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(54) Title: METHODS FOR TREATING TYROSINE-KINASE-INHIBITOR-RESISTANT MALIGNANCIES IN PATIENTS WITH GENETIC POLYMORPHISMS OR AHI1 DYSREGULATIONS OR MUTATIONS EMPLOYING DIANHYDROGALACTITOL, DIACETYLDIANHYDROGALACTITOL, DIBROMODULCITOL, OR ANALOGS OR DERIVATIVES THEREOF

(57) Abstract: Methods and compositions suitable for the treatment of malignancies in subjects with a germline deletion polymorphism that blocks the activity of thymidine kinase inhibitors in triggering apoptosis in tumor cells or in subjects having a mutation in or a dysregulation of the *AHI1* gene are disclosed. These methods employ an alkylating hexitol derivative such as dianhydrogalactitol, a derivative or analog of dianhydrogalactitol, diacetyldianhydrogalactitol, a derivative or analog of diacetyldianhydrogalactitol, dibromodulcitol, and a derivative or analog of dibromodulcitol. The compositions can include such alkylating hexitol derivatives. The methods can further include administration of a BH3 mimetic, and the compositions can further include a BH3 mimetic. In subjects having a dysregulation of the *AHI1* gene, the methods can further include the administration of an agent modulating the expression or activity of the *AHI1* gene or AHI1 protein, and the compositions can further include such an agent.