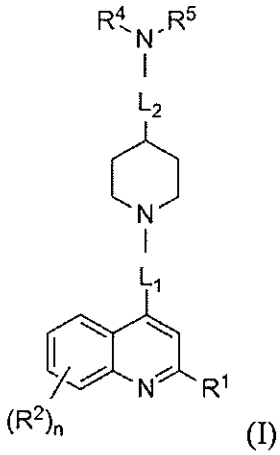
CLAIMS:

1. A compound of formula (I)



(I)

wherein

R^1 is selected from optionally substituted aryl;

R^2 is selected from Cl, F, I, Br, C_1-C_6 alkyl, C_1-C_6 alkyl substituted with one or more halogens, C_1-C_6 alkoxy, hydroxy, or nitro;

L^1 is selected from a bond or from optionally substituted C_1-C_{14}alkyl(-R^3), wherein R^3 is selected from H, optionally substituted C_1-C_8-alkyl, optionally substituted C_2-C_8-alkenyl, optionally substituted C_2-C_8-alkynyl, optionally substituted C_3-C_{12} cycloalkyl;

n is 0, 1, 2, 3 or 4;

L_2 is selected from a bond or from optionally substituted C_1-C_{14}alkyl(-R^3), wherein R^3 is defined as above;

R^4 and R^5 are independently selected from hydrogen, C_1-C_6 alkyl, cycloalkyl, phenyl, or benzyl, or CH_2-CH_2-Phenyl, or R^4 and R^5 are linked to form a heterocyclic group;

wherein the term "optionally substituted" means optionally substituted with one or more substituents independently selected from Cl, F, I, Br, C_1-C_6 alkyl, C_1-C_6 alkyl substituted with one or more halogens, C_1-C_6 alkoxy, hydroxy, cyano, or nitro;

and any pharmaceutically acceptable salt, or solvate thereof.

2. A compound according to claim 1 selected from:

2-phenyl-4-(4-*N*,*N*-diethylamino-piperidin-1-yl)quinoline (I-3);

7-chloro-2-phenyl-4-(4-*N*,*N*-diethylamino-piperidin-1-yl)quinoline (II-3);

2-phenyl-4-([1,4']-bipiperidin-1'-yl)quinoline (III-3);

2-phenyl-4-(4-*N*-*tert*-butylamino-piperidin-1-yl)quinoline (IV-1);

2-phenyl-4-[(4-morpholin-4-yl)piperidin-1yl]quinoline (V-1);

2-(2-naphtyl)-4-(4-*N*,*N*-diethylamino-piperidin-1-yl)quinoline (VI-5);

2-(4-bromo-phenyl)-7-chloro-4-(4-*N*,*N*-diethylamino-piperidin-1-yl)quinoline (VII-4);

2-(4-bromo-phenyl)-4-(4-*N*,*N*-diethylamino-piperidin-1-yl)quinoline (VIII-5);

2-(1,1'-biphenyl)-4-yl-4-(4-*N*,*N*-diethylamino-piperidin-1-yl)quinoline (IX-1);

2-(4-chloro-phenyl)-4-(4-*N*,*N*-diethylamino-piperidin-1-yl)quinoline (X-5);

2-(1,1'-biphenyl)-4-yl-7-chloro-4-(4-*N*,*N*-diethylamino-piperidin-1-yl)quinoline (XI-1);

2-(4-chloro-phenyl)-4-(4-*N*-*tert*-butylamino-piperidin-1-yl)quinoline (XII-3);

2-(4-methyl-phenyl)-4-(4-*N*-*tert*-butylamino-piperidin-1-yl)quinoline (XIII-7);

2-(3,4-dichloro-phenyl)-4-(4-*N*-*tert*-butylamino-piperidin-1-yl)quinoline (XIV-7);

2-(4-methoxy-phenyl)-4-(4-*N*-*tert*-butylamino-piperidin-1-yl)quinoline (XV-7);

7-Chloro-2-phenyl-4-{1-[4-(*N*,*N*-diethylamino)-piperidin-1-yl]-eth-1-yl}quinoline (XVI-3);

7-Chloro-2-phenyl-4-[4-(*N*,*N*-diethylamino)-piperidin-1-ylmethyl]quinoline (XVII-5);

2-phenyl-4-{1-[4-(*N*,*N*-diethylamino)-piperidin-1-yl]-eth-1-yl}quinoline (XIX-2);

2-phenyl-4-[4-(*N*,*N*-diethylamino)-piperidin-1-ylmethyl]quinoline (XX-4);

2-phenyl-4-{1-{4-[benzyl(phenethyl)amino]-piperidin-1-yl}-eth-1-yl}quinoline (XXI-3);

2-phenyl-4-{1-[(1.4'-bipiperidin)-1'-yl]-eth-1-yl}quinoline (XXII-3);

2-phenyl-4-{1-[4-(*tert*-butylamino)-piperidin-1-yl]-eth-1-yl}quinoline (XXIII-1);

2-(2-naphtyl)-4-{1-[4-(*N*,*N*-diethylamino)-piperidin-1-yl]-eth-1-yl}quinoline (XXIV-2);

2-phenyl-4-{2-[4-(*N*,*N*-diethylamino)-piperidin-1-yl]-propan-2-yl}quinoline trifluoroacetate salt (XXV-6).

7-chloro-2-phenyl-4-[4-(*N*,*N*-diethylaminomethyl)-piperidin-1-yl]quinoline (XXVI-3);

2-phenyl-4-[4-(*N*,*N*-diethylaminomethyl)-piperidin-1-yl)quinoline (XXVII-1);

2-phenyl-4-{1-[4-(morpholino)-piperidinyl]-eth-1-yl}quinoline (XLV-1);

3. A compound according to claim 1 selected from:

2-phenyl-4-(4-*N*,*N*-diethylamino-piperidin-1-yl)quinoline hydrochloride salt (I-4);

7-chloro-2-phenyl-4-(4-*N*,*N*-diethylamino-piperidin-1-yl)quinoline hydrochloride salt (II-4);

2-phenyl-4-([1,4']-bipiperidin-1'-yl)quinoline hydrochloride salt (III-4);

2-phenyl-4-(4-*N*-*tert*-butylamino-piperidin-1-yl)quinoline hydrochloride salt (IV-2);

2-phenyl-4-[(4-morpholin-4-yl)piperidin-1yl]quinoline hydrochloride salt (V-2);

2-(2-naphtyl)-4-(4-*N*,*N*-diethylamino-piperidin-1-yl)quinoline hydrochloride salt (VI-6);

2-(4-bromo-phenyl)-7-chloro-4-(4-*N*,*N*-diethylamino-piperidin-1-yl)quinoline hydrochloride salt (VII-5);

2-(4-bromo-phenyl)-4-(4-*N*,*N*-diethylamino-piperidin-1-yl)quinoline hydrochloride salt (VIII-6);

2-(1,1'-biphenyl)-4-yl-4-(4-*N*,*N*-diethylamino-piperidin-1-yl)quinoline hydrochloride salt (IX-2);

2-(4-chloro-phenyl)-4-(4-*N*,*N*-diethylamino-piperidin-1-yl)quinoline hydrochloride salt (X-6);

2-(1,1'-biphenyl)-4-yl-7-chloro-4-(4-*N*,*N*-diethylamino-piperidin-1-yl)quinoline hydrochloride salt (XI-2);

2-(4-chloro-phenyl)-4-(4-*N*-*tert*-butylamino-piperidin-1-yl)quinoline hydrochloride salt (XII-4);

2-(4-methyl-phenyl)-4-(4-*N*-*tert*-butylamino-piperidin-1-yl)quinoline hydrochloride salt (XIII-8);

2-(3,4-dichloro-phenyl)-4-(4-*N*-*tert*-butylamino-piperidin-1-yl)quinoline hydrochloride salt (XIV-8);

2-(4-methoxy-phenyl)-4-(4-*N*-*tert*-butylamino-piperidin-1-yl)quinoline *hydrochloride salt* (XV-8);

7-Chloro-2-phenyl-4-{1-[4-(*N*,*N*-diethylamino)-piperidin-1-yl]-eth-1-yl}quinoline hydrochloride salt (XVI-4);

7-Chloro-2-phenyl-4-[4-(*N*,*N*-diethylamino)-piperidin-1-ylmethyl]quinoline hydrochloride salt (XVII-6);

2-phenyl-4-{1-[4-(*N*,*N*-diethylamino)-piperidin-1-yl]-eth-1-yl}quinoline hydrochloride salt (XIX-3);

2-phenyl-4-[4-(*N*,*N*-diethylamino)-piperidin-1-ylmethyl]quinoline hydrochloride salt (XX-5);

2-phenyl-4-{1-{4-[benzyl(phenethyl)amino]-piperidin-1-yl}-eth-1-yl}quinoline hydrochloride salt (XXI-4);

2-phenyl-4-{1-[(1.4'-bipiperidin)-1'-yl]-eth-1-yl}quinoline hydrochloride salt (XXII-4);

2-phenyl-4-{1-[4-(*tert*-butylamino)-piperidin-1-yl]-eth-1-yl}quinoline hydrochloride salt (XXIII-2);

2-(2-naphtyl)-4-{1-[4-(*N*,*N*-diethylamino)-piperidin-1-yl]-eth-1-yl}quinoline hydrochloride salt (XXIV-3);

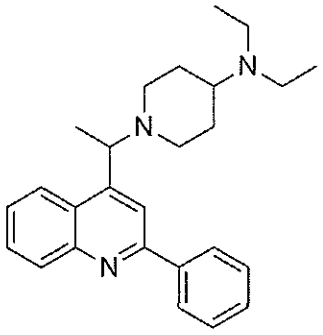
2-phenyl-4-{2-[4-(*N*,*N*-diethylamino)-piperidin-1-yl]-propan-2-yl}quinoline trifluoroacetate salt (XXV-6).

7-chloro-2-phenyl-4-[4-(*N*,*N*-diethylaminomethyl)-piperidin-1-yl]quinoline hydrochloride salt (XXVI-4);

2-phenyl-4-[4-(*N*,*N*-diethylaminomethyl)-piperidin-1-yl)quinoline hydrochloride salt (XXVII-2);

2-phenyl-4-{1-[4-(morpholino)-piperidinyl]-eth-1-yl}quinoline hydrochloride salt (XLV-1);

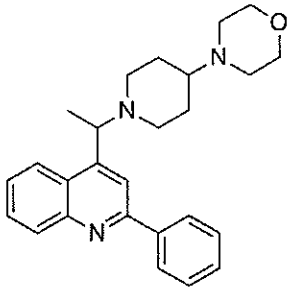
4. A compound according to claim 1 of formula (Ia) (XIX-2):



(Ia)

or a pharmaceutically acceptable salt, or solvate thereof.

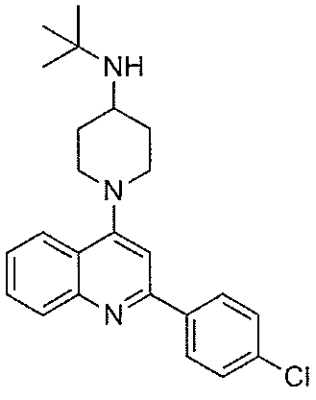
5. A compound according to claim 1 of formula (Ib) (XLV-1):



(Ib)

or a pharmaceutically acceptable salt, or solvate thereof.

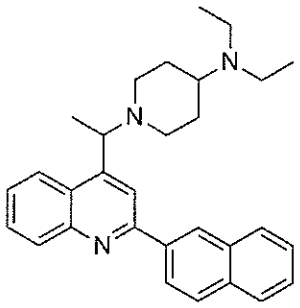
6. A compound according to claim 1 of formula (Ic) (XII-3):



(Ic)

or a pharmaceutically acceptable salt, or solvate thereof.

7. A compound according to claim 1 of formula (Id) (XXIV-2):

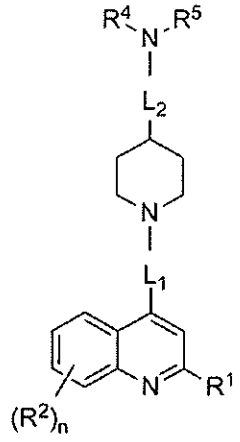


(1d)

or a pharmaceutically acceptable salt, or solvate thereof.

8. A pharmaceutical composition comprising a therapeutically effective amount of a compound according to any one of claims 1 to 7, or a pharmaceutically acceptable salt, or solvate thereof, and a pharmaceutically acceptable adjuvant, diluent or carrier.

9. A pharmaceutical composition comprising a therapeutically effective amount of a compound of formula (I)



(I)

wherein

L^1 is selected from a bond or from optionally substituted C_1-C_{14}alkyl(-R^3), wherein R^3 is as defined in claim 1;

L_2 is selected from a bond or from optionally substituted C_1-C_{14}alkyl(-R^3), wherein R^3 is as defined in claim 1;

And wherein R^1, R^2, n, R^4 and R^5 are defined as in claim 1;

And wherein the term "optionally substituted" has the same meaning as in claim 1;

further comprising in combination one or more anti-neoplastic agents.

10. A pharmaceutical composition according to any one of claims 8 and 9, wherein the therapeutically effective amount of the compound is formulated or co-formulated in nanoparticles.

11. The pharmaceutical composition according to claim 10, wherein the nanoparticles comprise a polymeric biodegradable composition.

12. The pharmaceutical composition according to claim 11, wherein the polymeric biodegradable composition is based on Poly (DL-Lactic-co-glycolic acid) having molecular weight from 7 to 240 kDa; or a copolymer of polylactic acid (PLA and polyglycolic acid (PGA) where the molecular ratio is between 95:5 and 50:50.

13. The pharmaceutical composition according to claim 10, wherein the nanoparticles comprise a lysosomal biodegradable composition.

14. The pharmaceutical composition according to claim 10, wherein the nanoparticles comprise a biocompatible polymer or copolymer.

15. The pharmaceutical composition according to any one of claims 10 to 14, wherein the nanoparticles are associated covalently or non-covalently with a polyethylene glycol (PEG).

16. The pharmaceutical composition according to any one of claims 10 to 15, wherein the nanoparticles have an average size of from about 80 to about 600 nm.

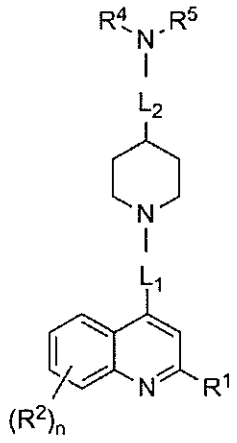
17. The pharmaceutical composition according to any one of claims 8 to 16, wherein the compound is associated with at least one therapeutically active anti-cancer agent.

18. The pharmaceutical composition according to any one of claims 8 to 17 which is suitable for oral-, parenteral-, ocular-, transdermal-, nasal-administration, or for inhalation.

19. A pharmaceutical composition according to claims 10, 11, and 14 to 18, wherein the nanoparticles comprise an item selected from PLGA nanoparticules, PLGA-PEG nanoparticles (block type AB, BA, ABA or BAB, where A = PLGA and B = PEG) and targeted nanoparticules

20. A pharmaceutical composition according to claims 19, wherein the nanoparticle is a targeted nanoparticle containing a signaling motif.

21. A pharmaceutical composition comprising a combination of a therapeutically effective amount of a compound of formula (I)



(I)

wherein

L^1 is selected from a bond or from optionally substituted C_1-C_{14}alkyl(-R^3), wherein R^3 is as defined as in claim 1;

L_2 is selected from a bond or from optionally substituted C_1-C_{14}alkyl(-R^3), wherein R^3 is as defined in claim 1;

And R^1, R^2, n, R^4 and R^5 are defined as in claim 1;

And wherein the term "optionally substituted" has the same meaning as in claim 1; and any pharmaceutically acceptable salt, or solvate thereof and a therapeutically effective amount of one or more anti-neoplastic agents, wherein the components

constituting said combination are for simultaneous, separate or sequential use in cancer therapy.

22. The pharmaceutical composition of claim 9 or claim 21, wherein the anti-neoplastic agent is selected from the group consisting of everolimus, chloroquine, hydroxychloroquine, trabectedin, abraxane, TLK 286, AV-299, DN-101, pazopanib, GSK690693, RTA 744, ON 0910.Na, AZD 6244 (ARRY-142886), AMN-107, TKI-258, GSK461364, AZD 1152, enzastaurin, vandetanib, ARQ-197, MK-0457, MLN8054, PHA-739358, R-763, AT-9263, pemetrexed, erlotinib. dasatanib, nilotinib, decatanib, panitumumab, amrubicin, oregovomab, Lep-etu, nolatrexed, azd2171, batabulin, ofatumumab, zanolimumab, edotecarin, tetrandrine, rubitecan, tesmilifene, oblimersen, ticilimumab, ipilimumab, gossypol, Bio 111, 131-I-TM-601, ALT-110, BIO 140, CC 8490, cilengitide, gimatecan. IL13-PE38QQR, TNO 1001, IPdR1 KRX-0402, lucanthone, LY 317615, neuradiab, vitespan, Rta 744, Sdx 102, talampanel, atrasentan, Xr 311, romidepsin, ADS-100380, sunitinib, 5-fluorouracil, vorinostat, etoposide, gemcitabine, doxorubicin, irinotecan, liposomal doxorubicin, 5'-deoxy-5-fluorouridine, vincristine, temozolomide, ZK-304709, seliciclib, PD0325901, AZD-6244, capecitabine, L-Glutamic acid, N-[4-[2-(2-amino-4,7-dihydro-4-oxo-1H-pyrrolo[2,3-d]pyrimidin-5-yl)ethyl]benzoyl]- disodium salt heptahydrate, camptothecin, PEG-labeled irinotecan, tamoxifen, toremifene citrate, anastrazole, exemestane, letrozole, DES(diethylstilbestrol), estradiol, estrogen, conjugated estrogen, bevacizumab, IMC-1C11, CHIR-258, 3-[5-(methylsulfonylpiperadinemethyl)-indolyl]-quinolone, vatalanib, AG-013736, AVE-0005, the acetate salt of [D-Ser(But)$_6$, Azgly$_{10}$](pyro-Glu-His-Trp-Ser-Tyr-D-Ser(But)-Leu-Arg-Pro-Azgly-NH_2 acetate [C59H84N18O14-(C2H4O2)x where x = 1 to 2.4], goserelin acetate, leuprolide acetate, triptorelin pamoate, medroxyprogesterone acetate, hydroxyprogesterone caproate, megestrol acetate, raloxifene, bicalutamide, flutamide, nilutamide, megestrol acetate, CP-724714; TAK-165, HKI-272, erlotinib, lapatanib, canertinib, ABX-EGF antibody, erbitux, EKB-569, PKI-166, GW-572016, lonafarnib, BMS-214662, tipifarnib; amifostine, NVP-LAQ824, suberoyl analide hydroxamic acid, valproic acid, trichostatin A,

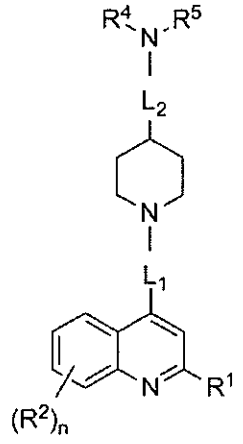
FK-228, SU11248, sorafenib, KRN951, aminoglutethimide, amsacrine, anagrelide, L-asparaginase, Bacillus Calmette-Guerin (BCG) vaccine, bleomycin, buserelin, busulfan, carboplatin, carmustine, chlorambucil, cisplatin, cladribine, clodronate, cyproterone, cytarabine, dacarbazine, dactinomycin, daunorubicin, diethylstilbestrol, epirubicin, fludarabine, fludrocortisone, fluoxymesterone, flutamide, gemcitabine, gleevec, hydroxyurea, idarubicin, ifosfamide, imatinib, leuprolide, levamisole, lomustine, mechlorethamine, melphalan, 6-mercaptopurine, mesna, methotrexate, mitomycin, mitotane, mitoxantrone, nilutamide, octreotide, oxaliplatin, pamidronate, pentostatin, plicamycin, porfimer, procarbazine, raltitrexed, rituximab, streptozocin, teniposide, testosterone, thalidomide, thioguanine, thiotepa, tretinoin, vindesine, 13-cis-retinoic acid, phenylalanine mustard, uracil mustard, estramustine, altretamine, floxuridine, 5-deoxyuridine, cytosine arabinoside, 6-mecaptopurine, deoxycoformycin, calcitriol, valrubicin, mithramycin, vinblastine, vinorelbine, topotecan, razoxin, marimastat, COL-3, neovastat, BMS-275291, squalamine, endostatin, SU5416, SU6668, EMD121974, interleukin-12, 1M862, angiostatin, vitaxin, droloxifene, idoxyfene, spironolactone, finasteride, cimitidine, trastuzumab, denileukin diftitox,gefitinib, bortezimib, paclitaxel, irinotecan, topotecan, doxorubicin, docetaxel, vinorelbine, bevacizumab (monoclonal antibody) and erbitux, cremophor-free paclitaxel, epithilone B, BMS-247550, BMS-310705, droloxifene, 4-hydroxytamoxifen, pipendoxifene, ERA-923, arzoxifene, fulvestrant, acolbifene, lasofoxifene, idoxifene, TSE-424, HMR-3339, ZK186619, PTK787/ZK 222584, VX-745, PD 184352, rapamycin, 40-O-(2-hydroxyethyl)-rapamycin, temsirolimus, AP-23573, RAD001, ABT-578, BC-210, LY294002, LY292223, LY292696, LY293684, LY293646, wortmannin, ZM336372, L-779,450, PEG-filgrastim, darbepoetin, erythropoietin, granulocyte colony-stimulating factor, zolendronate, prednisone, cetuximab, granulocyte macrophage colony-stimulating factor, histrelin, pegylated interferon alfa-2a, interferon alfa- 2a, pegylated interferon alfa-2b, interferon alfa-2b, azacitidine, PEG-L-asparaginase, lenalidomide, gemtuzumab, hydrocortisone, interleukin-11, dexrazoxane, alemtuzumab, all-transretinoic acid, ketoconazole, interleukin-2, megestrol, nitrogen mustard, methylprednisolone, ibritumomab tiuxetan, androgens, decitabine, hexamethylmelamine, bexarotene, tositumomab,

arsenic trioxide, cortisone, editronate, mitotane, cyclosporine, liposomal daunorubicin, Edwina-asparaginase, strontium 89, casopitant, netupitant, an NK-1 receptor antagonists, palonosetron, aprepitant,, diphenhydramine, hydroxyzine, metoclopramide, lorazepam, alprazolam, haloperidol, droperidol, dronabinol, dexamethasone, methylprednisolone, prochlorperazine, granisetron, ondansetron, dolasetron, tropisetron, sspegfilgrastim, epoetin alfa and darbepoetin alfa, ipilumumab, vemurafenib, FLT-3 inhibitor, a VEGFR inhibitor, an EGFR TK inhibitor, an aurora kinase inhibitor, a PIK-1 modulator, a mTOR inhibitor, a Bcl-2 inhibitor, an HDAC inhibitor, a c-MET inhibitor, a PARP inhibitor, a Cdk inhibitor, an EGFR TK inhibitor, an IGFR-TK inhibitor, an anti-HGF antibody, a PI3 kinase inhibitors, an AKT inhibitor, a JAK/STAT inhibitor, a checkpoint-1 or 2 inhibitor, a focal adhesion kinase inhibitor, a Map kinase kinase (mek) inhibitor, a VEGF trap antibody, and mixtures thereof.

23. The pharmaceutical composition according to any one of claims 8 to 22, which is suitable for slow- or sustained-release.

24. A compound according to any one of claims 1 to 7, for use in therapy.

25. A compound of formula (I)



(I)

wherein

L^1 is selected from a bond or from optionally substituted C_1-C_{14}alkyl(-R^3), wherein R^3 is as defined in claim 1,

L_2 is selected from a bond or from optionally substituted C_1-C_{14}alkyl(-R^3), wherein R^3 is as defined in claim 1;

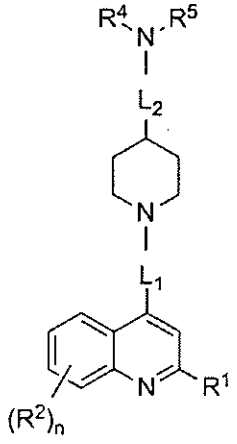
And wherein R^1, R^2, n, R^4 and R^5 are defined as in claim 1;

And wherein the term "optionally substituted" has the same meaning as in claim 1;

and any pharmaceutically acceptable salt, or solvate thereof, for use as a therapeutically active substance for the treatment and/or prevention of a proliferative and/or neoplastic disease.

26. A compound for use according to claim 25, wherein the proliferative and/or neoplastic disease is selected from the group consisting of: carcinoma; cancer of the esophagus, head, kidney, liver, lung, nasopharyngeal, neck, ovary, pancreas, prostate, or stomach; a leukemia (e.g. acute myelogenous leukemia, acute lymphocytic leukemia, acute promyelocytic leukemia (APL), acute T-cell lymphoblastic leukemia, adult T-cell leukemia, basophilic leukemia, eosinophilic leukemia, granulocytic leukemia, hairy cell leukemia, leukopenic leukemia, lymphatic leukemia, lymphoblastic leukemia, lymphocytic leukemia, megakaryocytic leukemia, micromyeloblastic leukemia, monocytic leukemia, neutrophilic leukemia and stem cell leukemia); a malignant lymphoma, a malignant melanoma; myeloproliferative diseases; a sarcoma; a tumor of the central nervous system; a germ-line tumor; testicular cancer; thyroid cancer; astrocytoma; colon cancer, melanoma, and a mixed type of neoplasia.

27. A therapeutically active amount of a compound of formula (I)



(I)

wherein

L^1 is selected from a bond or from optionally substituted C_1-C_{14}alkyl(-R^3 wherein R^3 is as defined in claim 1;

L_2 is selected from a bond or from optionally substituted C_1-C_{14}alkyl(-R^3), wherein R^3 is as defined in claim 1;

And wherein R^1, R^2, n, R^4 and R^5 are defined as in claim 1;

And wherein the term "optionally substituted" has the same meaning as in claim 1; and any pharmaceutically acceptable salt, or solvate thereof, for use as a therapeutically active substance for inhibiting the growth or differentiation of a Cancer Stem Cell (CSC), a tumor initiating cell, a mesenchymal cancerous cell.

28. Use of a pharmaceutical composition according to any one of claims 8 to 23, in the manufacture of a medicament for inhibiting the growth or differentiation of a Cancer Stem Cell (CSC), a tumor initiating cell, or a mesenchymal cancerous cell.