

citric, tartaric, lactic, benzoic, salicylic, glutamaic, aspartic, p-toluenesulfonic, benzenesulfonic, methanesulfonic, ethanesulfonic, naphthalenesulfonic such as 2-naphthalenesulfonic, or hexanoic acid), optionally in a suitable solvent such as an organic solvent, to give the salt which is usually isolated for example by crystallisation and filtration or by evaporation followed by trituration. A pharmaceutically acceptable acid addition salt of a compound of formula (I) can comprise or be for example a hydrobromide, hydrochloride, sulfate, nitrate, phosphate, succinate, maleate, acetate, propionate, fumarate, citrate, tartrate, lactate, benzoate, salicylate, glutamate, aspartate, p-toluenesulfonate, benzenesulfonate, methanesulfonate, ethanesulfonate, naphthalenesulfonate (e.g. 2-naphthalenesulfonate) or hexanoate salt. In one embodiment a pharmaceutically acceptable acid addition salt of a compound of formula (I) can comprise or be a hydrochloride, sulfate, maleate, fumarate, citrate, p-toluenesulfonate, benzenesulfonate or methanesulfonate salt. In a particular embodiment there is provided a compound of formula (IA) in the form of a hydrochloride salt.

Other non-pharmaceutically acceptable salts, e.g. formates, oxalates or trifluoroacetates, may be used, for example in the isolation of the compounds of formula (I), and are included within the scope of this invention.

The invention includes within its scope all possible stoichiometric and non-stoichiometric forms of the salts of the compounds of formula (I).

It will be appreciated that many organic compounds can form complexes with solvents in which they are reacted or from which they are precipitated or crystallized. These complexes are known as "solvates". For example, a complex with water is known as a "hydrate". Solvents with high boiling points and/or capable of forming hydrogen bonds such as water, xylene, *N*-methyl pyrrolidinone, methanol and ethanol may be used to form solvates. Methods for identification of solvates include, but are not limited to, NMR and microanalysis. Solvates of the compounds of formula (I) are within the scope of the invention.

The invention includes within its scope all possible stoichiometric and non-stoichiometric forms of the solvates of the compounds of formula (I).

The invention encompasses all prodrugs, of the compound of formula (I) or a pharmaceutically acceptable salt thereof, which upon administration to the recipient is capable of providing (directly or indirectly) the compound of formula (I) or a pharmaceutically acceptable salt thereof, or an active metabolite or residue thereof. Such derivatives are recognizable to those skilled in the art, without undue experimentation. Nevertheless, reference is made to the teaching of Burger's Medicinal Chemistry and Drug Discovery, 5th Edition, Vol 1: Principles and Practice, which is incorporated herein by reference to the extent of teaching such derivatives.

The compounds of formula (I) may be in crystalline or amorphous form. Furthermore, some of the crystalline forms of the compounds of formula (I) may exist as polymorphs, which are included within the scope of the present invention. Polymorphic forms of compounds of formula (I) may be characterized and differentiated using a number of conventional analytical techniques, including, but not limited to, X-ray powder diffraction (XRPD) patterns, infrared (IR) spectra, Raman spectra, differential scanning

as ointments, creams, suspensions, emulsions, lotions, powders, solutions, pastes, gels, foams, sprays, aerosols or oils. Such pharmaceutical compositions may include conventional additives which include, but are not limited to, preservatives, solvents to assist drug penetration, co-solvents, emollients, propellants, viscosity modifying agents (gelling agents), surfactants and carriers. In one embodiment there is provided a pharmaceutical composition adapted for topical administration which comprises between 0.01 – 10%, or between 0.01 – 1% of the compound of formula (I), or a pharmaceutically acceptable salt thereof, by weight of the composition.

For treatments of the eye or other external tissues, for example mouth and skin, the compositions are preferably applied as a topical ointment, cream, gel, spray or foam. When formulated in an ointment, the active ingredient may be employed with either a paraffinic or a water-miscible ointment base. Alternatively, the active ingredient may be formulated in a cream with an oil-in-water cream base or a water-in-oil base.

Pharmaceutical compositions adapted for topical administrations to the eye include eye drops wherein the active ingredient is dissolved or suspended in a suitable carrier, especially an aqueous solvent. Compositions to be administered to the eye will have ophthalmically compatible pH and osmolality. One or more ophthalmically acceptable pH adjusting agents and/or buffering agents can be included in a composition of the invention, including acids such as acetic, boric, citric, lactic, phosphoric and hydrochloric acids; bases such as sodium hydroxide, sodium phosphate, sodium borate, sodium citrate, sodium acetate, and sodium lactate; and buffers such as citrate/dextrose, sodium bicarbonate and ammonium chloride. Such acids, bases, and buffers can be included in an amount required to maintain pH of the composition in an ophthalmically acceptable range. One or more ophthalmically acceptable salts can be included in the composition in an amount sufficient to bring osmolality of the composition into an ophthalmically acceptable range. Such salts include those having sodium, potassium or ammonium cations and chloride, citrate, ascorbate, borate, phosphate, bicarbonate, sulfate, thiosulfate or bisulfite anions.

The ocular delivery device may be designed for the controlled release of one or more therapeutic agents with multiple defined release rates and sustained dose kinetics and permeability.

Pharmaceutical compositions for ocular delivery also include in situ gellable aqueous composition. Such a composition comprises a gelling agent in a concentration effective to promote gelling upon contact with the eye or with lacrimal fluid. Suitable gelling agents include but are not limited to thermosetting polymers. The term "in situ gellable" as used herein includes not only liquids of low viscosity that form gels upon contact with the eye or with lacrimal fluid, but also includes more viscous liquids such as semi-fluid and thixotropic gels that exhibit substantially increased viscosity or gel stiffness upon administration to the eye. See, for example, Ludwig (2005) Adv. Drug Deliv. Rev. 3;57:1595-639, herein incorporated by reference for purposes of its teachings of examples of polymers for use in ocular drug delivery.

Dosage forms for nasal or inhaled administration may conveniently be formulated as aerosols, solutions, suspensions, gels or dry powders.

The compound of Example 2 was also tested in accordance with an analogous procedure using 96 well plates along with appropriate modifications to volumes and concentrations that would be apparent to those skilled in the art. The compound of Example 2 was tested and found to have the gIC_{50} as shown in Table 3.

5 Table 3

Cell line type	n (number of lines)	gIC_{50}
Acute monocytic leukemia	1	123 nM
Acute promyelocytic leukemia	1	141 nM
Cutaneous T cell lymphoma	1	162 nM
Burkitt's lymphoma	3	181 – 807 nM
Chronic myeloid leukemia	1	776 nM
Breast cancer (ductal)	1	537 nM
Ovarian carcinoma	1	707 nM

10 These data demonstrate that the compound of Example 2 tested in the above assay inhibited cell growth in a panel of oncology cell lines and may therefore have utility in the treatment of one or more cancers.

15 ~~All publications, including but not limited to patents and patent applications, cited in this specification are herein incorporated by reference as if each individual publication were specifically and individually indicated to be incorporated by reference herein as though fully set forth.~~

4. A compound according to any one of claims 1 – 3 or a pharmaceutically acceptable salt thereof.

5. A pharmaceutical composition which comprises a compound or a pharmaceutically acceptable salt thereof as defined in claim 4 and one or more pharmaceutically acceptable carriers, diluents or excipients.

6. A combination pharmaceutical product comprising a compound or a pharmaceutically acceptable salt thereof as defined in claim 4 together with one or more other therapeutically active agents.

7. A compound or a pharmaceutically acceptable salt thereof as defined in claim 4 for use in therapy.

8. A compound or a pharmaceutically acceptable salt thereof as defined in claim 4 for use in the treatment of diseases or conditions for which a bromodomain inhibitor is indicated.

9. A compound for use according to claim 8, wherein the disease or condition is a chronic autoimmune and/or inflammatory condition.

10. A compound for use according to claim 8, wherein the disease or condition is cancer.

~~11. The use of a compound or a pharmaceutically acceptable salt thereof as defined in claim 4 in the manufacture of a medicament for the treatment of diseases or conditions for which a bromodomain inhibitor is indicated.~~

~~12. The use according to claim 11, wherein the disease or condition is a chronic autoimmune and/or inflammatory condition.~~

~~13. The use according to claim 11, wherein the disease or condition is cancer.~~

~~14. The use according to any one of claims 11 – 13 in which the subject is a human.~~

11. A compound for use according to claim 9 in which the cancer is selected from hematological, epithelial including lung, breast and colon carcinomas, midline carcinomas, mesenchymal, hepatic, renal and neurological tumours.

12. The use of a compound or a pharmaceutically acceptable salt thereof as defined in claim 4 in the manufacture of a medicament for the treatment of cancer or a chronic autoimmune and/or inflammatory condition.

13. The use of a compound or a pharmaceutically acceptable salt thereof as defined in claim 4 in the manufacture of a medicament for the treatment of cancer selected from hemotological, epithelial including lung, breast and colon carcinomas, midline carcinomas, mesenchymal, hepatic, renal and neurological tumours.