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(54) Title: SMOOTHENED ANTAGONISM FOR THE TREATMENT OF HEDGEHOG PATHWAY-RELATED DISORDERS

(57) Abstract: The invention provides methods for modulating, e.g., antagonizing, the activity of the Hedgehog signaling pathway, and for treating Hedgehog related disorders such as cancers (e.g., medulloblastoma). In particular, the invention provides methods for inhibiting aberrant growth states resulting from phenotypes such as Ptch Io ss-of- function, Hedgehog gain-of- function, smoothened gain-of- function or GIi gain-of-function by administering to a mammal combinations of Smoothened inhibitors (e.g., a compound of Formula I, Formula II, or Formula III, or any of the compounds listed herein or incorporated by reference) and cholesterol biosynthesis pathway inhibitors (e.g., statins), GIi inhibitors, and/or Phosphatidylinositol 3-kinase (P13K) inhibitors.