There is a need for leukemia selective chemotherapeutic agents that exhibit per se therapeutic activity, and improved efficacy in the treatment of a leukemia patient with a specific type of leukemia. The GSK3β inhibitor 7-(2,5-dihydro-4-imidazo[1,2-a]-pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinyl-carbonyl)pyrrolo[3,2,1-jk][1,4]benzodiazepine evidences selectivity, per se therapeutic activity, and improved efficacy over SB216763 and GSK3-IX, against several types of leukemia.

One embodiment~~aspect~~ of the disclosure~~invention~~ provides a method of treating a patient suffering from mixed lineage leukemia; translocated mixed lineage leukemia; translocated mixed lineage leukemia based acute myelogenous leukemia; translocated mixed lineage leukemia based acute lymphoid leukemia; a non-MLL based chronic myeloproliferative disorder; or a non-MLL based acute lymphoid leukemia comprising administering to a leukemia patient in need of such treatment an effective amount of 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof.

A second embodiment~~aspect~~ of the disclosure~~invention~~ provides a method of treating a patient suffering from mixed lineage leukemia; translocated mixed lineage leukemia; translocated mixed lineage leukemia based acute myelogenous leukemia; or translocated mixed lineage leukemia based acute lymphoid leukemia comprising administering to a leukemia patient in need of such treatment an effective amount of 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof.

A third embodiment~~aspect~~ of the disclosure~~invention~~ provides a method of treating a patient suffering from mixed lineage leukemia comprising administering to a leukemia patient in need of such treatment an effective amount of 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof.

A fourth embodiment~~aspect~~ of the disclosure~~invention~~ provides a method of treating a patient suffering from translocated mixed lineage leukemia comprising administering to a leukemia patient

in need of such treatment an effective amount of 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof.

A fifth embodimentaspect of the disclosureinvention provides a method of treating a patient suffering from translocated mixed lineage leukemia based acute myelogenous leukemia comprising administering to a leukemia patient in need of such treatment an effective amount of 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof.

A sixth embodimentaspect of the disclosureinvention provides a method of treating a patient suffering from translocated mixed lineage leukemia based acute lymphoid leukemia comprising administering to a leukemia patient in need of such treatment an effective amount of 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof.

A seventh embodimentaspect of the disclosureinvention provides a method of treating a patient suffering from a non-MLL based chronic myeloproliferative disorder comprising administering to a leukemia patient in need of such treatment an effective amount of 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof.

An eighth embodimentaspect of the disclosureinvention provides a method of treating a patient suffering from non-MLL based acute myelogenous leukemia; erythroleukemia; or chronic myelogenous leukemia comprising administering to a leukemia patient in need of such treatment an effective amount of 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof.

A ninth embodimentaspect of the disclosureinvention provides a method of treating a patient suffering from non-MLL based erythroleukemia comprising administering to a leukemia patient in need of such treatment an effective amount of 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-

pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof.

A tenth embodimentaspect of the disclosureinvention provides a method of treating a patient suffering from non-MLL based chronic myelogenous leukemia comprising administering to a leukemia patient in need of such treatment an effective amount of 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof.

An eleventh embodimentaspect of the disclosureinvention provides a method of treating a patient suffering from non-MLL based acute myelogenous leukemia comprising administering to a leukemia patient in need of such treatment an effective amount of 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof.

A twelfth embodimentaspect of the disclosureinvention provides a method of treating a patient suffering from non-MLL based acute lymphoid leukemia comprising administering to a patient in need of such treatment an effective amount of 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof.

A thirteenth embodimentaspect of the disclosureinvention provides a method of treating a patient suffering from a non-MLL based JAK2 (+) chronic myeloproliferative disorder comprising administering to a leukemia patient in need of such treatment an effective amount of 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof.

A fourteenth embodimentaspect of the disclosureinvention provides a method of treating a patient suffering from non-MLL based Philadelphia positive chronic myelogenous leukemia comprising administering to a patient in need of such treatment an effective amount of 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof.

In one aspect, there is~~A fifteenth aspect of the invention~~ provided~~s~~ the use of 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof in~~for~~ the preparation of a medicament for treating~~the treatment of~~ mixed lineage leukemia; translocated mixed lineage leukemia; translocated mixed lineage leukemia based acute myelogenous leukemia; translocated mixed lineage leukemia based acute lymphoid leukemia; a non-MLL based chronic myeloproliferative disorder or a non-MLL based acute lymphoid leukemia.

A fifteenth~~sixteenth~~ embodiment~~aspect~~ of the disclosure~~invention~~ provides the use of 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof for the preparation of a medicament for the treatment of mixed lineage leukemia; translocated mixed lineage leukemia; translocated mixed lineage leukemia based acute myelogenous leukemia; or translocated mixed lineage leukemia based acute lymphoid leukemia.

A sixteenth~~eventeenth~~ embodiment~~aspect~~ of the disclosure~~invention~~ provides the use of 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof for the preparation of a medicament for the treatment of mixed lineage leukemia.

A seventeenth~~An eighteenth~~ embodiment~~aspect~~ of the disclosure~~invention~~ provides the use of 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof for the preparation of a medicament for the treatment of translocated mixed lineage leukemia.

An eighteenth~~A nineteenth~~ embodiment~~aspect~~ of the disclosure~~invention~~ provides the use of 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof for the preparation of a medicament for the treatment of translocated mixed lineage leukemia based acute myelogenous leukemia.

A nineteenthtwentieth embodimentaspect of the disclosureinvention provides the use of 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof for the preparation of a medicament for the treatment of translocated mixed lineage leukemia based acute lymphoid leukemia.

A twentieth embodimenttwenty-first aspect of the disclosureinvention provides the use of 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof for the preparation of a medicament for the treatment of a non-MLL based chronic myeloproliferative disorder.

A twenty-first embodimentsecond aspect of the disclosureinvention provides the use of 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof for the preparation of a medicament for the treatment of non-MLL based acute myelogenous leukemia; erythroleukemia; or chronic myelogenous leukemia

A twenty-second embodimentthird aspect of the disclosureinvention provides the use of 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof for the preparation of a medicament for the treatment of non-MLL based erythroleukemia.

A twenty-third embodimentfourth aspect of the disclosureinvention provides the use of 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof for the preparation of a medicament for the treatment of non-MLL based chronic myelogenous leukemia.

A twenty-fourthfifth aspect embodiment of the disclosureinvention provides the use of 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof for the preparation of a medicament for the treatment of non-MLL based acute myelogenous leukemia.

A twenty-fifth~~sixth~~ embodiment~~aspect~~ of the disclosure~~invention~~ provides the use of 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof for the preparation of a medicament for the treatment of a non-MLL based JAK2 (+) chronic myeloproliferative disorder.

A twenty-sixth~~seventh~~ embodiment~~aspect~~ of the disclosure~~invention~~ provides the use of 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof for the preparation of a medicament for the treatment of non-MLL based Philadelphia positive chronic myelogenous leukemia.

A twenty-seventh~~eighth~~ embodiment~~aspect~~ of the disclosure~~invention~~ provides the use of 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof for the preparation of a medicament for the treatment of non-MLL based acute lymphoid leukemia.

A twenty-eighth~~ninth~~ embodiment~~aspect~~ of the disclosure~~invention~~ provides a compound 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine or a pharmaceutically acceptable salt or solvate thereof, for use in the treatment of mixed lineage leukemia; translocated mixed lineage leukemia; translocated mixed lineage leukemia based acute myelogenous leukemia; translocated mixed lineage leukemia based acute lymphoid leukemia; a non-MLL based chronic myeloproliferative disorder; or a non-MLL based acute lymphoid leukemia. In a particular embodiment, the leukemia is translocated mixed lineage leukemia based acute myelogenous leukemia; translocated mixed lineage leukemia based acute lymphoid leukemia; non-MLL based chronic myeloproliferative disorder selected from non-MLL based acute myelogenous leukemia, erythroleukemia, or chronic myelogenous leukemia; non-MLL based acute myelogenous leukemia; or non-MLL based chronic myelogenous leukemia.

The compound 7-(2,5-dihydro-4-imidazo[1,2-a]pyridine-3-yl-2,5-dioxo-1H-pyrrol-3-yl)-9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinyl-carbonyl)-pyrrolo[3,2,1-jk][1,4]benzodiazepine is taught to be an inhibitor of GSK-3β in WO 03/076442, where it is referred to as 3-(9-fluoro-6-(piperidin-1-yl)carbonyl)-6,7-dihydro-6H-[1,4]diazepino-