-C₆)acylamino, amino(C₁-C₆)acyl, amino(C₁-C₆)acyl(C₁-C₆)alkyl, (C₁-C₆)alkylamino(C₁-C₆)acyl, ((C₁-C₆)alkyl)₂acyl, amino(C₁-C₆)acyl, R¹⁶⁺R¹⁶-N-CO-O⁻, R¹⁵⁺R¹⁶-N-CO-(C₁-C₆)alkyl, R¹⁵⁺OC(O)NH, R¹⁵⁺OC(O)NH, R¹⁵⁺NHC(O)NH, (C₁-C₆)alkyl-S(O)ₘ, (C₁-C₆)alkyl-S(O)ₙ(C₁-C₆)alkyl, R¹⁵⁺R¹⁶NS(O)ₘ, R¹⁵⁺R¹⁶NS(O)ₙ(C₁-C₆)alkyl, R¹⁵⁺S(O)ₘR¹⁶N, R¹⁵⁺S(O)ₙR¹⁶N(C₁-C₆)alkyl
\end{align*}
\]
wherein m is 0, 1 or 2 and R^{15} and R^{16} are each independently selected from hydrogen or (C_{1}-C_{6})alkyl;

R^2 and R^3 are each independently selected from the group consisting of hydrogen, deuterium, amino, halo, hydroxy, nitro, carboxy, (C_{2}-C_{6})alkenyl, (C_{2}-C_{6})alkynyl, trifluoromethyl, trifluoromethoxy, (C_{1}-C_{6})alkyl, (C_{1}-C_{6})alkoxy, (C_{3}-C_{10})cycloalkyl wherein the alkyl, alkoxy or cycloalkyl groups are optionally substituted by one to three groups selected from halo, hydroxy, carboxy, amino (C_{1}-C_{6})alkylthio, (C_{1}-C_{6})alkylamino, ((C_{1}-C_{6})alkyl)_{2}amino, (C_{2}-C_{6})heteroaryl, (C_{2}-C_{6})heterocycloalkyl, (C_{3}-C_{6})cycloalkyl or (C_{6}-C_{10})aryl; or R^2 and R^3 are each independently (C_{3}-C_{10})cycloalkyl, (C_{3}-C_{10})cycloalkoxy, (C_{1}-C_{6})alkylamino, ((C_{1}-C_{6})alkyl)_{2}amino, (C_{6}-C_{10})arylamino, (C_{1}-C_{6})alkylthio, (C_{6}-C_{10})arylthio, (C_{1}-C_{6})alkylsulfanyl, (C_{6}-C_{10})aryl sulfanyl, (C_{1}-C_{6})acyl, (C_{1}-C_{6})alkoxyCO-NH- , (C_{1}-C_{6})alkylamino- CO- , (C_{2}-C_{6})heteroaryl, (C_{2}-C_{6})heterocycloalkyl or (C_{6}-C_{10})aryl wherein the heteroaryl, heterocycloalkyl and aryl groups are optionally substituted by one to three halo, (C_{1}-C_{6})alkyl, (C_{1}-C_{6})alkyl- CO-NH-, (C_{1}-C_{6})alkoxyCO-NH-, (C_{1}-C_{6})alkyl- CO-NH-(C_{1}-C_{6})alkyl, (C_{1}-C_{6})alkoxy- CO-NH-(C_{1}-C_{6})alkoxy, carboxy, carboxy(C_{1}-C_{6})alkyl, carboxy(C_{1}-C_{6})alkoxy, benzoxycarbonyl(C_{1}-C_{6})alkoxy, (C_{1}-C_{6})alkoxycarbonyl(C_{1}-C_{6})alkoxy, (C_{6}-C_{10})aryl, amino, amino(C_{1}-C_{6})alkyl, (C_{1}-C_{6})alkoxycarbonylamino, (C_{6}-C_{10})aryl(C_{1}-C_{6})alkoxycarbonylamino, (C_{1}-C_{6})alkoxycarbonylamino, (C_{1}-C_{6})alkylamino, ((C_{1}-C_{6})alkyl)_{2}amino, (C_{1}-C_{6})alkylamino(C_{1}-C_{6})alkyl, ((C_{1}-C_{6})alkyl)_{2}amino(C_{1}-C_{6})alkyl, hydroxy, (C_{1}-C_{6})alkoxy, carboxy, carboxy(C_{1}-C_{6})alkyl, (C_{1}-C_{6})alkoxycarbonyl, (C_{1}-C_{6})alkyl, (C_{1}-C_{6})alkoxyCO-NH-, (C_{1}-C_{6})alkyl- CO-NH-, cyano, (C_{2}-C_{6})heterocycloalkyl, amino-CO-NH-, (C_{1}-C_{6})alkylamino-CO-NH-, ((C_{1}-C_{6})alkyl)_{2}amino-CO-NH-, (C_{6}-C_{10})arylaminoco-NH-, (C_{5}-C_{6})heteroarylaminoco-NH-, (C_{1}-C_{6})alkylaminoco-NH-, (C_{1}-C_{6})alkylaminoco-NH-(C_{1}-C_{6})alkyl, ((C_{1}-C_{6})alkyl)_{2}amino-CO-NH-(C_{1}-C_{6})alkyl, (C_{6}-C_{10})arylaminoco-NH-(C_{1}-C_{6})alkyl, (C_{1}-C_{6})alkylsulfonlamino, (C_{1}-C_{6})alkylsulfonlamino(C_{1}-C_{6})alkyl, (C_{6}-C_{10})aryl sulfonlamino, (C_{1}-C_{6})alkylsulfonlamino, (C_{6}-C_{10})aryl sulfonlamino(C_{1}-C_{6})alkyl, (C_{1}-C_{6})alkylsulfonlamino, (C_{1}-C_{6})alkylsulfonlamino(C_{1}-C_{6})alkyl, (C_{6}-C_{9})heteroaryl or (C_{2}-C_{9})heterocycloalkyl,

wherein said compound of Formula I are contained in the coating at a weight percentage of 0.0001% to 30%, wherein the coating is a polymer.
14. The stent of claim 13 wherein said polymer is mixed to the compound of Formula I.

15. The stent of claim 4 wherein said polymer is bound to the compound of Formula I.

16. The stent of claim 13 wherein the compound of Formula I is entrapped on the surface of the stent by said polymer.

17. A stent containing a polymer and a compound of the formula

\[
\begin{align*}
R^1 & \quad R^2 \\
\text{N} & \quad \text{H}
\end{align*}
\]

or the pharmaceutically acceptable salt thereof; wherein

\[ R^1 \] is a group of the formula

\[
\begin{align*}
R^4 & \quad (\text{CH}_2)_y \\
\text{N} & \quad \text{R}^5
\end{align*}
\]

wherein \( y \) is 0, 1 or 2;

\( R^4 \) is selected from the group consisting of hydrogen, \((C_1-C_6)\text{alkyl}, \text{(C}_1-
C_6)\text{alkylsulfonyl}, \text{(C}_2-C_6)\text{alkenyl}, \text{(C}_2-C_6)\text{alkynyl} \) wherein the alkyl, alkenyl and alkynyl groups are optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, \((C_1-C_4)\text{alkoxy}, \text{(C}_1-C_6)\text{acyloxy}, \text{(C}_1-C_6)\text{alkylamino}, \text{((C}_1-C_6)\text{alkyl})_2\text{amino, cyano, nitro, (C}_2-C_6)\text{alkenyl, (C}_2-C_6)\text{alkynyl or (C}_1-C_6)\text{acylamino; or R}^4 \) is \((C_2-C_{10})\text{cycloalkyl}\) wherein the cycloalkyl group is optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, \((C_1-C_6)\text{acyloxy, (C}_1-C_6)\text{acylamino, (C}_1-C_6)\text{alkylamino, ((C}_1-C_6)\text{alkyl})_2\text{amino, cyano, cyano(C}_1-C_6)\text{alkyl, trifluoromethyl(C}_1-C_6)\text{alkyl, nitro, nitro(C}_1-C_6)\text{alkyl or (C}_1-C_6)\text{acylamino; R}^5 \) is \((C_2-C_9)\text{heterocycloalkyl}\) wherein the heterocycloalkyl groups must be substituted by one to five carboxy, cyano, amino, deuterium, hydroxy, \((C_1-C_6)\text{alkyl, (C}_1-C_6)\text{alkoxy, halo, (C}_1-C_6)\text{acyl, (C}_1-C_6)\text{alkylamino, amino(C}_1-C_6)\text{alkyl, (C}_1-
C_6)\text{alkoxy-CO-NH, (C}_1-C_6)\text{alkylamino-CO-, (C}_2-C_6)\text{alkenyl, (C}_2-C_6)\text{alkylamino, amino(C}_1-C_6)\text{alkyl, hydroxy(C}_1-C_6)\text{alkyl, (C}_1-C_6)\text{alkoxy(C}_1-C_6)\text{alkyl, (C}_1-C_6)\text{acyloxy(C}_1-C_6)\text{alkyl, nitro, cyano(C}_1-C_6)\text{alkyl, halo(C}_1-C_6)\text{alkyl, nitro(C}_1-
C₆)alkyl, trifluoromethyl, trifluoromethyl(C₁-C₆)alkyl, (C₁-C₆)acylamino, (C₁-C₆)acylamino(C₁-C₆)alkyl, (C₁-C₆)alkoxy(N₁-C₆)acylamino, amino(C₁-C₆)acyl, amino(C₁-C₆)acyl(C₁-C₆)alkyl, (C₁-C₆)alkylamino(C₁-C₆)acyl, ((C₁-C₆)alkyl)₂amino(C₁-C₆)acyl, R¹⁵R¹⁶N-CO–O–, R¹⁵R¹⁶N-CO-(C₁-C₆)alkyl, (C₁-C₆)alkyl-S(O)m, R¹⁵R¹⁶NS(O)m, R¹⁵R¹⁶NS(O)m(C₁-C₆)alkyl, R¹⁵S(O)mR¹⁶N, R¹⁵S(O)mR¹⁶N(C₁-C₆)alkyl wherein m is 0, 1 or 2 and R¹⁵ and R¹⁶ are each independently selected from hydrogen or (C₁-C₆)alkyl; or a group of the formula

wherein a is 0, 1, 2, 3 or 4;
10 b, c, e, f and g are each independently 0 or 1;
d is 0, 1, 2, or 3;
X is S(O)n wherein n is 0, 1 or 2; oxygen, carbonyl or –C(=N-cyano)–;
Y is S(O)n wherein n is 0, 1 or 2; or carbonyl; and
Z is carbonyl, C(O)O–, C(O)NR– or S(O)n wherein n is 0, 1 or 2;
15 R⁶, R⁷, R⁸, R⁹, R¹⁰ and R¹¹ are each independently selected from the group consisting of hydrogen or (C₁-C₆)alkyl optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C₁-C₆)acyloxy, (C₁-C₆)acylamino, (C₁-C₆)alkylamino, ((C₁-C₆)alkyl)₂amino, cyano, cyano(C₁-C₆)alkyl, trifluoromethyl(C₁-C₆)alkyl, nitro, nitro(C₁-C₆)alkyl or (C₁-C₆)acylamino;
20 R¹² is carboxy, cyano, amino, oxo, deuterium, hydroxy, trifluoromethyl, (C₁-C₆)alkyl, trifluoromethyl(C₁-C₆)alkyl, (C₁-C₆)alkoxy, halo, (C₁-C₆)acyl, (C₁-C₆)alkylamino, ((C₁-C₆)alkyl)₂ amino, amino(C₁-C₆)alkyl, (C₁-C₆)alkoxy-CO-NH, (C₁-C₆)alkylamino-CO–, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-C₆)alkynylamino, hydroxy(C₁-C₆)alkyl, (C₁-C₆)alkoxy(C₁-C₆)alkyl, (C₁-C₆)acyloxy(C₁-C₆)alkyl, nitro, cyano(C₁-C₆)alkyl, halo(C₁-C₆)alkyl, nitro(C₁-C₆)alkyl, trifluoromethyl, trifluoromethyl(C₁-C₆)alkyl, (C₁-C₆)acylamino, (C₁-C₆)acylamino(C₁-C₆)alkyl, (C₁-C₆)alkoxy(C₁-C₆)acylamino, amino(C₁-C₆)acyl, amino(C₁-C₆)acyl(C₁-C₆)alkyl, (C₁-C₆)alkynylamino(C₁-C₆)acyl, ((C₁-C₆)alkyl)₂ amino(C₁-C₆)acyl, R¹⁵R¹⁶N-CO–O–, R¹⁵R¹⁶N-CO-(C₁-C₆)alkyl, R¹⁵S(O)NH,
R^{15}OC(O)NH, R^{15}NHC(O)NH, (C_{1-6}alkyl-S(O)_{m}, (C_{1-6}alkyl-S(O)_{m}}(C_{1-6}alkyl,
R^{15}R^{16}NS(O)_{m}, R^{15}R^{16}NS(O)_{m}(C_{1-6}alkyl, R^{15}S(O)_{m}R^{16}N, R^{15}S(O)_{m}R^{16}N(C_{1-6}alkyl
wherein m is 0, 1 or 2 and R^{15} and R^{16} are each independently selected from
hydrogen or (C_{1-6}alkyl;

R^2 and R^3 are each independently selected from the group consisting of
hydrogen, deuterium, amino, halo, hydroxy, nitro, carboxy, (C_{2-6}alkenyl, (C_{2-6}
alkynyl, trifluoromethyl, trifluoromethoxy, (C_{1-6}alkyl, (C_{1-6}alkoxy, (C_{3-}
C_{10})cycloalkyl wherein the alkyl, alkoxy or cycloalkyl groups are optionally substituted
by one to three groups selected from halo, hydroxy, carboxy, amino (C_{1-6}alkylthio,
(C_{1-6}alkylamino, ((C_{1-6}alkyl)_{2}amino, (C_{5-6}heteroaryl, (C_{2-6}heterocycloalkyl,
(C_{3-6}C_{9})cycloalkyl or (C_{6-10})aryl; or R^2 and R^3 are each independently (C_{3-}
C_{10})cycloalkyl, (C_{3-6}C_{10})cycloalkoxy, (C_{1-6})alkylamino, ((C_{1-6})alkyl)_{2}amino, (C_{6-}
C_{10})arylamino, (C_{1-6}alkylthio, (C_{6-10})arylsulfonyl, (C_{6-}
C_{10})arylsulfonyl, (C_{6-10})arylsulfonyl, (C_{6-10})arylsulfonyl, (C_{1-6}acetyl, (C_{1-6}alkoxy-
CO-NH, (C_{1-6}alkoxyamino-CO-, (C_{5-6}heteroaryl, (C_{2-6}heterocycloalkyl or (C_{6-}
C_{10})aryl wherein the heteroaryl, heterocycloalkyl and aryl groups are optionally
substituted by one to three halo, (C_{1-6}alkyl, (C_{1-6})alkyl-CO-NH-, (C_{1-6})alkoxy-
CO-NH, (C_{1-6})alkyl-CO-NH-(C_{1-6})alkyl, (C_{1-6})alkoxy-CO-NH-(C_{1-6})alkyl, (C_{1-6}
alkoxy-CO-NH-(C_{1-6})alkoxy, carboxy, carboxy(C_{1-6}alkyl, carboxy(C_{1-6}alkoxy,
benzyloxy carbonyl(C_{1-6}alkoxy, (C_{1-6}alkoxy carbonyl(C_{1-6}alkoxy, (C_{6-10})aryl,
amino, amino(C_{1-6}alkyl, (C_{1-6})alkoxy carbonylamino, (C_{6-10})aryl(C_{1-}
C_{6})alkoxy carbonylalino, (C_{1-6}alkylamino, ((C_{1-6})alkyl)_{2}amino, (C_{1-}
C_{6})alkylamino(C_{1-6}alkyl, ((C_{1-6})alkyl)_{2}amino(C_{1-6}alkyl, hydroxy, (C_{1-6}alkoxy,
carboxy, carboxy(C_{1-6}alkyl, alkyl(C_{1-6}alkyl, alkyl(C_{1-6}alkoxy carbonyl(C_{1-}
C_{6})alkyl, (C_{1-6}alkoxy-CO-NH-, (C_{1-6}alkyl-CO-NH-, (C_{6-10})heterocycloalkyl,
amino-CO-NH-, (C_{1-6}alkylamino-CO-NH-, (C_{1-6})alkylamino-CO-NH-, (C_{1-6}
C_{10})arylamino-CO-NH-, (C_{6-10})heterocycloalkylamino-CO-NH-, (C_{1-6}alkylamino-CO-NH-
(C_{1-6}alkyl, ((C_{1-6})alkyl)_{2}amino-CO-NH-(C_{1-6})alkyl, (C_{6-10})arylamino-CO-NH-(C_{1-}
C_{6})alkyl, (C_{6-10})heterocycloalkylamino-CO-NH-(C_{1-6})alkyl, (C_{1-6})alkylsulfonyl, (C_{1-}
C_{6})alkylsulfonyl, amino(C_{1-6}alkylsulfonyl(C_{1-6}alkyl, (C_{6-10})aryl sulfonyl, (C_{6-}
C_{10})aryl sulfonyl, amino(C_{1-6}alkyl sulfonyl(C_{1-6}alkyl, (C_{1-6})alkyl sulfonyl,
(C_{1-6}alkyl sulfonyl(C_{1-6}alkyl, (C_{6-10})aryl sulfonyl, (C_{6-}
wherein said compound of Formula I are contained in a therapeutically beneficial amount to combat restenosis.

18. The stent of claim 17 wherein said polymer is mixed to the compound of Formula I.

19. The stent of claim 17 wherein said polymer is bound to the compound of Formula I.

20. The stent of claim 17 wherein the compound of Formula I is entrapped on the surface of the stent by said polymer.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61L31/00 A61K31/52 A61K9/00 A61P41/00 A61P43/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED
Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic database consulted during the International search (name of database and where practical, search terms used)
EPO-Internal, WPI Data, PAJ, CHEM ABS Data, MEDLINE, EMBASE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
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<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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<tbody>
<tr>
<td>X</td>
<td>EP 0 795 556 A (PHARMACIA &amp; UPJOHN S.P.A) 17 September 1997 (1997-09-17) abstract page 7, line 4 - line 13 claim 7</td>
<td>1-20</td>
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Further documents are listed in the continuation of box C. Patent family members are listed in annex.

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Date of the actual completion of the international search: 15 March 2005

Date of mailing of the international search report: 01/04/2005

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