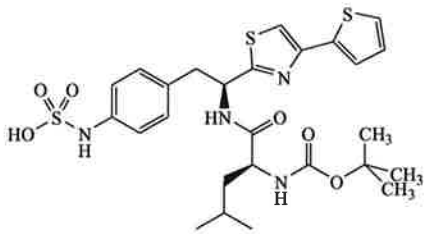
(d, J = 8.4 Hz, 2H), 7.39 (d, J = 8.4 Hz, 2H), 5.06 (d, J = 7.8 Hz, 1H), 4.80 (q, J = 6.3 Hz, 1H), 4.04 (s, 2H), 1.42 (s, 9H).

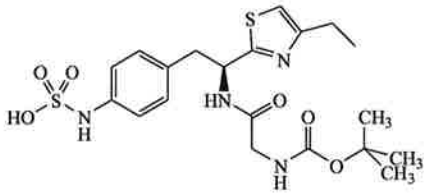
Preparation of *tert*-butyl (*S*)-1-(*S*)-2-(4-nitrophenyl)-1-(2-phenylthiazole-4-yl)ethylamino-1-oxo-3-phenylpropan-2-ylcarbamate (8): A mixture of thiobenzamide (0.117 g, 0.85 mmol) and (*S*)-*tert*-butyl 4-bromo-1-(4-nitrophenyl)-3-oxobutan-2-ylcarbamate, 7, (0.300 g, 0.77 mmol) in CH_3CN (4 mL) is refluxed 2 hours. The reaction mixture is cooled to room temperature and diethyl ether is added to precipitate the intermediate 2-(nitrophenyl)-(*S*)-1-(4-phenylthiazol-2-yl)ethylamine which is isolated by filtration as the hydrobromide salt. The hydrobromide salt is dissolved in DMF (3 mL) together with diisoproylethylamine (0.42 mL, 2.31 mmol), 1-hydroxybenzotriazole (0.118 g, 0.79 mmol) and (*S*)-(2-*tert*-butoxycarbonyl-amino)-3-phenylpropionic acid (0.212 g, 0.80 mmol). The mixture is stirred at 0 °C for 30 minutes then at room temperature overnight. The reaction mixture is diluted with water and extracted with EtOAc. The combined organic phase is washed with 1 N aqueous HCl, 5 % aqueous $NaHCO_3$, water and brine, and dried over Na_2SO_4. The solvent is removed *in vacuo* to afford 0.395 g (90 % yield) of the desired product which is used without further purification. LC/MS ESI+ 573 (M+1).

Preparation of (4-((*S*)-2-((*S*)-2-((*tert*-Butoxycarbonyl)amino)-3-phenylpropaneamido)-2-(2-phenylthiazol-4-yl)ethyl)phenyl)sulfamic acid ~~4-{(*S*)-2-(*S*)-2-(*tert*-butoxycarbonyl)-3-phenylpropaneamido-2-(2-phenylthiazole-4-yl)}phenylsulfamic acid~~ (9): *tert*-butyl (*S*)-1-(*S*)-2-(4-nitrophenyl)-1-(2-phenylthiazole-4-yl)ethylamino-1-oxo-3-phenylpropan-2-ylcarbamate, 8, (0.360 g) is dissolved in MeOH (4 mL). A catalytic amount of Pd/C (10% w/w) is added and the mixture is stirred under a hydrogen atmosphere 12 hours. The reaction mixture is filtered through a bed of CELITE™ and the solvent is removed under reduced pressure. The crude product is dissolved in pyridine (12 mL) and treated with SO_3-pyridine (0.296 g). The reaction is stirred at room temperature for 5 minutes after which a 7% solution of NH_4OH (10 mL) is added. The mixture is then concentrated and the resulting residue is purified by reverse phase chromatography to afford 0.050 g of the desired product as the ammonium salt. ^{1}H NMR (300 MHz, MeOH-d_4) δ 8.20 (d, J = 8.1 Hz, 1H), 7.96-7.99 (m, 2H), 7.48-7.52 (m, 3H), 7.00-7.23(m, 7H), 6.89 (s, 1H), 5.28 (q, J = 7.5 Hz, 1H), 4.33 (t, J = 6.6 Hz, 1H), 3.09-3.26 (m, 2H), 3.34 (dd, J = 13.2 and 8.4 Hz, 1H), 2.82 (dd, J = 13.2 and 8.4 Hz, 1H), 1.38 (s, 9H).

The first aspect of Category II of the present disclosure relates to compounds wherein R is a substituted or unsubstituted thiazol-4-yl unit having the formula:

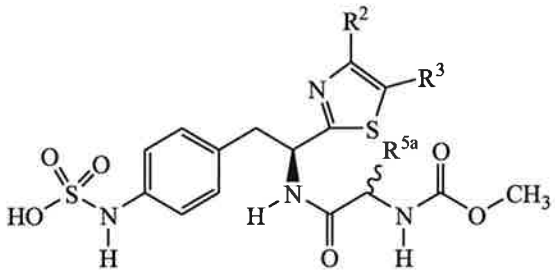


4-{(*S*)-2-[(*S*)-2-(*tert*-Butoxycarbonylamino)-4-methylpentanamido]-2-[2-(thiophen-2-yl)thiazol-4-yl]ethyl}phenylsulfamic acid: ^{1}H NMR (CD3OD) δ 8.06 (d, 1H, J = 8.4Hz), 7.61-7.58 (m, 1H), 7.57 (s, 1H), 7.15 (t, 1H, J = 0.6Hz), 7.09-6.98 (m, 6H), 5.30-5.20 (m, 1H), 4.10-4.00 (m, 1H), 3.19-3.13 (m, 2H), 1.63-1.55 (m, 2H), 1.48-1.33 (m, 10H), 0.95-0.89 (m, 6H).



(*S*)-4-{2-[2-(*tert*-Butoxycarbonyl)amino]acetamido-2-(4-ethylthiazol-2-yl)ethyl}-phenylsulfamic acid ~~(*S*)-4-{2-[2-(*tert*-Butoxycarbonyl)acetamide]-2-(4-ethylthiazol-2-yl)ethyl}-phenylsulfamic acid~~: ^{1}H NMR (CD_3OD): δ 7.09-6.91 (m, 5H), 5.30 (t, 1H, *J*=8.4 Hz), 3.60-2.64 (m, 6H), 1.34 (s, 9H), 1.16 (t, 3H, *J*=7.5 Hz).

A further embodiment of Category IV relates to inhibitors having the formula:



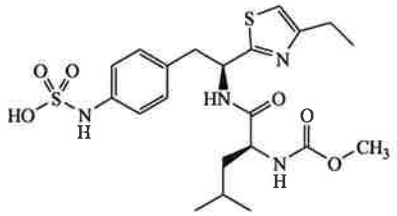
wherein R units and R^{5a} units further described in Table VII.

TABLE VII

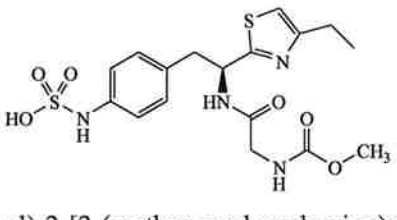
No.	R	R^{5a}
G151	thiazol-2-yl	hydrogen
G152	4-methylthiazol-2-yl	hydrogen
G153	4-ethylthiazol-2-yl	hydrogen
G154	4-propylthiazol-2-yl	hydrogen
G155	4-*iso*-propylthiazol-2-yl	hydrogen
G156	4-cyclopropylthiazol-2-yl	hydrogen
G157	4-butylthiazol-2-yl	hydrogen
G158	4-*tert*-butylthiazol-2-yl	hydrogen
G159	4-cyclohexylthiazol-2-yl	hydrogen
G160	4,5-dimethylthiazol-2-yl	hydrogen

No.	R	R^{5a}
G161	4-methyl-5-ethylthiazol-2-yl	hydrogen
G162	4-phenylthiazol-2-yl	hydrogen
G163	thiazol-2-yl	(*S*)-*iso*-propyl
G164	4-methylthiazol-2-yl	(*S*)-*iso*-propyl
G165	4-ethylthiazol-2-yl	(*S*)-*iso*-propyl
G166	4-propylthiazol-2-yl	(*S*)-*iso*-propyl
G167	4-*iso*-propylthiazol-2-yl	(*S*)-*iso*-propyl
G168	4-cyclopropylthiazol-2-yl	(*S*)-*iso*-propyl
G169	4-butylthiazol-2-yl	(*S*)-*iso*-propyl
G170	4-*tert*-butylthiazol-2-yl	(*S*)-*iso*-propyl
G171	4-cyclohexylthiazol-2-yl	(*S*)-*iso*-propyl
G172	4,5-dimethylthiazol-2-yl	(*S*)-*iso*-propyl
G173	4-methyl-5-ethylthiazol-2-yl	(*S*)-*iso*-propyl
G174	4-phenylthiazol-2-yl	(*S*)-*iso*-propyl
G175	4-(thiophen-2-yl)thiazol-2-yl	(*S*)-*iso*-propyl

The compounds encompassed within this embodiment of Category IV can be made according to the procedure outlined in Scheme V and described in Example 6 by substituting the corresponding methylcarbamate for the Boc-protected reagent. The following are non-limiting examples of this embodiment.

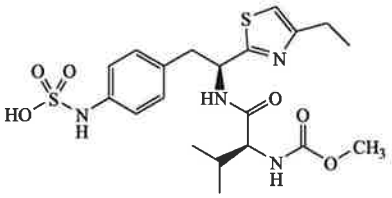


4-{(*S*)-2-(4-Ethylthiazol-2-yl)-2-[(*S*)-2-(methoxycarbonylamino)-4-methylpentan-amido]ethyl}phenylsulfamic acid ~~4-{(*S*)-2-(4-Ethylthiazol-2-yl)-2-[(*S*)-2-(methoxycarbonyl)-4-methylpentan-amido]ethyl}phenylsulfamic acid~~: ^{1}H NMR (CD3OD) δ 7.12-7.03 (m, 5H), 6.84 (d, 1H, J = 8.4Hz), 5.40 (t, 1H, J = 5.7Hz), 4.16 (t, 1H, J = 6.3Hz), 3.69 (s, 3H), 3.61-3.55 (m, 1H), 3.29-3.27 (m, 1H), 3.14-3.07 (m, 1H), 2.81 (q, 2H, J = 3.9, 11.2Hz), 1.66-1.59 (m, 1H), 1.48-1.43 (m, 2H), 1.31 (t, 3H, J = 4.5Hz), 0.96-0.90 (m, 6H).

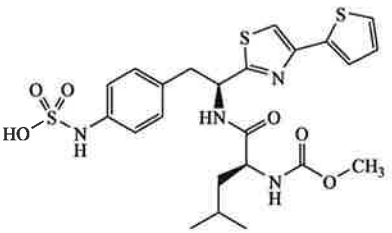


(*S*)-4-{2-(4-Ethylthiazol-2-yl)-2-[2-(methoxycarbonylamino)acetamido]ethyl}-phenylsulfamic acid ~~(*S*)-4-{2-(4-Ethylthiazol-2-yl)-2-[2-(methoxycarbonyl)acetamido]ethyl}phenyl-sulfamic acid:~~ ^{1}H NMR (CD_3OD): δ 7.12-7.07 (m, 4H), 7.03 (s, 1H), 5.42 (t, 1H, *J*=5.7 Hz), 3.83-3.68 (q,

2H, *J*=11.4 Hz), 3.68 (s, 3H), 3.34-3.04 (m, 2H), 2.83-2.76 (q, 2H, *J*=7.8 Hz), 1.31 (t, 3H, *J*=7.5 Hz).

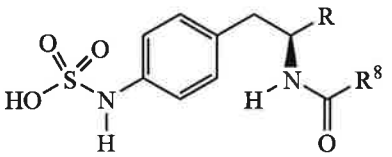


4-{(*S*)-2-(4-Ethylthiazol-2-yl)-2-[(*S*)-2-(methoxycarbonylamino)-3-methylbutanamido]-ethyl}phenylsulfamic acid ~~4-{(*S*)-2-(4-Ethylthiazol-2-yl)-2-[(*S*)-2-(methoxycarbonyl)-3-methylbutanamido]-ethyl}phenylsulfamic acid:~~ ^{1}H NMR (CD_3OD) δ 8.56 (d, 1H, J = 7.8Hz), 7.09 (s, 4H), 7.03 (s, 1H), 5.26-5.20 (m, 1H), 3.90 (d, 1H, J = 7.8Hz), 3.70 (s, 3H), 3.30 (1H, A of ABX, obscured by solvent), 3.08 (1H, B of ABX, J = 9.9, 9Hz), 2.79 (q, 2H, J = 11.1, 7.2Hz), 2.05-1.97 (m, 1H), 1.31 (t, 3H, J = 7.5Hz), 0.88 (s, 3H), 0.85 (s, 3H), 0.79-0.75 (m, 1H).



4-{(*S*)-2-[(*S*)-2-(Methoxycarbonylamino)-4-methylpentanamido]-2-[2-(thiophen-2-yl)thiazol-4-yl]ethyl}phenylsulfamic acid ~~4-{(*S*)-2-[(*S*)-2-(Methoxycarbonyl)-4-methylpentanamido]-2-[2-(thiophen-2-yl)thiazol-4-yl]ethyl}phenylsulfamic acid~~: ^{1}H NMR (CD3OD) δ 8.22 (d, 1H, J = 9Hz), 7.62-7.57 (m, H), 7.15 (t, 1H, J = 0.6Hz), 7.10-6.97 (m, 4H), 5.30-5.20 (m, 1H), 4.16-4.11 (m, 1H), 3.67 (s, 2H), 3.22 (1H, A of ABX, J = 6.9, 13.5Hz), 3.11 (1H, B of ABX, J = 7.8, 13.6Hz), 1.65-1.58 (m, 1H), 1.50-1.45 (m, 2H), 0.95-0.88 (m, 6H).

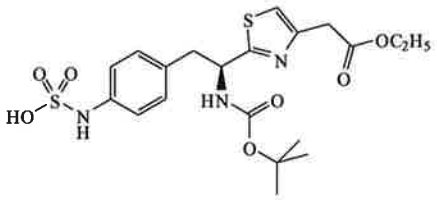
Category IV of the present disclosure relates to compounds having the formula:



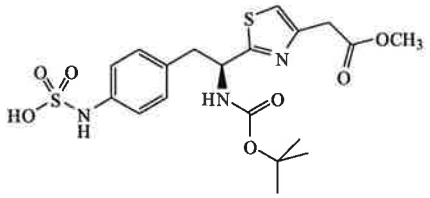
wherein R is a substituted or unsubstituted thiophen-2-yl or thiophen-4-yl unit and non-limiting examples of R^2 are further described in Table VIII.

TABLE VIII

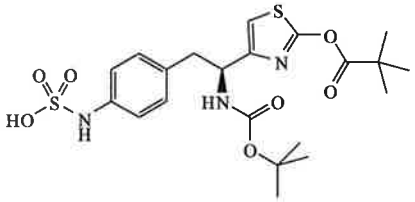
No.	R	R^8
H176	thiazol-2-yl	$-OC(CH_3)_3$
H177	4-methylthiazol-2-yl	$-OC(CH_3)_3$
H178	4-ethylthiazol-2-yl	$-OC(CH_3)_3$
H179	4-cyclopropylthiazol-2-yl	$-OC(CH_3)_3$



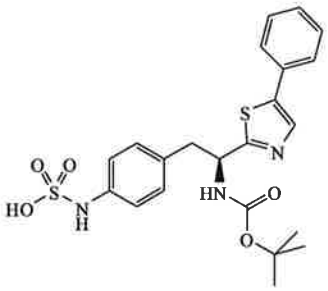
(S)-(4-(2-*tert*-Butoxycarbonylamino)-2-(4-(2-ethoxy-2-oxoethyl)-thiazole-2-yl)-ethyl)phenylsulfamic acid ~~*(S)*-4-(2-*tert*-Butoxycarbonylamino)-2-(4-(2-ethoxy-2-oxoethyl)-thiazole-2-yl)-ethyl)phenylsulfamic acid~~: ^{1}H NMR (300 MHz, MeOH-d_4) δ 7.29 (s, 1H), 7.09-7.16 (m, 4H), 5.04-5.09 (m, 1H), 4.20 (q, J = 6.9 Hz, 2H), 3.84 (s, 2H), 3.30 (dd, J = 4.8 and 14.1 HZ, 1H), 2.97 (dd, J = 9.6 Hz and 13.8 Hz, 1H), 1.41 (s, 9H), 1.29 (t, J = 7.2 Hz, 3H).



(*S*)-4-(2-(*tert*-Butoxycarbonylamino)-2-(4-(2-methoxy-2-oxoethyl)thiazol-2-yl)ethyl)phenylsulfamic acid: ^{1}H NMR (300 MHz, MeOH-d_4) δ 7.31 (s, 1H), 7.01-7.16 (m, 4H), 5.04-5.09 (m, 1H), 4.01 (s, 2H), 3.78 (s, 2H), 3.74 (s, 3H), 3.29 (dd, J = 5.1 and 13.8 Hz, 1H), 2.99 (dd, J = 9.3 and 13.8 Hz, 1H), 1.41 (s, 9H).



(S)-4-(2-(*tert*-Butoxycarbonylamino)-2-(2-(pivaloyloxy)thiazol-4-yl)ethyl)phenylsulfamic acid: ^{1}H NMR (300 MHz, D_2O) δ 6.95 (s, 4H), 6.63 (s, 1H), 2.94 (dd, J = 13.5 and 4.8 Hz, 1H), 2.75 (dd, J =13.5 and 4.8 Hz, 1H), 1.16 (s, 9H), 1.13 (s, 9H).



(S)-4-(2-(*tert*-Butoxycarbonylamino)-2-(5-phenylthiazol-2-yl)ethyl)-phenyl sulfamic acid: ^{1}H NMR (300 MHz, CD_3OD): δ 7.98 (s, 1H), 7.62 (d, J=7.2 Hz, 2H), 7.46-7.35 (m, 4H), 7.14 (s, 4H), 5.09 (bs, 1H), 3.07-2.99 (m, 2H), 1.43 (s, 9H).

EXAMPLE 9

(S)-(4-(2-(2-(3-chlorophenyl)acetylamino]-2-(2-(thiophen-2-ylthiazol-4-yl)ethyl]phenyl)sulfamic acid ~~4-((*S*)-2-(2-(3-chlorophenyl)acetamido)-2-(2-(thiophen-2-yl)thiazol-4-yl)ethyl)phenylsulfamic acid (23)~~

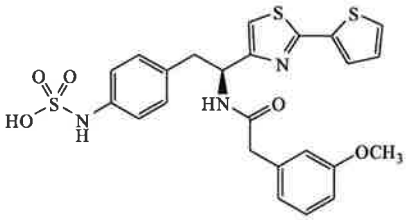
Preparation of (*S*)-2-(4-nitrophenyl)-1-[(thiophen-2-yl)thiazol-4-yl]ethanamine hydrobromide salt (22): A mixture of (*S*)-tert-butyl 4-bromo-1-(4-nitrophenyl)-3-oxobutan-2-ylcarbamate, 7, (7.74g, 20mmol), and thiophen-2-carbothioic acid amide (3.14g, 22mmol) in CH_3CN (200 mL) is refluxed for 5 hours. The reaction mixture is cooled to room temperature and diethyl ether (50 mL) is added to the solution. The precipitate which forms is collected by filtration. The solid is dried under vacuum to afford 7.14 g (87 % yield) of the desired product. ESI+ MS 332 (M+1).

Preparation of 2-(3-chlorophenyl)-*N*-{(*S*)-2-(4-nitrophenyl)-1-[2-(thiophen-2-yl)thiazol-4-yl]ethyl}acetamide (23): To a solution of 2-(4-nitrophenyl)-1-(2-thiophene2-ylthiazol-4-yl)ethylamine, 22, (0.41 g, 1mmol) 3-chlorophenylacetic acid (0.170g, 1mmol) and 1-hydroxybenzotriazole (HOBt) (0.070g, 0.50mmol) in DMF (5 mL) at 0°, is added 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (EDCI) (0.190g, 1mmol) followed by triethylamine (0.42mL, 3mmol). The mixture is stirred at 0 °C for 30 minutes then at room temperature overnight. The reaction mixture is diluted with water and extracted with EtOAc. The combined organic phase is washed with 1 N aqueous HCl, 5 % aqueous $NaHCO_3$, water and brine, and dried over Na_2SO_4. The solvent is removed *in vacuo* to afford 0.290 g (60 % yield) of the desired product which is used without further purification. ESI- MS 482 (M-1).

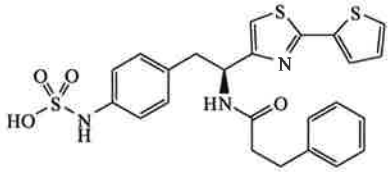
Preparation of (S)-(4-(2-(2-(3-chlorophenyl)acetylamino]-2-(2-(thiophen-2-ylthiazol-4-yl)ethyl]phenyl)sulfamic acid ~~{4-[2-(3-chlorophenyl)acetylamino]-2-(2-thiophen-2-ylthiazol-4-yl)ethyl]phenyl}sulfamic acid~~ (24): 2-(3-chlorophenyl)-*N*-{(*S*)-2-(4-nitrophenyl)-1-[2-(thiophene2-yl)thiazol-4-yl]ethyl}acetamide, 23, (0.290 g) is dissolved in MeOH (4 mL). A catalytic amount of Pd/C (10% w/w) is added and the mixture is stirred under a hydrogen atmosphere 18 hours. The reaction mixture is filtered through a bed of CELITE™ and the solvent is removed under reduced pressure. The crude product is dissolved in pyridine (12 mL) and treated with SO_3-pyridine (0.157 g). The reaction is stirred at room temperature for 5 minutes after which a 7% solution of NH_4OH is added. The mixture is then concentrated and the resulting residue is purified by reverse phase chromatography to afford 0.078 g of the desired product as the ammonium salt. ^1H NMR (CD3OD) δ 7.61 (d, 1H, J = 3.6Hz), 7.58 (d, 1H, J =

5.1Hz), 7.41-7.35 (m, 1H), 7.28-7.22 (m, 2H), 7.18-6.98 (m, 6H), 5.33 (t, 1H, J = 6.6Hz), 3.70 (d, 2H, J = 3.9Hz), 3.23 (1H, A of ABX, J = 6.6, 13.8Hz), 3.07 (1H, B of ABX, J = 8.1, 13.5Hz).

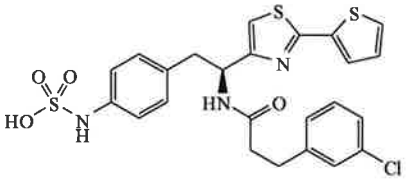
The following are non-limiting examples of compounds encompassed within the second aspect of Category V of the present disclosure.



4-((*S*)-2-(2-(3-Methoxyphenyl)acetamido)-2-(2-(thiophen-2-yl)thiazol-4-yl)ethyl)-phenylsulfamic acid ~~4-((*S*)-2-(2-(3-Methoxyphenyl)acetamido)-2-(2-(thiophene2-yl)thiazol-4-yl)ethyl)-phenylsulfamic acid~~: ^{1}H NMR (CD_3OD) δ 8.35 (d, 1H, J = 8.7Hz), 7.61-7.57 (m, 2H), 7.25-7.20 (m, 2H), 7.25-7.20 (m, 2H), 7.09 (s, 1H), 7.05 (d, 2H, J = 4.2Hz), 6.99 (d, 1H, J = 8.7Hz), 6.81 (d, 1H, J = 7.8Hz), 6.77 (s, 1H), 5.30-5.28 (m, 1H), 3.76 (s, 3H), 3.51 (s, 2H), 3.20 (1H, A of ABX, J = 6.3, 13.6Hz), 3.06 (1H, B of ABX, J = 8.1, 13.8Hz).



4-{(*S*)-2-(3-Phenylpropanamido)-2-[2-(thiophen-2-yl)thiazol-4-yl]ethyl}-phenylsulfamic acid ~~4-{(*S*)-2-(3-Phenylpropanamido)-2-[2-(thiophene2-yl)thiazol-4-yl]ethyl}-phenylsulfamic acid~~: ^{1}H NMR (CD_3OD) δ 8.30 (d, 1H, J = 9Hz), 7.61-7.56 (m, 2H), 7.26-7.14 (m, 7H), 7.12 (d, 1H, J = 1.5Hz), 7.09 (d, 1H, J = 2.1Hz), 6.89 (s, 1H), 5.28-5.26 (m, 1H), 3.18 (1H, A of ABX, J = 6.2, 13.8Hz), 2.96 (1H, B of ABX, J = 8.4, 13.6Hz).



4-{(*S*)-2-(3-(3-Chlorophenyl)propanamido)-2-[2-(thiophen-2-yl)thiazol-4-yl]ethyl}phenylsulfamic acid ~~4-{(*S*)-2-(3-(3-Chlorophenyl)propanamido)-2-[2-(thiophene2-yl)thiazol-4-yl]ethyl}phenylsulfamic acid~~: ^{1}H NMR (CD_3OD) δ 7.61-7.56 (m, 3H), 7.22-7.14 (m, 6H), 7.08 (d, 1H), 7.00 (d, 1H, J = 77.5Hz), 6.870 (s, 1H), 5.25 (t, 1H, J = 7.8Hz), 3.18 (1H, A of ABX, J = 6.6, 13.8Hz), 2.97 (1H, B of ABX, J = 7.8, 13.8Hz), 2.87 (t, 2H, J = 7.5Hz), 2.51 (t, 2H, J = 7.2Hz).



40 41

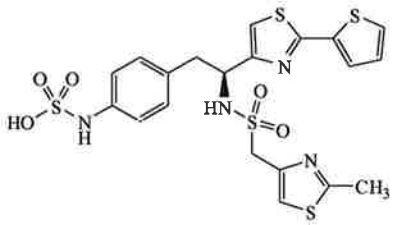
Reagents and conditions: (b) PCl_5, $POCl_3$; 50 °C, 3 hrs.

EXAMPLE 17

(2-Methylthiazol-4-yl)methanesulfonyl chloride (41)

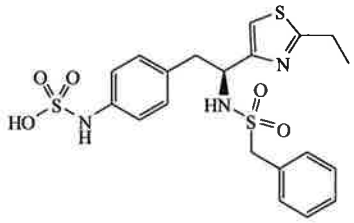
Preparation of sodium (2-methylthiazol-4-yl)methanesulfonate (40): 4-Chloromethyl-2-methylthiazole (250 mg, 1.69 mmol) is dissolved in H_2O (2 mL) and treated with sodium sulfite (224 mg, 1.78 mmol). The reaction mixture is subjected to microwave irradiation for 20 minutes at 200°C. The reaction mixture is diluted with H_2O (30 mL) and washed with EtOAc (2 x 25 mL). The aqueous layer is concentrated to afford 0.368g of the desired product as a yellow solid. LC/MS ESI+ 194 (M+1, free acid).

Preparation of (2-methylthiazol-4-yl)methanesulfonyl chloride (41): Sodium (2-methylthiazol-4-yl)methanesulfonate, 40, (357 mg, 1.66 mmol) is dissolved in phosphorous oxychloride (6 mL) and is treated with phosphorous pentachloride (345 mg, 1.66 mmol). The reaction mixture is stirred at 50 °C for 3 hours, then allowed to cool to room temperature. The solvent is removed under reduced pressure and the residue is re-dissolved in CH_2Cl_2 (40 mL) and is washed with sat. $NaHCO_3$ and brine. The organic layer is dried over $MgSO_4$, filtered, and the solvent removed *in vacuo* to afford 0.095 g of the desired product as a brown oil. LC/MS ESI+ 211 (M+1). Intermediates are obtained in sufficient purity to be carried forward according to Scheme IX without the need for further purification.

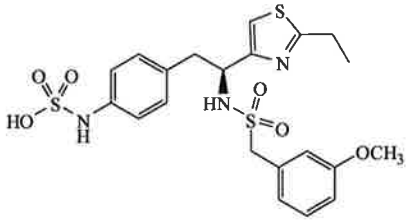


(*S*)-(4-(2-((2-Methylthiazol-4-yl)methylsulfonamido)-2-(2-(2-(thiophen-2-yl)thiazol-4-yl)ethyl)phenyl)sulfamic acid ~~4-{(S)-2-[(2-methylthiazol-4-yl)methylsulfonamido]-2-[2-(thiophen-2-yl)thiazol-4-yl]ethyl}phenylsulfamic acid~~: ^{1}H NMR (CD_3OD): δ 7.71-7.66 (m, 2H), 7.27-7.10 (m, 7H), 4.87 (t, 1H, *J*=7.3 Hz), 4.30-4.16 (q, 2H, *J*=13.2 Hz), 3.34-3.13 (m, 2H), 2.70 (s, 3H).

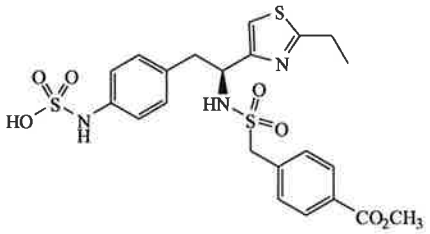
The following are non-limiting examples of compounds encompassed within Category VIII of the present disclosure.



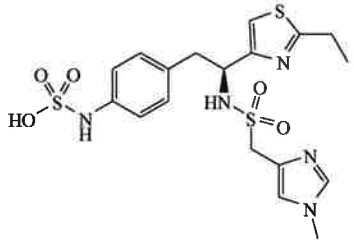
{4-(*S*)-[2-Phenylmethanesulfonylamino-2-(2-ethylthiazol-4-yl)ethyl]phenyl}-sulfamic acid: ^{1}H NMR (300 MHz, MeOH-d_4) δ 7.27–7.32 (m, 3H), 7.16-7.20 (m, 3H), 7.05-7.6 (m, 2H), 6.96 (d, J = 8.4 Hz, 2H), 4.70 (t, J = 9.0 Hz, 1H), 3.91-4.02 (m, 2H), 2.95-3.18 (m, 4H), 1.41 (t, J = 7.5 Hz, 3H).



(S)-(4-(2-(2-Ethylthiazol-4-yl)-2-((3-ethoxyphenyl)methylsulfonamido)ethyl)-phenyl)sulfamic acid~~{4-(*S*)-[2-(3-Methoxyphenyl)methanesulfonylamino-2-(2-ethylthiazol-4-yl)ethyl]phenyl}sulfamic acid~~: ^{1}H NMR (300 MHz, MeOH-d_4) δ 7.20 (t, J = 8.1 Hz. 1H), 6.94-7.08 (m,4H), 6.88-6.94 (m, 3H), 6.75-6.80 (m, 1H), 4.67 (t, J = 7.2 Hz, 1H), 3.90-4.0 (m, 2H), 3.76 (s, 3H), 2.95-3.16 (m, 4H), 1.40 (t, J = 7.5 HZ, 3H).

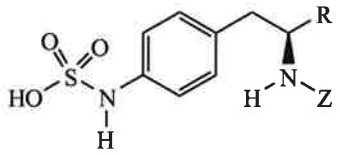


(*S*)-4-{[1-(2-Ethylthiazol-4-yl)-2-(4-sulfoaminophenyl)ethylsulfamoyl]methyl}-benzoic acid methyl ester: ^{1}H NMR (300 MHz, MeOH-d_4) δ 7.90–7.94– (m, 2H), 7.27-7.30 (m, 2H), 7.06-7.11 (m, 3H), 6.97-7.00 (m, 2H), 4.71 (t, J = 7.2 Hz, 1H), 3.95-4.08 (4, 2H), 3.92 (s, 3H), 2.80-3.50 (m, 4H), 1.38-1.44 (m, 3H).

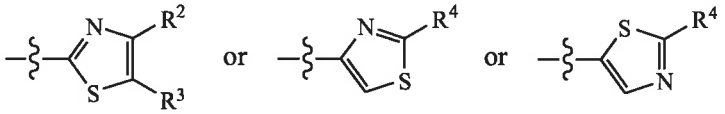


Claims

1. The use of a compound for making a medicament for preventing metastasis of cancer cells in a subject, the compound having the formula:



wherein R is a substituted or unsubstituted thiazolyl unit having the formula:



R^2, R^3, and R^4 are each independently:

i) hydrogen;

ii) substituted or unsubstituted C_1-C_6 linear, C_3-C_6 branched, or C_3-C_6 cyclic alkyl;

iii) substituted or unsubstituted C_2-C_6 linear, C_3-C_6 branched, or C_3-C_6 cyclic alkenyl;

iv) substituted or unsubstituted C_2-C_6 linear or C_3-C_6 branched alkynyl;

v) substituted or unsubstituted C_6 or C_{10} aryl;

vi) substituted or unsubstituted C_1-C_9 heteroaryl;

vii) substituted or unsubstituted C_1-C_9 heterocyclic; or

viii) R^2 and R^3 can be taken together to form a saturated or unsaturated ring having from 5 to 7 atoms; wherein from 1 to 3 atoms can optionally be heteroatoms chosen from oxygen, nitrogen, and sulfur;

Z is a unit having the formula:

$$—(L)_n—R^1$$

R^1 is chosen from:

i) hydrogen;

ii) hydroxyl;

iii) amino;

iv) s substituted or unsubstituted C_1-C_6 linear, C_3-C_6 branched, or C_3-C_6 cyclic alkyl;

v) substituted or unsubstituted C_1-C_6 linear, C_3-C_6 branched, or C_3-C_6 cyclic alkoxy;

vi) substituted or unsubstituted C_6 or C_{10} aryl;

xv) –NHC(=NH)NH–;

R^{5a} and R^{5b} are each independently:

i) hydrogen;

ii) hydroxy;

iii) halogen;

iv) substituted or unsubstituted C_1-C_6 linear or C_3-C_6 branched alkyl; or

v) a unit having the formula:

$$-[C(R^{7a}R^{7b})]_tR^8$$

R^{7a} and R^{7b} are each independently:

i) hydrogen; or

ii) substituted or unsubstituted C_1-C_6 linear, C_3-C_6 branched, or C_3-C_6 cyclic alkyl;

R^8 is:

i) hydrogen;

ii) substituted or unsubstituted C_1-C_6 linear, C_3-C_6 branched, or C_3-C_6 cyclic alkyl;

iii) substituted or unsubstituted C_6 or C_{10} aryl;

iv) substituted or unsubstituted C_1-C_9 heteroaryl; or

v) substituted or unsubstituted C_1-C_9 heterocyclic;

R^{6a} and R^{6b} are each independently:

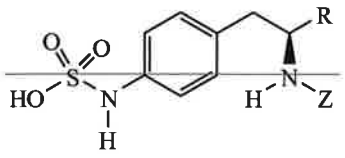
i) hydrogen; or

ii) C_1-C_4 linear or C_3-C_4 branched alkyl;

the index n is 0 or 1; the indices t, w and x are each independently from 0 to 4; the indices y and z are each independently 0 or 1; or

a pharmaceutically acceptable salt thereof.

~~3. The use of a compound for making a medicament for treating a subject diagnosed with cancer, the compound having the formula:~~



~~wherein R is a substituted or unsubstituted thiazolyl unit having the formula:~~

v) NHC(O)NH ;

vi) NHC(O)O ;

vii) C(O)O ;

viii) C(O)NHC(O) ;

ix) O ;

x) S ;

xi) SO_2 ;

xii) C(=NH) ;

xiii) C(=NH)NH ;

xiv) NHC(=NH) ; or

xv) NHC(=NH)NH ;

R^{5a} and R^{5b} are each independently:

i) hydrogen;

ii) hydroxy;

iii) halogen;

iv) substituted or unsubstituted C_1-C_6 linear or C_3-C_6 branched alkyl; or

v) a unit having the formula:

$$-[C(R^{7a}R^{7b})]_tR^8$$

R^{7a} and R^{7b} are each independently:

i) hydrogen; or

ii) substituted or unsubstituted C_1-C_6 linear, C_3-C_6 branched, or C_3-C_6 cyclic alkyl;

R^8 is:

i) hydrogen;

ii) substituted or unsubstituted C_1-C_6 linear, C_3-C_6 branched, or C_3-C_6 cyclic alkyl;

iii) substituted or unsubstituted C_6 or C_{10} aryl;

iv) substituted or unsubstituted C_1-C_9 heteroaryl; or

v) substituted or unsubstituted C_1-C_9 heterocyclic;

R^{6a} and R^{6b} are each independently:

i) hydrogen; or

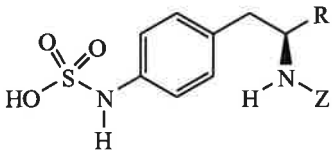
ii) C_1-C_4 linear or C_3-C_4 branched alkyl;

~~the index n is 0 or 1; the indices t, w and x are each independently from 0 to 4; the indices y and z are each independently 0 or 1; or~~

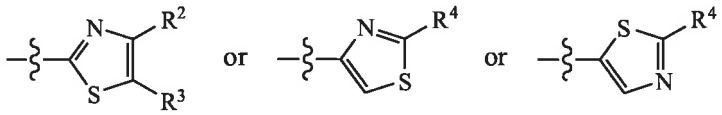
~~a pharmaceutically acceptable salt thereof.~~

43. The use of a compound for making a medicament for preventing metastasis <u>of cancer cells</u> in a subject, the medicament comprising:

A) an effective amount of one or more compounds having the formula:



wherein R is a substituted or unsubstituted thiazolyl unit having the formula:



R^2, R^3, and R^4 are each independently:

i) hydrogen;

ii) substituted or unsubstituted C_1-C_6 linear, C_3-C_6 branched, or C_3-C_6 cyclic alkyl;

iii) substituted or unsubstituted C_2-C_6 linear, C_3-C_6 branched, or C_3-C_6 cyclic alkenyl;

iv) substituted or unsubstituted C_2-C_6 linear or C_3-C_6 branched alkynyl;

v) substituted or unsubstituted C_6 or C_{10} aryl;

vi) substituted or unsubstituted C_1-C_9 heteroaryl;

vii) substituted or unsubstituted C_1-C_9 heterocyclic; or

viii) R^2 and R^3 can be taken together to form a saturated or unsaturated ring having from 5 to 7 atoms; wherein from 1 to 3 atoms can optionally be heteroatoms chosen from oxygen, nitrogen, and sulfur;

Z is a unit having the formula:

$$—(L)_n—R^1$$

R^1 is chosen from:

i) hydrogen;

ii) hydroxyl;

iii) amino;

iv) substituted or unsubstituted C_1-C_6 linear, C_3-C_6 branched, or C_3-C_6 cyclic alkyl;

v) substituted or unsubstituted C_1-C_6 linear, C_3-C_6 branched, or C_3-C_6 cyclic alkoxy;

vi) substituted or unsubstituted C_6 or C_{10} aryl;

vii) substituted or unsubstituted C_1-C_9 heterocyclic rings; or

viii) substituted or unsubstituted C_1-C_9 heteroaryl rings;

L is a linking unit having the formula:

$$-[Q]_y[C(R^{5a}R^{5b})]_x[Q^1]_z[C(R^{6a}R^{6b})]_w-$$

Q and Q^1 are each independently:

i) –C(O)–;

ii) –NH–;

iii) –C(O)NH–;

iv) –NHC(O)–;.

v) –NHC(O)NH–;

vi) –NHC(O)O–;

vii) –C(O)O–;

viii) –C(O)NHC(O)–;

ix) –O–;

x) –S–;

xi) $–SO_2–$;

xii) –C(=NH)–;

xiii) –C(=NH)NH–;

xiv) –NHC(=NH)–; or

xv) –NHC(=NH)NH–;

R^{5a} and R^{5b} are each independently:

i) hydrogen;

ii) hydroxy;

iii) halogen;

iv) substituted or unsubstituted C_1-C_6 linear or C_3-C_6 branched alkyl; or

v) a unit having the formula:

$$-[C(R^{7a}R^{7b})]_t R^8$$

R^{7a} and R^{7b} are each independently:

i) hydrogen; or

ii) substituted or unsubstituted C_1-C_6 linear, C_3-C_6 branched, or C_3-C_6 cyclic alkyl;

R^8 is:

i) hydrogen;

ii) substituted or unsubstituted C_1-C_6 linear, C_3-C_6 branched, or C_3-C_6 cyclic alkyl;

iii) substituted or unsubstituted C_6 or C_{10} aryl;

iv) substituted or unsubstituted C_1-C_9 heteroaryl; or

v) substituted or unsubstituted C_1-C_9 heterocyclic;

R^{6a} and R^{6b} are each independently:

i) hydrogen; or

ii) C_1-C_4 linear or C_3-C_4 branched alkyl;

the index n is 0 or 1; the indices t, w and x are each independently from 0 to 4; the indices y and z are each independently 0 or 1; or

a pharmaceutically acceptable salt thereof; and

B) an effective amount of one or more chemotherapeutic agents.

54. The use according to Claim 43, wherein the chemotherapeutic agent is chosen from vincristine, vinblastine, vindesine, vinorelbine-5'-noranhydroblastine, irinotecan, topotecan, cisplatin, cyclophosphamide, nitrogen mustard, trimethylene thiophosphoramide, carmustine, busulfan, chlorambucil, belustine, ~~uracil mustard,~~ chlomaphazin, dacarbazine, cytosine arabinoside, fluorouracil, methotrexate, mercaptopurine, azathioprime, procarbazine, doxorubicin, bleomycin, dactinomycin, daunorubicin, mithramycin, mitomycin, mytomycin C, daunomycin, ~~dacarbazine,~~ azacytidine, amsacrine, melphalan, ifosfamide, mitoxantrone, cis-platin, ~~cyclophosphamide, nitrogen mustard, trimethylene thiophosphoramide, carmustine,~~

~~busulfan~~, ~~chlorambucil, belustine, uracil mustard, chlomaphazin, dacabazine, cytosine arabinoside, fluorouracil, methotrexate, mercaptopuirine, azathioprime, procarbazine, doxorubicin, bleomycin, dactinomycin, daunorubicin, mithramycin, mitomycin, mytomycin C, daunomycin~~, ~~vincristine~~, ~~vinblastine~~, etoposide, taxol, ~~L-asparaginase, anti-tumor antibodies, dacarbazine~~, ~~azacytidine~~, ~~amsacrine, melphalan, VM-26, ifosfamide~~, ~~mitoxantrone~~, ~~vindesine~~, acivicin; aclarubicin; acodazole hydrochloride; acronine; adozelesin; aldesleukin; altretamine; ambomycin; ametantrone acetate; aminoglutethimide; ~~amsacrine~~; anastrozole; anthramycin; ~~asparaginase~~; asperlin; azacitidine; azetepa; azotomycin; batimastat; benzodepa; bicalutamide; bisantrene hydrochloride; bisnafide dimesylate; bizelesin; ~~bleomycin~~ sulfate; brequinar sodium; bropirimine; ~~busulfan~~; cactinomycin; calusterone; caracemide; carbetimer; carboplatin; ~~carmustine~~; carubicin hydrochloride; carzelesin; cedefingol; ~~chlorambucil~~; cirolemycin; ~~cisplatin~~; cladribine; crisnatol mesylate; ~~cyclophosphamide~~; cytarabine; ~~dacarbazine~~; ~~dactinomycin~~; ~~daunorubicin hydrochloride~~; decitabine; dexormaplatin; dezaguanine; ~~dezaguanine mesylate~~; diaziquone; docetaxel; ~~doxorubicin~~; ~~doxorubicin hydrochloride~~; droloxifene; ~~droloxifene citrate~~; ~~dromostanolone propionate~~; duazomycin; edatrexate; eflornithine hydrochloride; elsamitrucin; enloplatin; enpromate; epipropidine; epirubicin hydrochloride; erbulozole; esorubicin hydrochloride; estramustine; ~~estramustine phosphate sodium~~; etanidazole; ~~etoposide~~; ~~etoposide phosphate~~; etoprine; fadrozole hydrochloride; fazarabine; fenretinide; floxuridine; fludarabine phosphate; ~~fluorouracil~~; flurocitabine; fosquidone; fostriecin sodium; gemcitabine; ~~gemcitabine hydrochloride~~; hydroxyurea; idarubicin hydrochloride; ~~ifosfamide~~; ilmofosine; interleukin II ~~(including recombinant interleukin II, or rIL2)~~, interferon alfa-2a; interferon alfa-2b; interferon alfa-n1; interferon alfa-n3; interferon beta-I a; interferon gamma-I b; iproplatin; ~~irinotecan hydrochloride~~; lanreotide acetate; letrozole; leuprolide acetate; liarozole hydrochloride; lometrexol sodium; lomustine; losoxantrone hydrochloride; masoprocol; maytansine; mechlorethamine hydrochloride; megestrol acetate; melengestrol acetate; ~~melphalan~~; menogaril; ~~mercaptopurine~~; ~~methotrexate; methotrexate sodium~~; metoprine; meturedepa; mitindomide; mitocarcin; mitocromin; mitogillin; mitomalcin; ~~mitomycin~~; mitosper; mitotane; ~~mitoxantrone hydrochloride~~; mycophenolic acid; nocodazole; nogalamycin; ormaplatin; oxisuran; paclitaxel; pegaspargase; peliomycin; pentamustine; peplomycin

sulfate; perfosfamide; pipobroman; piposulfan; piroxantrone hydrochloride; plicamycin; plomestane; porfimer sodium; porfiromycin; prednimustine; ~~procarbazine hydrochloride;~~ puromycin; ~~puromycin hydrochloride;~~ pyrazofurin; riboprine; rogletimide; safingol; ~~safingol hydrochloride;~~ semustine; simtrazene; sparfosate sodium; sparsomycin; spirogermanium hydrochloride; spiromustine; spiroplatin; streptonigrin; streptozocin; sulofenur; talisomycin; tecogalan sodium; tegafur; teloxantrone hydrochloride; temoporfin; teniposide; teroxirone; testolactone; thiamiprine; thioguanine; thiotepa; tiazofurin; tirapazamine; toremifene citrate; trestolone acetate; triciribine phosphate; trimetrexate; ~~trimetrexate glucuronate;~~ triptorelin; tubulozole hydrochloride; ~~uracil mustard;~~ uredepa; vapreotide; verteporfin; ~~vinblastine sulfate; vincristine sulfate; vindesine; vindesine sulfate;~~ vinepidine sulfate; vinglycinate sulfate; vinleurosine sulfate; ~~vinorelbine tartrate;~~ vinrosidine sulfate; vinzolidine sulfate; vorozole; zeniplatin; zinostatin; and zorubicin hydrochloride~~, 20-epi-1,25 dihydroxyvitamin D3; 5-ethynyluracil; abiraterone; aclarubicin; acylfulvene; adecypenol; adozelesin; aldesleukin; ALL-TK antagonists; altretamine; ambamustine; amidox; amifostine; aminolevulinic acid; amrubicin; amsacrine; anagrelide; anastrozole; andrographolide; angiogenesis inhibitors; antagonist D; antagonist G; antarelix; anti-dorsalizing morphogenetic protein-1; antiandrogen, prostatic carcinoma; antiestrogen; antineoplaston; antisense oligonucleotides; aphidicolin glycinate; apoptosis gene modulators; apoptosis regulators; apurinic acid; ara-CDP-DL-PTBA; arginine deaminase; asulacrine; atamestane; atrimustine; axinastatin 1; axinastatin 2; axinastatin 3; azasetron; azatoxin; azatyrosine; baccatin III derivatives; balanol; batimastat; BCR/ABL antagonists; benzochlorins; benzoylstaurosporine; beta lactam derivatives; beta-alethine; betaclamycin B; betulinic acid; bFGF inhibitor; bicalutamide; bisantrene; bisaziridinylspermine; bisnafide; bistratene A; bizelesin; breflate; bropirimine; budotitane; buthionine sulfoximine; calcipotriol; calphostin C; camptothecin derivatives; canarypox IL-2; capecitabine; carboxamide-amino-triazole; carboxyamidotriazole; CaRest M3; CARN 700; cartilage derived inhibitor; carzelesin; casein kinase inhibitors (ICOS); castanospermine; cecropin B; cetrorelix; chlorlns; chloroquinoxaline sulfonamide; cicaprost; cis-porphyrin; cladribine; clomifene analogues; clotrimazole; collismycin A; collismycin B; combretastatin A4; combretastatin analogue; conagenin; crambescidin 816; crisnatol;~~

~~cryptophycin 8; cryptophycin A derivatives; curacin A; cyclopentanthraquinones; cycloplatam; cypemycin; cytarabine ocfosfate; cytolytic factor; cytostatin; dacliximab; decitabine; dehydrodidemnin B; deslorelin; dexamethasone; dexifosfamide; dexrazoxane; dexverapamil; diaziquone; didemnin B; didox; diethylnorspermine; dihydro-5-azacytidine; dihydrotaxol, 9-; dioxamycin; diphenyl spiromustine; docetaxel; docosanol; dolasetron; doxifluridine; droloxifene; dronabinol; duocarmycin SA; ebselen; ecomustine; edelfosine; edrecolomab; eflornithine; elemene; emitefur; epirubicin; epristeride; estramustine analogue; estrogen agonists; estrogen antagonists; etanidazole; etoposide phosphate; exemestane; fadrozole; fazarabine; fenretinide; filgrastim; finasteride; flavopiridol; flezelastine; fluasterone; fludarabine; fluorodaunorunicin hydrochloride; forfenimex; formestane; fostriecin; fotemustine; gadolinium texaphyrin; gallium nitrate; galocitabine; ganirelix; gelatinase inhibitors; gemcitabine; glutathione inhibitors; hepsulfam; heregulin; hexamethylene bisacetamide; hypericin; ibandronic acid; idarubicin; idoxifene; idramantone; ilmofosine; ilomastat; imidazoacridones; imiquimod; immunostimulant peptides; insulin-like growth factor-1 receptor inhibitor; interferon agonists; interferons; interleukins; iobenguane; iododoxorubicin; ipomeanol, 4-; iroplact; irsogladine; isobengazole; isohomohalicondrin B; itasetron; jasplakinolide; kahalalide F; lamellarin-N triacetate; lanreotide; leinamycin; lenograstim; lentinan sulfate; leptolstatin; letrozole; leukemia inhibiting factor; leukocyte alpha interferon; leuprolide+estrogen+progesterone; leuprorelin; levamisole; liarozole; linear polyamine analogue; lipophilic disaccharide peptide; lipophilic platinum compounds; lissoclinamide 7; lobaplatin; lombricine; lometrexol; lonidamine; losoxantrone; lovastatin; loxoribine; lurtotecan; lutetium texaphyrin; lysofylline; lytic peptides; maitansine; mannostatin A; marimastat; masoprocol; maspin; matrilysin inhibitors; matrix metalloproteinase inhibitors; menogaril; merbarone; meterelin; methioninase; metoclopramide, and mitoguazone; mitolactol; mitomycin analogues; mitonafide; mitotoxin fibroblast growth factor-saporin; mitoxantrone; mofarotene; molgramostim; monoclonal antibody, human chorionic gonadotrophin; monophosphoryl lipid A+myobacterium cell wall sk; mopidamol; multiple drug resistance gene inhibitor; multiple tumor suppressor 1-based therapy; mustard anticancer agent; mycaperoxide B; mycobacterial cell wall extract; myriaporone; N-acetyldinaline; N-substituted benzamides; nafarelin; nagrestip;~~

~~naloxone+pentazocine; napavin; naphterpin; nartograstim; nedaplatin; nemorubicin; neridronic acid; neutral endopeptidase; nilutamide; nisamycin; nitric oxide modulators; nitroxide antioxidant; nitrullyn; O6-benzylguanine; octreotide; okicenone; oligonucleotides; onapristone; ondansetron; ondansetron; oracin; oral cytokine inducer; ormaplatin; osaterone; oxaliplatin; oxaunomycin; paclitaxel; paclitaxel analogues; paclitaxel derivatives; palauamine; palmitoylrhizoxin; pamidronic acid; panaxytriol; panomifene; parabactin; pazelliptine; pegaspargase; peldesine; pentosan polysulfate sodium; pentostatin; pentrozole; perflubron; perfosfamide; perillyl alcohol; phenazinomycin; phenylacetate; phosphatase inhibitors; picibanil; pilocarpine hydrochloride; pirarubicin; piritrexim; placetin A; placetin B; plasminogen activator inhibitor; platinum complex; platinum compounds; platinum-triamine complex; porfimer sodium; porfiromycin; prednisone; propyl bis-acridone; prostaglandin J2; proteasome inhibitors; protein A-based immune modulator; protein kinase C inhibitor; protein kinase C inhibitors, microalgal; protein tyrosine phosphatase inhibitors; purine nucleoside phosphorylase inhibitors; purpurins; pyrazoloacridine; pyridoxylated hemoglobin polyoxyethylene conjugate; raf antagonists; raltitrexed; ramosetron; ras farnesyl protein transferase inhibitors; ras inhibitors; ras-GAP inhibitor; retelliptine demethylated; rhenium Re 186 etidronate; rhizoxin; ribozymes; RII retinamide; rogletimide; rohitukine; romurtide; roquinimex; rubiginone B1; ruboxyl; safingol; saintopin; SarCNU; sarcophytol A; sargramostim; Sdi 1 mimetics; semustine; senescence derived inhibitor 1; sense oligonucleotides; signal transduction inhibitors; signal transduction modulators; single chain antigen binding protein; sizofiran; sobuzoxane; sodium borocaptate; sodium phenylacetate; solverol; somatomedin binding protein; sonermin; sparfosic acid; spicamycin D; spiromustine; splenopentin; spongistatin 1; squalamine; stem cell inhibitor; stem-cell division inhibitors; stipiamide; stromelysin inhibitors; sulfinosine; superactive vasoactive intestinal peptide antagonist; suradista; suramin; swainsonine; synthetic glycosaminoglycans; tallimustine; tamoxifen methiodide; tauromustine; tazarotene; tecogalan sodium; tegafur; tellurapyrylium; telomerase inhibitors; temoporfin; temozolomide; teniposide; tetrachlorodecaoxide; tetrazomine; thaliblastine; thiocoraline; thrombopoietin; thrombopoietin mimetic; thymalfasin; thymopoietin receptor agonist; thymotrinan; thyroid stimulating hormone; tin ethyl etiopurpurin; tirapazamine;~~

~~titanocene bichloride; topsentin; toremifene; totipotent stem cell factor; translation inhibitors; tretinoin; triacetyluridine; triciribine; trimetrexate; triptorelin; tropisetron; turosteride; tyrosine kinase inhibitors; tyrphostins; UBC inhibitors; ubenimex; urogenital sinus-derived growth inhibitory factor; urokinase receptor antagonists; vapreotide; variolin B; vector system, erythrocyte gene therapy; velaresol; veramine; verdins; verteporfin; vinorelbine; vinxaltine; vitaxin; vorozole; zanoterone; zeniplatin; zilascorb; and zinostatin stimalamer~~.

~~6~~5. The use according to Claim 4~~3~~, wherein the chemotherapeutic agent is chosen from taxol, IL-2, gemcitabine, erlotinib, doxil, irinortecan, and bevacizumab.

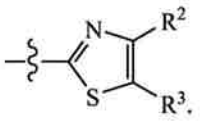
~~7~~6. The use according to any of Claims 1 to 5 ~~Claims 1 to 6~~, wherein the cancer is chosen from Acute Lymphoblastic; Acute Myeloid Leukemia; Adrenocortical Carcinoma; Adrenocortical Carcinoma, Childhood; Appendix Cancer; Basal Cell Carcinoma; Bile Duct Cancer, Extrahepatic; Bladder Cancer; Bone Cancer; Osteosarcoma and Malignant Fibrous Histiocytoma; Brain Stem Glioma, Childhood; Brain Tumor, Adult; Brain Tumor, Brain Stem Glioma, Childhood; Brain Tumor, Central Nervous System Atypical Teratoid/Rhabdoid Tumor, Childhood; Central Nervous System Embryonal Tumors; Cerebellar Astrocytoma; Cerebral Astrocytoma/Malignant Glioma; Craniopharyngioma; Ependymoblastoma; Ependymoma; Medulloblastoma; Medulloepithelioma; Pineal Parenchymal Tumors of Intermediate Differentiation; Supratentorial Primitive Neuroectodermal Tumors and Pineoblastoma; Visual Pathway and Hypothalamic Glioma; Brain and Spinal Cord Tumors; Breast Cancer; Bronchial Tumors; Burkitt Lymphoma; Carcinoid Tumor; Carcinoid Tumor, Gastrointestinal; Central Nervous System Atypical Teratoid/Rhabdoid Tumor; Central Nervous System Embryonal Tumors; Central Nervous System Lymphoma; Cerebellar Astrocytoma; Cerebral Astrocytoma/Malignant Glioma, Childhood; Cervical Cancer; Chordoma, Childhood; Chronic Lymphocytic Leukemia; Chronic Myelogenous Leukemia; Chronic Myeloproliferative Disorders; Colon Cancer; Colorectal Cancer; Craniopharyngioma; Cutaneous T-Cell Lymphoma; Esophageal Cancer; Ewing Family of Tumors; Extragonadal Germ Cell Tumor; Extrahepatic Bile Duct Cancer; Eye Cancer Intraocular

Melanoma; Eye Cancer, Retinoblastoma; Gallbladder Cancer; Gastric (Stomach) Cancer; Gastrointestinal Carcinoid Tumor; Gastrointestinal Stromal Tumor (GIST); Germ Cell Tumor, Extracranial; Germ Cell Tumor, Extragonadal; Germ Cell Tumor, Ovarian; Gestational Trophoblastic Tumor; Glioma; Glioma, Childhood Brain Stem; Glioma, Childhood Cerebral Astrocytoma; Glioma, Childhood Visual Pathway and Hypothalamic; Hairy Cell Leukemia; Head and Neck Cancer; ;Hepatocellular (Liver) Cancer; Histiocytosis, Langerhans Cell; Hodgkin Lymphoma; Hypopharyngeal Cancer; Hypothalamic and Visual Pathway Glioma; Intraocular Melanoma; Islet Cell Tumors; Kidney (Renal Cell) Cancer; Langerhans Cell Histiocytosis; Laryngeal Cancer; Leukemia, Acute Lymphoblastic; Leukemia, Acute Myeloid; Leukemia, Chronic Lymphocytic; Leukemia, Chronic Myelogenous; Leukemia, Hairy Cell; Lip and Oral Cavity Cancer; Liver Cancer; Lung Cancer, Non-Small Cell; Lung Cancer, Small Cell; Lymphoma, AIDS-Related; Lymphoma, Burkitt; Lymphoma, Cutaneous T-Cell; Lymphoma, Hodgkin; Lymphoma, Non-Hodgkin; Lymphoma, Primary Central Nervous System; Macroglobulinemia, Waldenström; Malignant Fibrous Histiocytoma of Bone and Osteosarcoma; Medulloblastoma; Melanoma; Melanoma, Intraocular (Eye); Merkel Cell Carcinoma; Mesothelioma; Metastatic Squamous Neck Cancer with Occult Primary; Mouth Cancer; Multiple Endocrine Neoplasia Syndrome, (Childhood); Multiple Myeloma/Plasma Cell Neoplasm; Mycosis Fungoides; Myelodysplastic Syndromes; Myelodysplastic/Myeloproliferative Diseases; Myelogenous Leukemia, Chronic; Myeloid Leukemia, Adult Acute; Myeloid Leukemia, Childhood Acute; Myeloma, Multiple; Myeloproliferative Disorders, Chronic; Nasal Cavity and Paranasal Sinus Cancer; Nasopharyngeal Cancer; Neuroblastoma; Non-Small Cell Lung Cancer; Oral Cancer; Oral Cavity Cancer; Oropharyngeal Cancer; Osteosarcoma and Malignant Fibrous Histiocytoma of Bone; Ovarian Cancer; Ovarian Epithelial Cancer; Ovarian Germ Cell Tumor; Ovarian Low Malignant Potential Tumor; Pancreatic Cancer; Pancreatic Cancer, Islet Cell Tumors; Papillomatosis; Parathyroid Cancer; Penile Cancer; Pharyngeal Cancer; Pheochromocytoma; Pineal Parenchymal Tumors of Intermediate Differentiation; Pineoblastoma and Supratentorial Primitive Neuroectodermal Tumors; Pituitary Tumor; Plasma Cell Neoplasm/Multiple Myeloma; Pleuropulmonary Blastoma; Primary Central Nervous System Lymphoma; Prostate Cancer; Rectal Cancer; Renal Cell

(Kidney) Cancer; Renal Pelvis and Ureter, Transitional Cell Cancer; Respiratory Tract Carcinoma Involving the NUT Gene on Chromosome 15; Retinoblastoma; Rhabdomyosarcoma; Salivary Gland Cancer; Sarcoma, Ewing Family of Tumors; Sarcoma, Kaposi; Sarcoma, Soft Tissue; Sarcoma, Uterine; Sézary Syndrome; Skin Cancer (Nonmelanoma); Skin Cancer (Melanoma); Skin Carcinoma, Merkel Cell; Small Cell Lung Cancer; Small Intestine Cancer; Soft Tissue Sarcoma; Squamous Cell Carcinoma, Squamous Neck Cancer with Occult Primary, Metastatic; Stomach (Gastric) Cancer; Supratentorial Primitive Neuroectodermal Tumors; T-Cell Lymphoma, Cutaneous; Testicular Cancer; Throat Cancer; Thymoma and Thymic Carcinoma; Thyroid Cancer; Transitional Cell Cancer of the Renal Pelvis and Ureter; Trophoblastic Tumor, Gestational; Urethral Cancer; Uterine Cancer, Endometrial; Uterine Sarcoma; Vaginal Cancer; Vulvar Cancer; Waldenström Macroglobulinemia; or Wilms Tumor.

~~8~~7. The use according to any of Claims 1 to 6 ~~Claims 1 to 8~~, wherein the cancer is renal cell carcinoma, lung cancer, malignant melanoma, or pancreatic cancer.

~~9~~8. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein R has the formula:



~~10~~9. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein R^2 and R^3 are each independently hydrogen or substituted or unsubstituted C_1-C_6 linear, C_3-C_6 branched, or C_3-C_6 cyclic alkyl.

~~11~~10. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein R^2 is chosen from methyl, ethyl, n-propyl, *iso*-propyl, n-butyl, *iso*-butyl, *sec*-butyl, and *tert*-butyl; and R^3 is hydrogen.

~~12~~11. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein R^2 is methyl or ethyl.

~~13~~12. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein R^2 is an alkyl unit wherein one or more hydrogen atoms are substituted with one or more substitutions chosen from:

i) halogen;

ii) $-N(R^{11})_2$; and

iii) $-OR^{11}$;

wherein each R^{11} is independently hydrogen or C_1-C_4 linear or C_3-C_4 branched alkyl.

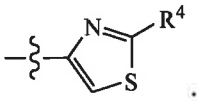
~~14~~13. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein R^2 is substituted or unsubstituted phenyl and R^3 is hydrogen.

~~15~~14. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein R^2 is substituted or unsubstituted heteroaryl and R^3 is hydrogen.

~~16~~15. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein R^2 is a heteroaryl unit chosen from 1,2,3,4-tetrazol-1-yl ,1,2,3,4-tetrazol-5-yl, [1,2,3]triazol-4-yl, [1,2,3]triazol-5-yl, [1,2,4]triazol-4-yl, [1,2,4]triazol-5-yl, imidazol-2-yl, imidazol-4-yl, pyrrol-2-yl, pyrrol-3-yl, oxazol-2-yl, oxazol-4-yl, oxazol-5-yl, isoxazol-3-yl, isoxazol-4-yl, isoxazol-5-yl, [1,2,4]oxadiazol-3-yl, [1,2,4]oxadiazol-5-yl, [1,3,4]oxadiazol-2-yl, furan-2-yl, furan-3-yl, thiophen-2-yl, thiophen-3-yl, isothiazol-3-yl, isothiazol-4-yl, isothiazol-5-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, [1,2,4]thiadiazol-3-yl, [1,2,4]thiadiazol-5-yl, or [1,3,4]thiadiazol-2-yl.

~~17~~16. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein R^2 is thiophen-2-yl or thiophen-3-yl.

~~18~~17. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein R has the formula:



~~19~~18. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein R^4 is hydrogen or substituted or unsubstituted C_1-C_6 linear, C_3-C_6 branched, or C_3-C_6 cyclic alkyl.

~~20~~19. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein R^4 is chosen from methyl, ethyl, n-propyl, *iso*-propyl, n-butyl, *iso*-butyl, *sec*-butyl, and *tert*-butyl; and R^3 is hydrogen.

~~21~~20. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein R^4 is methyl or ethyl.

~~22~~21. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein R^4 is substituted or unsubstituted phenyl and R^3 is hydrogen.

~~23~~22. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein R^4 is an alkyl unit wherein one or more hydrogen atoms are substituted with one or more substitutions chosen from:

i) halogen;

ii) $-N(R^{11})_2$; and

iii) $-OR^{11}$;

wherein each R^{11} is independently hydrogen or C_1-C_4 linear or C_3-C_4 branched alkyl.

~~24~~23. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein R^4 is substituted or unsubstituted heteroaryl.

~~25~~24. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein R^4 is a heteroaryl unit chosen from 1,2,3,4-tetrazol-1-yl ,1,2,3,4-tetrazol-5-yl, [1,2,3]triazol-4-yl, [1,2,3]triazol-5-yl, [1,2,4]triazol-4-yl, [1,2,4]triazol-5-yl, imidazol-2-yl, imidazol-4-yl, pyrrol-2-yl, pyrrol-3-yl, oxazol-2-yl, oxazol-4-yl, oxazol-5-yl, isoxazol-3-yl, isoxazol-4-yl, isoxazol-5-yl, [1,2,4]oxadiazol-3-yl, [1,2,4]oxadiazol-5-yl, [1,3,4]oxadiazol-2-yl, furan-2-yl, furan-3-yl, thiophen-2-yl, thiophen-3-yl, isothiazol-3-yl, isothiazol-4-yl, isothiazol-5-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, [1,2,4]thiadiazol-3-yl, [1,2,4]thiadiazol-5-yl, and [1,3,4]thiadiazol-2-yl.

~~26~~25. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein R^4 is thiophen-2-yl or thiophen-3-yl.

~~27~~26. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein R^1 is hydrogen, methyl, ethyl, *tert*-butyl, or methyl substituted with phenyl.

~~28~~27. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein L has the formula:

$$-C(O)[C(R^{5a}R^{5b})]_xNHC(O)-$$

R^{5a} is hydrogen, substituted or unsubstituted phenyl, and substituted or unsubstituted heteroaryl; the index x is 1 or 2.

~~29~~28. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein R^{5a} has the formula:

$$-[C(R^{7a}R^{7b})]_wR^8$$

each R^{7a} is independently hydrogen, methyl, or ethyl; each R^{7b} is hydrogen; R^8 is hydrogen, substituted or unsubstituted C_1-C_4 linear, C_3-C_4 branched, or C_3-C_4 cyclic alkyl, or substituted or unsubstituted phenyl, wherein the substitutions are chosen from one or more hydroxy, halogen, or C_1-C_4 alkyl; R^{5b} is hydrogen; the index w is 1 or 2.

~~30~~29. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein L has the formula chosen from:

i) $-C(O)[C(R^{5a}H)]NHC(O)O-$;

ii) $-C(O)[C(R^{5a}H)][CH_2]NHC(O)O-$;

ii) $-C(O)[CH_2][C(R^{5a}H)]NHC(O)O-$;

iv) $-C(O)[C(R^{5a}H)]NHC(O)-$;

v) $-C(O)[C(R^{5a}H)][CH_2]NHC(O)-$; or

vi) $-C(O)[CH_2][C(R^{5a}H)]NHC(O)-$;

wherein R^{5a} is:

i) hydrogen;

ii) methyl;

iii) ethyl;

iv) isopropyl;

v) phenyl;

vi) benzyl;

vii) 4-hydroxybenzyl;

viii) hydroxymethyl; or

ix) 1-hydroxyethyl.

~~31~~30. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, R^1 is chosen from phenyl, 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 2,3-difluorophenyl, 3,4-difluorophenyl, 3,5-difluorophenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 2,3-dichlorophenyl, 3,4-dichlorophenyl, 3,5-dichlorophenyl, 2-hydroxyphenyl, 3-hydroxyphenyl, 4-hydroxyphenyl, 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 2,3-dimethoxyphenyl, 3,4-dimethoxyphenyl, and 3,5-dimethoxyphenyl.

~~32~~31. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein R^2 is methyl or ethyl, R^3 is hydrogen, and L has the formula $–C(O)CH_2–$.

~~33~~32. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein R^2 is methyl or ethyl, R^3 is hydrogen, and L has the formula $–C(O)CH_2CH_2–$.

~~34~~33. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein R^4 is methyl, ethyl, phenyl, thiophen-2-yl, thiazol-2-yl, oxazol-2-yl, and isoxazol-3-yl; and L has the formula $–C(O)CH_2–$.

~~35~~34. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein R^4 is methyl, ethyl, phenyl, thiophen-2-yl, thiazol-2-yl, oxazol-2-yl, and isoxazol-3-yl; and L has the formula $–C(O)CH_2CH_2–$.

~~36~~35. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein R^1 is a substituted or unsubstituted heteroaryl unit, said substitutions chosen from:

i) C_1-C_6 linear, branched, and cyclic alkyl;

ii) substituted or unsubstituted phenyl and benzyl;

iii) substituted of unsubstituted heteroaryl;

iv) $–C(O)R^9$; or

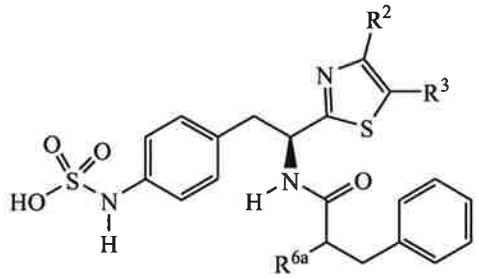
v) $–NHC(O)R^9$;

R^9 is C_1-C_6 linear or C_3-C_6 branched alkyl; C_1-C_6 linear or C_3-C_6 branched alkoxy; or $-NHCH_2C(O)R^{10}$; R^{10} is chosen from hydrogen, methyl, ethyl, or *tert*-butyl.

~~37~~36. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein R^1 is a heteroaryl unit substituted by an alkyl unit chosen from methyl, ethyl, n-propyl, *iso*-propyl, n-butyl, *iso*-butyl, *sec*-butyl, or *tert*-butyl.

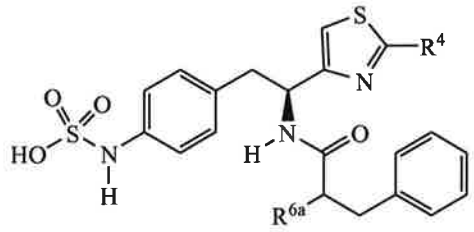
~~38~~37. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein R^1 is a heteroaryl unit substituted by a carboxy unit having the formula $-NHC(O)R^9$; R^9 is chosen from methyl, methoxy, ethyl, ethoxy, *tert*-butyl, and *tert*-butoxy.

~~39~~38. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein the compound has the formula:



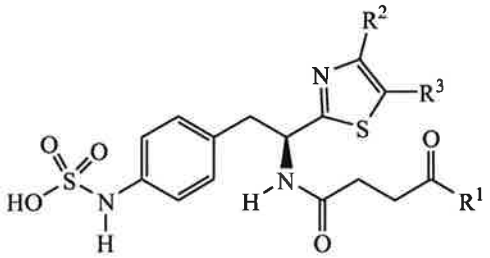
wherein R^2 is methyl or ethyl, R^3 is hydrogen, R^{6a} is chosen from phenyl, 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 2,3-difluorophenyl, 3,4-difluorophenyl, 3,5-difluorophenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 2,3-dichlorophenyl, 3,4-dichlorophenyl, 3,5-dichlorophenyl, 2-hydroxyphenyl, 3-hydroxyphenyl, 4-hydroxyphenyl, 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 2,3-dimethoxyphenyl, 3,4-dimethoxyphenyl, 3,5-dimethoxyphenyl, 3-methyl-1,2,4-oxadiazol-5-yl, thiophen-2-yl, thiophen-3-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, oxazol-2-yl, oxazol-4-yl, oxazol-5-yl, or isoxazol-3-yl.

~~40~~39. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein the compound has the formula:



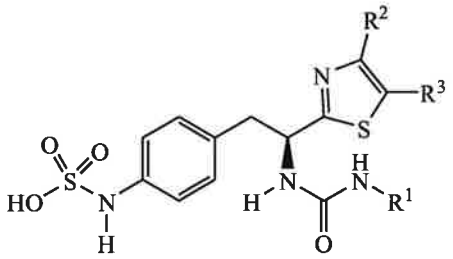
wherein R^4 is methyl, ethyl, phenyl, or thiophen-2-yl, R^{6a} is chosen from phenyl, 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 2,3-difluorophenyl, 3,4-difluorophenyl, 3,5-difluorophenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 2,3-dichlorophenyl, 3,4-dichlorophenyl, 3,5-dichlorophenyl, 2-hydroxyphenyl, 3-hydroxyphenyl, 4-hydroxyphenyl, 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 2,3-dimethoxyphenyl, 3,4-dimethoxyphenyl, 3,5-dimethoxyphenyl, 3-methyl-1,2,4-oxadiazol-5-yl, thiophen-2-yl, thiophen-3-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, oxazol-2-yl, oxazol-4-yl, oxazol-5-yl, or isoxazol-3-yl.

4140. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein the compound has the formula:



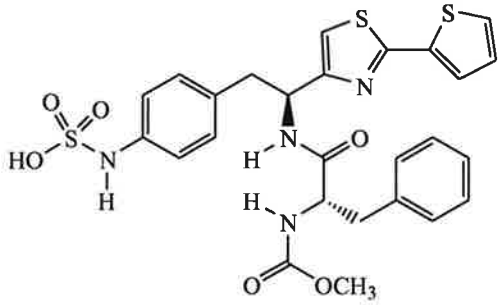
wherein R^2 is chosen from methyl, ethyl, phenyl, and thiophen-2-yl, R^3 is hydrogen or methyl; R^1 is chosen from phenyl, thiophen-2-yl, thiophen-3-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, oxazol-2-yl, oxazol-4-yl, oxazol-5-yl, and isoxazol-3-yl.

4241. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein the compound has the formula:



wherein R^2 and R^3 are each independently hydrogen, methyl or ethyl; R^1 is chosen from phenyl, 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 2,3-difluorophenyl, 3,4-difluorophenyl, 3,5-difluorophenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 2,3-dichlorophenyl, 3,4-dichlorophenyl, 3,5-dichlorophenyl, 2-hydroxyphenyl, 3-hydroxyphenyl, 4-hydroxyphenyl, 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 2,3-dimethoxyphenyl, 3,4-dimethoxyphenyl, and 3,5-dimethoxyphenyl.

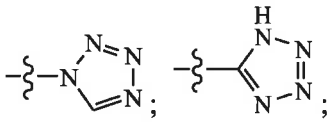
4342. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein the compound has the formula:



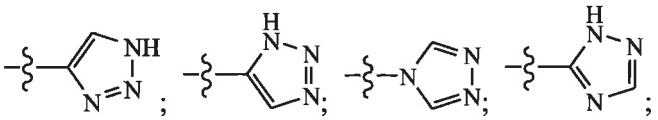
or the ammonium salt thereof.

4443. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein R^1 is a substituted or unsubstituted heteroaryl unit chosen from:

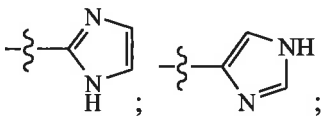
i) 1,2,3,4-tetrazol-1-yl and 1,2,3,4-tetrazol-5-yl having the respective formulae:



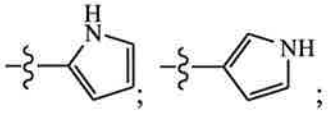
ii) [1,2,3]triazol-4-yl, [1,2,3]triazol-5-yl, [1,2,4]triazol-4-yl, and [1,2,4]triazol-5-yl having the respective formulae:



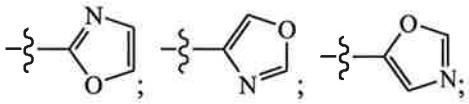
iii) imidazol-2-yl and imidazol-4-yl having the respective formulae:



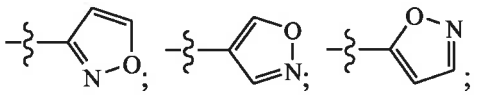
iv) pyrrol-2-yl and pyrrol-3-yl having the respective formulae:



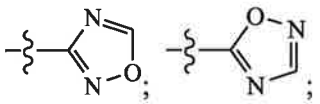
v) oxazol-2-yl, oxazol-4-yl, and oxazol-5-yl having the respective formulae:



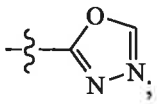
vi) isoxazol-3-yl, isoxazol-4-yl, and isoxazol-5-yl having the respective formulae:



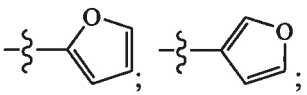
vii) [1,2,4]oxadiazol-3-yl and [1,2,4]oxadiazol-5-yl having the respective formulae:



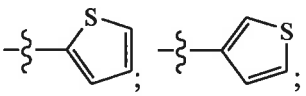
viii) [1,3,4]oxadiazol-2-yl having the formula:



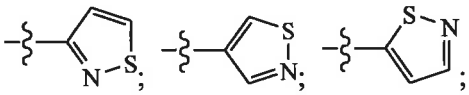
ix) furan-2-yl and furan-3-yl having the respective formulae:



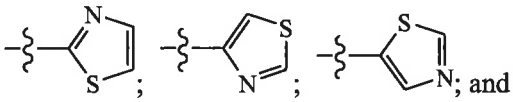
x) thiophen-2-yl and thiophen-3-yl having the respective formulae:



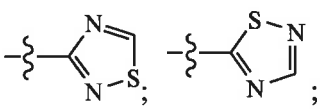
xi) isothiazol-3-yl, isothiazol-4-yl and isothiazol-5-yl having the respective formulae:



xii) thiazol-2-yl, thiazol-4-yl and thiazol-5-yl having the respective formulae:


; and

xiii) [1,2,4]thiadiazol-3-yl and [1,2,4]thiadiazol-5-yl having the respective formulae:



said heteroaryl unit substitutions chosen from:

i) C_1-C_6 linear, C_3-C_6 branched, or C_3-C_6 cyclic alkyl;

ii) substituted or unsubstituted phenyl and benzyl;

iii) substituted of unsubstituted heteroaryl;

iv) $-C(O)R^9$; and

v) $-NHC(O)R^9$;

R^9 is C_1-C_6 linear and C_3-C_6 branched alkyl; C_1-C_6 linear and C_3-C_6 branched alkoxy; or $NHCH_2C(O)R^{10}$; R^{10} is chosen from hydrogen, methyl, ethyl, and *tert*-butyl;

R^4 is a unit chosen from:

i) hydrogen;

ii) substituted or unsubstituted C_1-C_6 linear, C_3-C_6 branched, or C_3-C_6 cyclic alkyl;

iii) substituted or unsubstituted C_2-C_6 linear, C_3-C_6 branched, or C_3-C_6 cyclic alkenyl;

iv) substituted or unsubstituted C_2-C_6 linear or C_3-C_6 branched alkynyl;

v) substituted or unsubstituted C_6 or C_{10} aryl;

vi) substituted or unsubstituted C_1-C_9 heteroaryl;

vii) substituted or unsubstituted C_1-C_9 heterocyclic.

4544. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein the compound is chosen from:
(*S*)-4-[2-Benzamido-2-(4-ethylthiazol-2-yl)ethyl]phenylsulfamic acid;
(*S*)-4-{2-(4-Ethylthiazol-2-yl)-2-[2-(2-fluorophenyl)acetamido]ethyl}phenyl-sulfamic acid;
(*S*)-4-(2-(4-Ethylthiazol-2-yl)-2-(2-(3-fluorophenyl)acetamido)ethyl)phenylsulfamic acid;
(*S*)-4-(2-(2-(2,3-Difluorophenyl)acetamido)-2-(4-ethylthiazol-2-yl)ethyl)phenyl-sulfamic acid;
(*S*)-4-(2-(2-(3,4-Difluorophenyl)acetamido)-2-(4-ethylthiazol-2-yl)ethyl)phenyl-sulfamic acid;
(*S*)-4-(2-(2-(2-Chlorophenyl)acetamido)-2-(4-ethylthiazol-2-yl)ethyl)phenylsulfamic acid;
(*S*)-4-(2-(2-(3-Chlorophenyl)acetamido)-2-(4-ethylthiazol-2-yl)ethyl)phenyl-sulfamic acid;

(*S*)-4-(2-(4-Ethylthiazol-2-yl)-2-(2-(3-hydroxyphenyl)acetamido)ethyl)phenyl-sulfamic acid;

(*S*)-4-(2-(4-Ethylthiazol-2-yl)-2-(2-(2-methoxyphenyl)acetamido)ethyl)phenyl-sulfamic acid;

(*S*)-4-(2-(4-Ethylthiazol-2-yl)-2-(2-(3-methoxyphenyl)acetamido)ethyl)phenyl-sulfamic acid;

(*S*)-4-(2-(4-Ethylthiazol-2-yl)-2-(3-phenylpropanamido)ethyl)phenylsulfamic acid;

(*S*)-4-(2-(2-(3,4-Dimethoxyphenyl)acetamido)-2-(4-ethylthiazol-2-yl)ethyl)-phenylsulfamic acid;

(*S*)-4-(2-(2-(2,3-Dimethoxyphenyl)acetamido)-2-(4-ethylthiazol-2-yl)ethyl)-phenylsulfamic acid;

(*S*)-4-(2-(3-(3-Chlorophenyl)propanamido)-2-(4-ethylthiazol-2-yl)ethyl)phenyl-sulfamic acid;

(*S*)-4-(2-(4-Ethylthiazol-2-yl)-2-(3-(2-methoxyphenyl)propanamido)ethyl)phenyl-sulfamic acid;

(*S*)-4-(2-(4-Ethylthiazol-2-yl)-2-(3-(3-methoxyphenyl)propanamido)ethyl)pheny-lsulfamic acid;

(*S*)-4-(2-(4-Ethylthiazol-2-yl)-2-(3-(4-methoxyphenyl)propanamido)ethyl)phenyl-sulfamic acid;

(*S*)-4-{2-[2-(4-Ethyl-2,3-dioxopiperazin-1-yl)acetamido]-2-(4-ethylthiazol-2-yl)ethyl}phenylsulfamic acid;

(*S*)-4-{2-(4-Ethylthiazol-2-yl)-2-[2-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)acetamide]ethyl}phenylsulfamic acid;

(*S*)-4-[2-(Benzo[*d*][1,3]dioxole-5-carboxamido)-2-(4-ethylthiazol-2-yl)ethyl]-phenylsulfamic acid;

4-((*S*)-2-(2-(2-Chlorophenyl)acetamido)-2-(2-(thiophene2-yl)thiazol-4-yl)ethyl)-phenylsulfamic acid;

4-((*S*)-2-(2-(3-Methoxyphenyl)acetamido)-2-(2-(thiophene2-yl)thiazol-4-yl)ethyl)-phenylsulfamic acid;

4-{(*S*)-2-(3-Phenylpropanamido)-2-[2-(thiophene2-yl)thiazol-4-yl]ethyl}phenyl-sulfamic acid;

4-{(*S*)-2-(3-(3-Chlorophenyl)propanamido)-2-[2-(thiophene2-yl)thiazol-4-yl]ethyl}-phenylsulfamic acid;

4-{(*S*)-2-[2-(3-Fluorophenyl)acetamide]-2-[2-(thiophene2-yl)thiazol-4-yl]ethyl}-phenylsulfamic acid;

(*S*)-4-{2-[2-(2,5-Dimethylthiazol-4-yl)acetamide]-2-(4-ethylthiazol-2-yl]ethyl}-phenylsulfamic acid;

(*S*)-4-{2-[2-(2,4-Dimethylthiazol-5-yl)acetamide]-2-(4-methylthiazol-2-ylethyl}-phenylsulfamic acid;

(*S*)-4-{2-(4-Ethylthiazol-2-yl)-2-[3-(thiazol-2-yl)propanamido]ethyl}phenylsulfamic acid;

(*S*)-4-{2-(4-Ethylthiazol-2-yl)-2-[2-(4-ethylthiazol-2-yl)acetamide]ethyl}phenyl-sulfamic acid;

(*S*)-4-{2-[2-(3-Methyl-1,2,4-oxadiazol-5-yl)acetamide]-2-(2-phenylthiazol-4-yl)ethyl}phenylsulfamic acid;

4-{(*S*)-2-[2-(4-Ethyl-2,3-dioxopiperazin-1-yl)acetamide]-2-[2-(thiophen-2-yl)thiazol-4-yl]ethyl}phenylsulfamic acid;

(*S*)-4-(2-(2,3-Diphenylpropanamido)-2-(4-ethylthiazol-2-yl)ethyl)phenylsulfamic acid;

(*S*)-4-{2-(4-Ethylthiazol-2-yl)-2-[2-(2-methoxyphenyl)-3-phenylpropanamido]-ethyl)phenylsulfamic acid;

(*S*)-4-{2-(4-Ethylthiazol-2-yl)-2-[2-(3-fluorophenyl)-3-phenylpropanamido]-ethyl}phenylsulfamic acid;

(*S*)-4-{2-(4-Ethylthiazol-2-yl)-2-[2-(3-methoxyphenyl)-3-phenylpropanamido]-ethyl}phenylsulfamic acid;

4-{(*S*)-2-(4-Ethylthiazol-2-yl)-2-[2-(3-methyl-1,2,4-oxadiazol-5-yl)-3-phenylpropanamido]ethyl}phenylsulfamic acid;

(*S*)-4-[2-(4-Ethylthiazol-2-yl)-2-(4-oxo-4-phenylbutanamido)-ethyl]phenylsulfamic acid;

(*S*)-4-(2-(4-Ethylthiazol-2-yl)-2-(5-methyl-4-oxohexanamido)ethyl)phenylsulfamic acid;

(*S*)-4-{2-[4-(3,4-Dihydro-2H-benzo[b][1,4]dioxepin-7-yl)-4-oxobutanamido]-2-(4-ethylthiazol-2-yl)ethyl}phenylsulfamic acid;

(*S*)-4-{2-[4-(2,3-Dimethoxyphenyl)-4-oxobutanamido]-2-(4-ethylthiazol-2-yl)ethyl}phenylsulfamic acid;

(*S*)-4-{2-(4-Ethylthiazol-2-yl)-2-[4-oxo-4-(pyridin-2-yl)butanamido]ethyl}phenyl-sulfamic acid;

(S)-4-{2-[4-(2,3-Dihydrobenzo[b][1,4]dioxin-6-yl)-4-oxobutanamido]-2-(4-ethylthiazol-2-yl)ethyl}phenylsulfamic acid;

(*S*)-4-[2-(4-*tert*-Butoxy-4-oxobutanamido)-2-(4-ethylthiazol-2-yl)ethyl]phenyl-sulfamic acid;

(*S*)-4-[2-(4-Ethoxy-4-oxobutanamido)-2-(4-ethylthiazol-2-yl)ethyl]phenylsulfamic acid;

(S)-4-(2-(3-Benzylureido)-2-(4-ethylthiazol-2-yl)ethyl)phenylsulfamic acid;

4-{[(*S*)-2-(2-Ethylthiazol-4-yl)-2-(3-(*R*)-1methoxy-1-oxo-3-phenylpropan-2-yl)ureido]ethyl}phenylsulfamic acid;

4-{(*S*)-2-(3-Benzylureido)-2-[2-(thiophen-2-yl)thiazol-4-yl]ethyl}phenylsulfamic acid;

{4-(*S*)-[2-Phenylmethanesulfonylamino-2-(2-thiophen-2-ylthiazol-4-yl)ethyl]-phenylsulfamic acid;

4-{(S)-2-[(2-Methylthiazol-4-yl)methylsulfonamido]-2-[2-(thiophen-2-yl)thiazol-4-yl]ethyl}phenylsulfamic acid;

{4-(*S*)-[2-Phenylmethanesulfonylamino-2-(2-ethylthiazol-4-yl)ethyl]phenyl}-sulfamic acid;

{4-(*S*)-[2-(3-Methoxyphenyl)methanesulfonylamino-2-(2-ethylthiazol-4-yl)ethyl]phenyl}sulfamic acid;

(*S*)-4-{[1-(2-Ethylthiazol-4-yl)-2-(4-sulfoaminophenyl)ethylsulfamoyl]methyl}-benzoic acid methyl ester;

(*S*)-4-[2-(2-Ethylthiazol-4-yl)-2-(1-methyl-1*H*-imidazol-4-sulfonamido)ethyl]-phenylsulfamic acid;

4-{(*S*)-2-[2-(Thiophen-2-yl)thiazol-4-yl]-2-(2,2,2-trifluoroethylsulfonamido)-ethyl}phenylsulfamic acid;

{4-(*S*)-[2-(Phenylethanesulfonylamino)-2-(2thiophen-2-ylthiazol-4-yl)ethyl]-phenyl}sulfamic acid;

{4-(*S*)-[3-(Phenylpropanesulfonylamino)-2-(2thiophen-2-ylthiazol-4-yl)ethyl]-phenyl}sulfamic acid;

(*S*)-{4-[2-(4-Methyl-3,4-dihydro-2H-benzo[1,4]oxazine-7-sulfonylamino)-2-(2-thiophen-2-ylthiazol-4-yl)ethyl]phenyl}sulfamic acid;

4-{(*S*)-2-(4-Acetamidophenylsulfonamido)-2-[2-(thiophen-2-yl)thiazol-4-yl]ethyl}phenylsulfamic acid;

4-{(S)-2-(2-cyclopropylthiazol-4-yl)-2-[4-(3-methoxyphenyl)-thiazol-2-ylamino]ethyl}phenylsulfamic acid;

(*S*)-4-(2-(4-((2-Methoxy-2-oxoethyl)carbamoyl)thiazole-5-ylamino)2-(2-ethylthiazole-4-yl)ethyl)phenylsulfamic acid;

4-((*S*)-2-(5-(1-*N*-(2-Methoxy-2-oxoethyl)-1-*H*-indol-3-yl)oxazole-2-ylamino)-2-(2-methylthiazol-4-yl)ethyl))phenylsulfamic acid;

4-((S)-2-(5-(2-Methoxyphenyl)oxazol-2-ylamino)-2-(2-methylthiazol-4-yl)ethyl)-phenylsulfamic acid;

4-((*S*)-2-(5-((*S*)-1-(*tert*-Butoxycarbonyl)-2-phenylethyl)oxazole-2-ylamino)-2-(2-methylthiazole-4-yl)ethyl)phenylsulfamic acid;

(*S*)-4-(2-(5-(4-Methoxycarbonyl)phenyl)oxazole-2-ylamino)2-(2-methylthiazole-4-yl)ethyl)phenylsulfamic acid;

(*S*)-4-(2-(5-(3-Methoxybenzyl)oxazole-2-ylamino)-2-(2-methylthiazole-4-yl)ethyl)-phenylsulfamic acid;

(*S*)-4-(2-(2-Methylthiazole-4-yl)2-(5-phenyloxazole-2-ylamino)ethyl)phenyl-sulfamic acid;

4-((S)-2-(2-Cyclopropylthiazol-4-yl)-2-(4-(3-methoxyphenyl)thiazol-2-ylamino)-ethyl)phenylsulfamic acid;

(*S*)-4-(2-(2-cyclopropylthiazol-4-yl)-2-(4-(4-fluorophenyl)thiazol-2-ylamino)ethyl)-phenylsulfamic acid;

4-((*S*)-2-(2-cyclopropylthiazol-4-yl)-2-(4-(2-methoxyphenyl)thiazol-2-ylamino)-ethyl)phenylsulfamic acid;

4-((*S*)-2-(2-cyclopropylthiazol-4-yl)-2-(4-(2,4-difluorophenyl)thiazol-2-ylamino)-ethyl)phenylsulfamic acid;

(*S*)-4-(2-(4-(3-methoxybenzyl)thiazol-2-ylamino)-2-(2-cyclopropylthiazol-4-yl)ethyl)phenylsulfamic acid;

(*S*)-{5-[1-(2-Ethylthiazol-4-yl)-2-(4-sulfoaminophenyl)ethylamino]-2-methyl-2H-[1,2,4]triazole-3-yl}carbamic acid methyl ester;

4-{(S)-2-[4-(2-Methoxyphenyl)thiazol-2-ylamino)-2-[2-(thiophen-2-yl)thiazol-4-yl]ethyl}phenylsulfamic acid;

4-{(*S*)-2-[5-(3-Methoxyphenyl)oxazole-2-ylamino]-2-(2-phenylthiazole-4-yl)ethyl}phenylsulfamic acid;

4-{(*S*)-2-[4-(2,4-Difluorophenyl)thiazol-2-ylamino]-2-[2-(thiophen-2-yl)thiazol-4-yl]ethyl}phenylsulfamic acid;

(*S*)-4-{2-[4-(Ethoxycarbonyl)thiazol-2-ylamino]-2-(2-phenylthiazol-4-yl)ethyl}-phenylsulfamic acid;

(*S*)-4-{2-[4-(2-Ethoxy-2-oxoethyl)thiazol-2-ylamino]-2-(2-phenylthiazol-4-yl)ethyl}phenylsulfamic acid;

(*S*)-4-{2-[4-(4-Acetamidophenyl)thiazol-2-ylamino]-2-(2-phenylthiazol-4-yl)ethyl}phenylsulfamic acid;

(S)-4-[2-(4-Phenylthiazol-2-ylamino)-2-(2-phenylthiazol-4-yl)ethyl]phenylsulfamic acid;

(*S*)-4-{2-[4-(4-(Methoxycarbonyl)phenyl)thiazol-2-ylamino]-2-(2-phenylthiazol-4-yl)ethyl}phenylsulfamic acid;

4-{(S)-2-[4-(Ethoxycarbonyl)thiazol-2-ylamino]-2-[2-(thiophen-2-yl)thiazol-4-yl]ethyl}phenylsulfamic acid;

(*S*)-4-[2-(4-(Methoxycarbonyl)thiazol-5-ylamino)-2-(2-phenylthiazole-4-yl)ethyl]-phenylsulfamic acid;

(*S*)-4-[2-(5-Phenyloxazole-2-ylamino)]-2-(2-phenylthiazole-4-yl)phenylsulfamic acid;

(*S*)-4-{2-[5-(4-Acetamidophenyl)oxazole-2-ylamino]-2-(2-phenylthiazole-4-yl)ethyl}phenylsufamic acid;

4-((*S*)-2-(5-(2,4-Difluorophenyl)oxazole-2-ylamino)-2-(2-phenylthiazole-4-yl)ethyl)phenylsulfamic acid;

4-{(*S*)-2-[5-(3-Methoxyphenyl)oxazol-2-ylamino]-2-[(2-thiophen-2-yl)thiazole-4-yl]ethyl}phenylsulfamic acid;

(*S*)-4-[2-(4,6-Dimethylpyrimidene-2-ylamino)-2-(2-methylthiazole-4-yl)ethyl]-phenylsulfamic acid;

(*S*)-4-[2-(4-Hydroxy-6-methylpyrimidine-2-ylamino)-2-(2-methylthiazole-4-yl)ethyl]phenylsulfamic acid; 4-{(S)-2-[(S)-2-(*tert*-Butoxycarbonylamino)-3-phenylpropanamido]-2-(4-ethylthiazol-2-yl)ethyl}phenylsulfamic acid;

4-{(*S*)-2-[(*R*)-2-(*tert*-Butoxycarbonylamino)-3-phenylpropanamido]-2-(4-ethylthiazol-2-yl)ethyl}phenylsulfamic acid;

{1-[1-(5-Ethylthiazol-2-yl)-(*S*)-2-(4-sulfoaminophenyl)ethylcarbamoyl]-(*S*)-2-phenylethyl}methyl carbamic acid *tert*-butyl ester;

{(*S*)-2-Phenyl-1-[1-(4-phenylthiazol-2-yl)-(*S*)-2-(4-sulfoaminophenyl)ethyl-carbamoyl]ethyl}carbamic acid *tert*-butyl ester;

4-{(*S*)-2-(*S*)-2-(*tert*-Butoxycarbonylamino)-3-phenylpropaneamido-2-(2-phenylthiazole-4-yl)}phenylsulfamic acid;

4-{(*S*)-2-(4-Ethylthiazol-2-yl)-2-[(*S*)-2-(methoxycarbonylamino)-3-phenyl-propanamido]ethyl}phenylsulfamic acid;

4-{(*S*)-2-[(*S*)-2-(Methoxycarbonylamino)-3-phenylpropanamido]-2-(thiazol-2-yl)ethyl}phenylsulfamic acid;

4-{(*S*)-2-[(*S*)-2-(Methoxycarbonylamino)-3-phenylpropanamido]-2-(4-methylthiazol-2-yl)ethyl}phenylsulfamic acid;

4-{(*S*)-2-[(*S*)-2-(Methoxycarbonylamino)-3-phenylpropanamido]-2-(4-propylthiazol-2-yl)ethyl}phenylsulfamic acid;

4-{(*S*)-2-(4-*tert*-Butylthiazol-2-yl)-2-[(*S*)-2-(methoxycarbonylamino)-3-phenylpropanamido]ethyl}phenylsulfamic acid;

4-{(*S*)-2-(4-Cyclopropylthiazol-2-yl)-2-[(*S*)-2-(methoxycarbonylamino)-3-phenylpropanamido]ethyl}phenylsulfamic acid;

4-{(*S*)-2-(4-Cyclohexylthiazol-2-yl)-2-[(*S*)-2-(methoxycarbonylamino)-3-phenyl-propanamido]ethyl}phenylsulfamic acid;

4-{(*S*)-2-(4,5-Dimethylthiazol-2-yl)-2-[(*S*)-2-(methoxycarbonylamino)-3-phenyl-propanamido]ethyl}phenylsulfamic acid;

4-{(*S*)-2-Phenyl-1-[1-(2-phenylthiazol-4-yl)-(*S*)-2-(4-sulfoaminophenyl)ethyl-carbamoyl]ethyl}carbamic acid *tert*-butyl ester;

4-{(*S*)-2-(4-Ethyl-5-methylthiazol-2-yl)-2-[(S)-2-(methoxycarbonylamino)-3-phenyl-propanamido]ethyl}phenylsulfamic acid;

4-{(*S*)-2-[(S)-2-(Methoxycarbonylamino)-3-phenylpropanamido]-2-[4-(2,2,2-trifluoroethyl)thiazol-2-yl]ethyl}phenylsulfamic acid;

4-{(*S*)-2-[(*S*)-2-(Methoxycarbonylamino)-3-phenylpropanamido)-2-[4-(3,3,3-trifluoropropyl)thiazol-2-yl]ethyl}phenylsulfamic acid;

4-{(*S*)-2-[4-(2,2-Difluorocyclopropyl)thiazol-2-yl]-2-[(*S*)-2-(methoxycarbonylamino)-3-phenylpropanamido]ethyl}phenylsulfamic acid;

4-{(*S*)-2-[(*S*)-2-(Methoxycarbonylamino)-3-phenylpropanamido]-2-[4-(methoxy-methyl)thiazol-2-yl]ethyl}phenylsulfamic acid;

4-{(*S*)-2-(4-(Ethoxycarbonylamino)thiazol-2-yl)-2-[(*S*)-2-(methoxycarbonylamino)-3-phenylpropanamido]ethyl}phenylsulfamic acid;

4-{(*S*)-2-[(*S*)-2-(Methoxycarbonylamino)-3-phenylpropanamido]-2-(5-phenylthiazol-2-yl))ethyl}phenylsulfamic acid;

4-{(*S*)-2-(4-*tert*-Butylthiazol-2-yl)-2-[(*S*)-2-(methoxycarbonylamino)-3-phenyl-propanamido]ethyl}phenylsulfamic acid;

4-{(*S*)-2-(4-Ethyl-5-phenylthiazol-2-yl)-2-[(*S*)-2-(methoxycarbonylamino)-3-phenyl-propanamido]ethyl}phenylsulfamic acid;

4-{(*S*)-2-[4-(3,4-Dimethylphenyl)thiazol-2-yl]-2-[(*S*)-2-(methoxycarbonylamino)-3-phenylpropanamido]ethyl}phenylsulfamic acid;

4-{(S)-2-[4-(4-Chlorophenyl)thiazol-2-yl]-2-[(S)-2-(methoxycarbonylamino)-3-phenylpropanamido]ethyl}phenylsulfamic acid;

4-{(*S*)-2-[(*S*)-2-(Methoxycarbonylamino)-3-phenylpropanamido]-2-(4-phenylthiazol-2-yl)ethyl}phenylsulfamic acid;

4-{(*S*)-2-[(*S*)-2-(Methoxycarbonylamino)-3-phenylpropanamido]-2-[4-(thiophen-2-yl)thiazol-2-yl]ethyl}phenylsulfamic acid;

4-{(*S*)-2-[(*S*)-2-(Methoxycarbonylamino)-3-phenylpropanamido]-2-[4-(thiophen-3-yl)thiazol-2-yl]ethyl}phenylsulfamic acid;

4-{(*S*)-2-(4-Ethylthiazol-2-yl)-2-[(*S*)-2-(methoxycarbinyl)-3-phenylpropion-amido]ethyl}phenylsulfamic acid;

4-{(*S*)-2-(5,6-Dihydro-4*H*-cyclopenta[*d*]thiazol-2-yl)-2-[(*S*)-2-(methoxy-carbonyl)-3-phenylpropanamido]ethyl}phenylsulfamic acid;

4-{(*S*)-2-[(*S*)-2-(Methoxycarbonylamino)-3-phenylpropanamido]-2-(4,5,6,7-tetrahydrobenzo[*d*]thiazol-2-yl)ethyl}phenylsulfamic acid;

4-{(*S*)-2-[4-(5-Chlorothiophen-2-yl)thiazol-2-yl]-2-[(*S*)-2-(methoxycarbonylamino)-3-phenylpropanamido]ethyl}phenylsulfamic acid;

4-{(*S*)-2-[(*S*)-2-(Ethoxycarbonylamino)-3-phenylpropanamido]-2-(4-ethylthiazol-2-yl)ethyl}phenylsulfamic acid;

4-{(*S*)-2-[(*S*)-2-(Methoxycarbonylamino)-3-phenylpropanamido]-2-(2-ethylthiazol-4-yl) ethyl}phenylsulfamic acid;

4-{(*S*)-2-[(*S*)-2-(Methoxycarbonylamino)-3-phenylpropanamido]-2-(2-methyl-thiazol-4-yl)ethyl}phenylsulfamic acid;

4-{(S)-2-(2-Ethylthiazole-4-yl)-2-[(S)-2-(methoxycarbonylamino)-3-phenylpropan-amido]ethyl}phenylsulfamic acid;

4-{(*S*)-2-(2-Isopropylthiazol-4-yl)-2-[(*S*)-2-(methoxycarbonylamino)-3-phenyl-propan-amido]ethyl}phenylsulfamic acid;

4-{(*S*)-2-(2-Cyclopropylthiazol-4-yl)-2-[(*S*)-2-(methoxycarbonylamino)-3-phenylpropanamido]ethyl}phenylsulfamic acid;

4-{(S)-2-{2-[(4-Chlorophenylsulfonyl)methyl]thiazol-4-yl}-2-[(S)-2-(methoxy-carbonyl)-3-phenylpropanamido]ethyl}phenylsulfamic acid;

4-{(S)-2-[2-(*tert*-Butylsulfonylmethyl)thiazol-4-yl]-2-[(S)-2-(methoxycarbonylamino)-3-phenylpropanamido]ethyl}phenylsulfamic acid;

4-{(*S*)-2-[(*S*)-2-(Methoxycarbonylamino)-3-phenylpropionamido]-2-(2-phenyl-thiazole-4-yl)ethyl}phenylsulfamic acid;

4-{(*S*)-2-[(*S*)-2-(Methoxycarbonylamino)-3-phenylpropanamido]-2-[2-(thiophen-2-yl)thiazol-4-yl]ethyl}phenylsulfamic acid;

4-{(*S*)-2-[2-(3-Chlorothiophen-2-yl)thiazol-4-yl]-2-[(*S*)-2-(methoxycarbonylamino)-3-phenylpropanamido]ethyl}phenylsulfamic acid;

4-{(*S*)-2-[(*S*)-2-(Methoxycarbonylamino)-3-phenylpropanamido]-2-[2-(3-methylthiophen-2-yl)thiazol-4-yl]ethyl}phenylsulfamic acid;

4-{[(*S*)-2-(2-(Furan-2-yl)thiazol-4-yl]-2-[(*S*)-2-(methoxycarbonylamino)-3-phenyl-propanamido]ethyl}phenylsulfamic acid;

4-{(*S*)-2-[(*S*)-2-(Methoxycarbonylamino)-3-phenylpropanamido]-2-[2-(2-methyl-thiazole-4-yl)thiazol-4yl]ethyl}phenylsulfamic acid;

4-{(*S*)-2-[(*S*)-2-(Methoxycarbonylamino)-3-phenylpropanamido]-2-(2-pyrazine-2-yl)thiazole-4-yl}phenylsulfamic acid;

4-{(*S*)-2-[(*S*)-2-(Methoxycarbonylamino)-3-phenylpropanamido]-2-[2-(6-methyl-pyridin-3-yl)thiazol-4-yl]ethyl}phenylsulfamic acid;

4-[(*S*)-2-((*S*)-2-Acetamido-3-phenylpropanamido)-2-(4-ethylthiazol-2-yl)ethyl]-phenylsulfamic acid ;

4-[(*S*)-2-((*S*)-2-Acetamido-3-phenylpropanamido)-2-(4-*tert*-butylthiazol-2-yl)ethyl]-phenylsulfamic acid;

4-{(*S*)-2-((*S*)-2-Acetamido-3-phenylpropanamido)-2-[4-(thiophen-3-yl)thiazol-2-yl]ethyl)phenylsulfamic acid;

4-{(*S*)-2-[(*S*)-2-(*tert*-Butoxycarbonyl)-3-methylbutanamido]-2-(4-ethylthiazol-2-yl)ethyl}phenylsulfamic acid;

(*S*)-4-{2-[2-(*tert*-Butoxycarbonyl)acetamide]-2-(4-ethylthiazol-2-yl)ethyl}phenyl-sulfamic acid;

(*S*)-4-{2-(4-Ethylthiazol-2-yl)-2-[2-(methoxycarbonyl)acetamido]ethyl}phenyl-sulfamic acid;

4-{(*S*)-2-(4-Ethylthiazol-2-yl)-2-[(*S*)-2-(methoxycarbonyl)-3-methylbutanamido]-ethyl}phenylsulfamic acid;

4-{(*S*)-2-[(*S*)-2-(*tert*-Butoxycarbonyl)-4-methylpentanamido]-2-(4-ethylthiazol-2-yl)ethyl}phenylsulfamic acid;

4-{(*S*)-2-(4-Ethylthiazol-2-yl)-2-[(*S*)-2-(methoxycarbonyl)-4-methylpentan-amido]ethyl}phenylsulfamic acid;

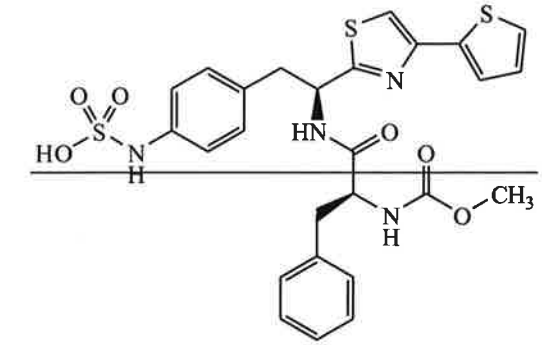
4-((*S*)-2-(4-Ethylthiazol-2-yl)-2-{(*S*)-2-[2-(methoxycarbonyl)acetamide]-3-phenylpropanamido}ethyl)phenylsulfamic acid;

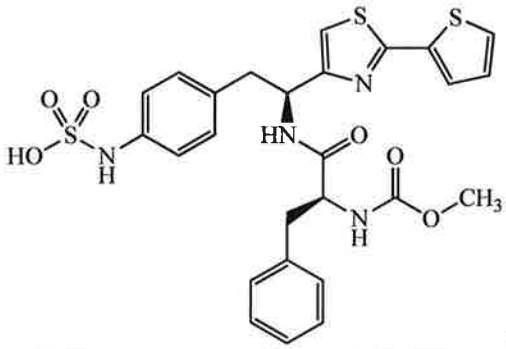
4-{(*S*)-2-[(*S*)-2-(*tert*-Butoxycarbonyl)-4-methylpentanamido]-2-[2-(thiophen-2-yl)thiazol-4-yl]ethyl}phenylsulfamic acid;

4-{(*S*)-2-[(*S*)-2-(Methoxycarbonyl)-4-methylpentanamido]-2-[2-(thiophen-2-yl)thiazol-4-yl]ethyl}phenylsulfamic acid; and

(*S*)-4-{2-[2-(*tert*-Butoxycarbonyl)acetamide]-2-(4-ethylthiazol-2-yl)ethyl}-phenylsulfamic acid.

4645. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein the compound has the formula:



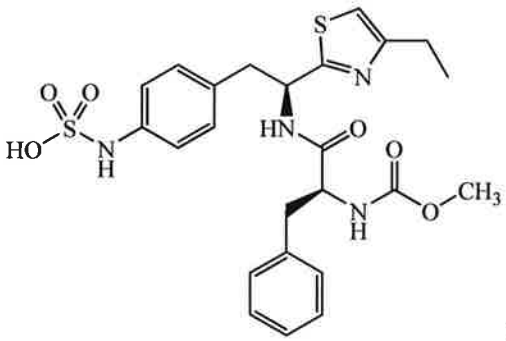


; and

pharmaceutically acceptable salts thereof.

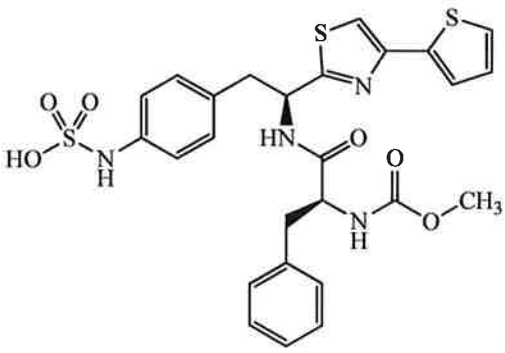
4746. The use according to any of Claims 1 to 7 ~~Claims 1 to 8~~, wherein the compound is chosen from a compound having the formula:

i)



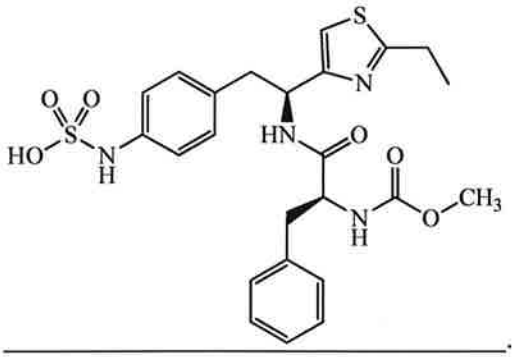
; ~~and~~

ii)



; and

iii)

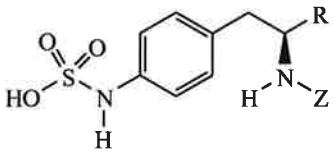


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4847. The use according to any of Claims 1 to 46 ~~Claims 1 to 47~~, wherein the compound is in the form of a salt of a cation chosen from ammonium, sodium, lithium, potassium, calcium, magnesium, bismuth, and lysine.

4948. A composition for treating cancer in a subject, comprising:

a) an effective amount of one or more compounds having the formula:



wherein R is a substituted or unsubstituted thiazolyl unit having the formula:

i) hydrogen;

ii) substituted or unsubstituted C_1-C_6 linear, C_3-C_6 branched, or C_3-C_6 cyclic alkyl;

iii) substituted or unsubstituted C_2-C_6 linear, C_3-C_6 branched, or C_3-C_6 cyclic alkenyl;

iv) substituted or unsubstituted C_2-C_6 linear or C_3-C_6 branched alkynyl;

v) substituted or unsubstituted C_6 or C_{10} aryl;

vi) substituted or unsubstituted C_1-C_9 heteroaryl;

vii) substituted or unsubstituted C_1-C_9 heterocyclic; or

viii) R^2 and R^3 can be taken together to form a saturated or unsaturated ring having from 5 to 7 atoms; wherein from 1 to 3 atoms can optionally be heteroatoms chosen from oxygen, nitrogen, and sulfur;

Z is a unit having the formula:

$$—(L)_n—R^1$$

R^1 is chosen from:

i) hydrogen;

ii) hydroxyl;

iii) amino;

iv) s substituted or unsubstituted C_1-C_6 linear, C_3-C_6 branched, or C_3-C_6 cyclic alkyl;

v) substituted or unsubstituted C_1-C_6 linear, C_3-C_6 branched, or C_3-C_6 cyclic alkoxy;

vi) substituted or unsubstituted C_6 or C_{10} aryl;

vii) substituted or unsubstituted C_1-C_9 heterocyclic rings; or

viii) substituted or unsubstituted C_1-C_9 heteroaryl rings;

L is a linking unit having the formula:

$$–[Q]_y[C(R^{5a}R^{5b})]_x[Q^1]_z[C(R^{6a}R^{6b})]_w–$$

Q and Q^1 are each independently:

i) –C(O)–;

ii) –NH–;

iii) –C(O)NH–;

iv) –NHC(O)–;

v) –NHC(O)NH–;

vi) –NHC(O)O–;

vii) –C(O)O–;

viii) –C(O)NHC(O)–;

ix) –O–;

x) –S–;

xi) $–SO_2–$;

xii) –C(=NH)–;

xiii) –C(=NH)NH–;

xiv) –NHC(=NH)–; or

xv) –NHC(=NH)NH–;

R^{5a} and R^{5b} are each independently:

i) hydrogen;

ii) hydroxy;

iii) halogen;

iv) substituted or unsubstituted C_1-C_6 linear or C_3-C_6 branched alkyl; or

v) a unit having the formula:

$$-[C(R^{7a}R^{7b})]_tR^8$$

R^{7a} and R^{7b} are each independently:

i) hydrogen; or

ii) substituted or unsubstituted C_1-C_6 linear, C_3-C_6 branched, or C_3-C_6 cyclic alkyl;

R^8 is:

i) hydrogen;

ii) substituted or unsubstituted C_1-C_6 linear, C_3-C_6 branched, or C_3-C_6 cyclic alkyl;

iii) substituted or unsubstituted C_6 or C_{10} aryl;

iv) substituted or unsubstituted C_1-C_9 heteroaryl; or

v) substituted or unsubstituted C_1-C_9 heterocyclic;

R^{6a} and R^{6b} are each independently:

i) hydrogen; or

ii) C_1-C_4 linear or C_3-C_4 branched alkyl;

the index n is 0 or 1; the indices t, w and x are each independently from 0 to 4; the indices y and z are each independently 0 or 1; or

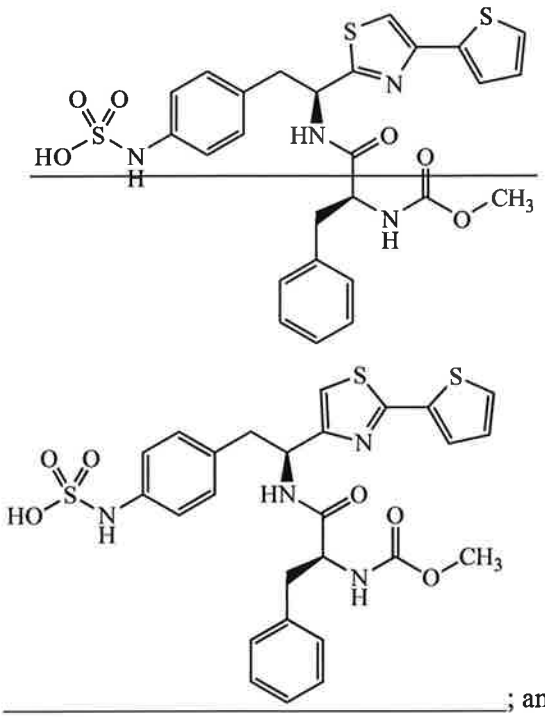
a pharmaceutically acceptable salt thereof; and

b) an effective amount of one or more chemotherapeutic agents;

wherein the one or more compounds and the chemotherapeutic agents can be administered together or in any order.

~~50~~49. A composition according to Claim ~~49~~48, wherein the chemotherapeutic agent is chosen from taxol, IL-2, gemcitabine, erlotinib, doxil, irinortecan, and bevacizumab.

~~51~~50. A composition according to Claim ~~49~~48, wherein the compound has the formula:



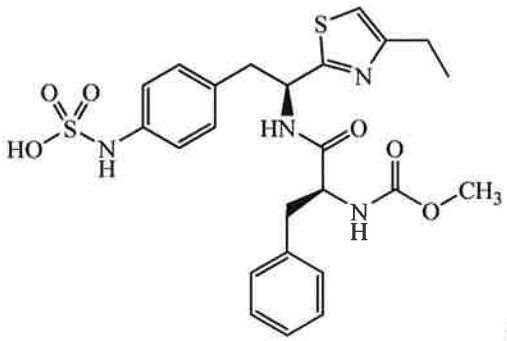
; and

pharmaceutically acceptable salts thereof.

~~52~~51. A composition according to Claim ~~49~~48, wherein the compound is in the form of a salt of a cation chosen from ammonium, sodium, lithium, potassium, calcium, magnesium, bismuth, and lysine.

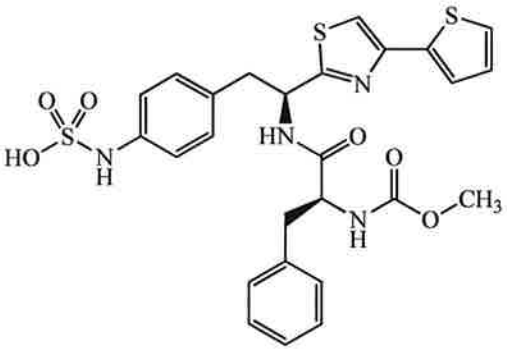
~~53~~52. A composition according to Claim ~~49~~48, wherein the compound is chosen from a compound having the formula:

i)



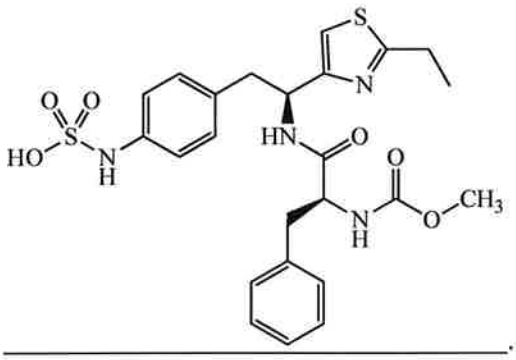
; ~~and~~

ii)



; and

iii)



.

5453. A composition according to any of Claims 49 48 to 5352, wherein the cancer is renal cell carcinoma, lung cancer, malignant melanoma, or pancreatic cancer.