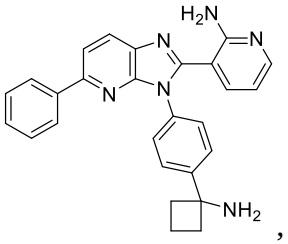
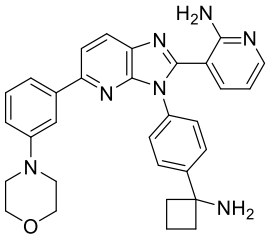
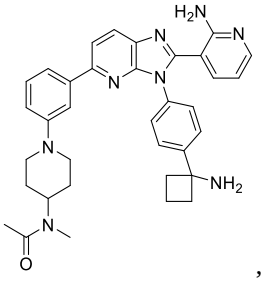
[0005] Accordingly, there is a need for pharmaceutical combinations and methods for modulating various genes and signaling pathways (*e.g.*, the AKT proteins), and methods for treating proliferation disorders, including cancer. The present application addresses these needs.

SUMMARY

[0006] In one aspect, the present application provides a pharmaceutical composition comprising a therapeutically effective amount of at least one of



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Compound 1 Compound 2 Compound 3

or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof, and at least one second therapeutic agent or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof.

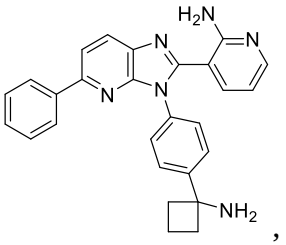
[0007] The present application provides a kit comprising a therapeutically effective amount of at least one of Compound 1, Compound 2, and Compound 3, or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof, and at least one second therapeutic agent or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof.

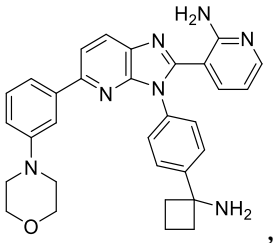
[0008] The present application provides a pharmaceutical package comprising a therapeutically effective amount of at least one of Compound 1, Compound 2, and Compound 3, or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof, and at least one second therapeutic agent or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof.

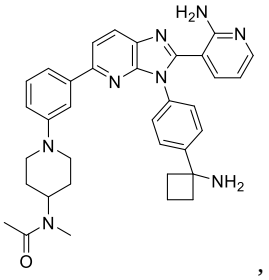
[0009] The present application provides a method of treating or preventing a cell proliferative disorder, comprising administering to a subject in need thereof a therapeutically effective amount of at least one of Compound 1, Compound 2, and Compound 3, or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof, and at least one second therapeutic agent or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof, wherein the cell proliferative disorder is treated or prevented.

[00010] The present application provides a method of treating or preventing a cell proliferative disorder, comprising administering to a subject in need thereof a therapeutically effective amount of a composition comprising at least one of Compound 1, Compound 2, and Compound 3, or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof, and at least one second therapeutic agent or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof, wherein the cell proliferative disorder is treated or prevented.

[00010a] In another aspect, the present application relaets to use of at least one of



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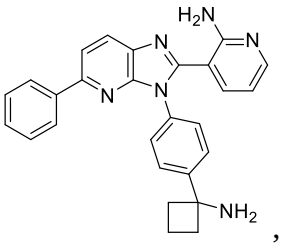
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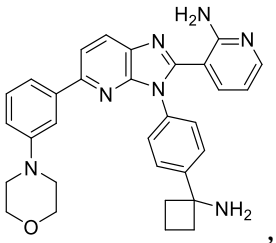
Compound 1 Compound 2 Compound 3

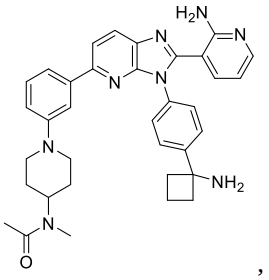
or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof,

in combination with at least one second therapeutic agent or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof, in the manufacture of a medicament for treating a cell proliferative disorder.

[00010b] In another aspect, the present application relates to a compound of



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Compound 1 Compound 2 Compound 3

or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof, for use

in combination with at least one second therapeutic agent or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof, in treating or preventing a cell proliferative disorder.

[00011] The cell proliferative disorder can be the result of a mutation in at least one of AKT, PIK3CA, PTEN, androgen receptor, and estrogen receptor. The cell proliferative disorder can be cancer. The cancer can be lung cancer, small cell lung cancer, non-small cell lung cancer, colon cancer, breast cancer, pancreatic cancer, prostate cancer, anal cancer, renal cancer, cervical cancer, brain cancer, gastric/stomach cancer, head and neck cancer, thyroid

cancer, bladder cancer, endometrial cancer, uterine cancer, intestinal cancer, hepatic cancer, leukemia, lymphoma, T-cell lymphoblastic leukemia, primary effusion lymphoma, chronic myelogenous leukemia, melanoma, Merkel cell cancer, ovarian cancer, alveolar soft part sarcoma (ASPS), clear cell sarcoma (CCS), Paget's disease, rhabdomysarcoma, angiosarcoma, cholangiocarcinoma, or hepatocellular carcinoma. The cancer can be endometrial cancer, ovarian cancer, primary effusion lymphoma, T-cell lymphoblastic leukemia, rhabdomysarcoma, Paget's disease, angiosarcoma, pancreatic endocrine tumor, anal squamous cell carcinoma, Merkel cell cancer, hormone receptor positive breast cancer or luminal breast cancer, head and neck squamous cell carcinoma, lung squamous cell carcinoma, gastric/stomach cancer, or thyroid cancer. In some embodiments, the cancer is a solid tumor. In some embodiments, the cancer is colon cancer, prostate cancer, breast cancer, endometrial cancer, head and neck cancer, or osteosarcoma.

[00012] The cell proliferative disorder can be a non-cancer condition, disease, or disorder. The non-cancer condition, disease or disorder can be pituitary adenoma, leishmaniasis, skin-related hyperproliferative disorders, psoriasis, eczema, hyperpigmentation disorders, eye-related hyperproliferative disorders, age-related macular degeneration, Herpes simplex virus, PIK3CA-related overgrowth spectrum (PROS), Proteus syndrome macrodactyly syndrome, Harlequin ichthyosis, CLOVES syndrome, atopic dermatitis, LEOPARD syndrome, systemic sclerosis, Spinocerebullar ataxia type 1, fibroadipose hyperplasia, hemihyperplasia-multiple lipomatosis syndrome, megalencephaly, rare hypoglycemia, Klippel-Trenaunay syndrome, harmatoma, Cowden syndrome, or overgrowth-hyperglycemia. The cell proliferative disorder can be pituitary adenoma, Proteus syndrome, fibroadipose hyperplasia, CLOVES syndrome, macrodactyly syndrome, Harlequin