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(71) Applicant: **DEL MAR PHARMACEUTICALS** [CA/CA]; 999 West Broadway, Suite 720, Vancouver, British Columbia V57 1K5 (CA).

(72) Inventors; and
(71) Applicants : **BROWN, Dennis M.** [US/US]; 3475 Edison Way, Suite R, Menlo Park, California 94025 (US). **BACHA, Jeffrey A.** [CA/CA]; c/o Del Mar Pharmaceuticals, Suite 115, Vancouver, British Columbia V5T 4T5 (CA). **GARNER, William J.** [US/US]; 1701 Jackson Street, #102, San Francisco, California 94109 (US).

(74) Agents: **DITTHAVONG MORI & STEINER P.C.** et al.; 44 Canal Center Plaza, Suite 322, Alexandria, Virginia 22314 (US).

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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.