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(54) Title: ENZYME CATALYZED THERAPEUTIC ACTIVATION

(57) Abstract: This invention provides novel substrate compounds that selectively inhibit the proliferation of pathological cells, for example, pathological cells that endogenously overexpress a target enzyme that confers resistance to biologic and chemotherapeutic agents. The enzyme acts on a substrate compound to 1) convert it to a cellular toxin and/or 2) release a toxic byproduct. In one embodiment, the activity of the target enzyme has been greatly enhanced in a target cell as a result of loss of tumor suppressor function and/or selection resulting from previous exposure to chemotherapy. In another embodiment, the pathological cell contains a target enzyme that is an expression product of an infectious agent in the cell. Further provided by this invention is a method for treating a subject by delivering to the subject a prodrug as described herein. The prodrugs of this invention may be used alone or in combination with other chemotherapeutics or alternative anti-cancer therapies such as radiation.

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