Lipophilic Bisphosphonates and Their Therapeutic Use in Cancer

INVENTION:
Investigators at the Salk, working with colleagues at the University of Illinois have designed and tested novel bisphosphonate compounds which show less polarity that typically associated with this class of compound. These compounds have shown efficacy in KRAS/p53 mutation animal models of cancer.

APPLICATIONS:
Treatment of adenocarcinomas with KRAS mutation such as lung adenocarcinoma and pancreatic adenocarcinoma

ADVANTAGES:
The combination therapy (lipophilic bisphosphonates plus rapamycin analogs) is much more potent than either single agent alone

STAGE OF DEVELOPMENT:
The combination therapy has been fully tested in mouse models; toxicity/toxicokinetic studies of the lipophilic bisphosphonates in big animals are underway.

BACKGROUND:
Currently available bisphosphonates are very polar. They enter cells, primarily macrophages and osteoclasts, via fluid-phase endocytosis. Bisphosphonates are also rapidly removed from circulation. These properties are good for a bone drug, but are undesirable for a drug that targets tumor cells in other organs, therefore there is a need to develop bisphosphonate to meet non-skeletal medical needs.

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PATENT STATUS: PCT patent application WO 2016/081281 is pending

PUBLICATIONS:

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TECHNOLOGY ID: RD 1330