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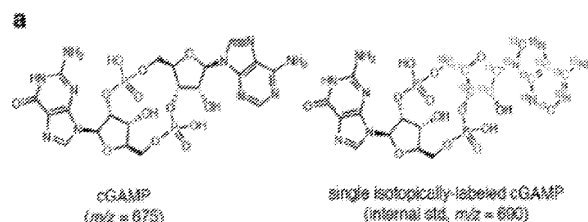


FIG. 1

(57) Abstract: Compounds, compositions and methods are provided for the inhibition of ENPP1. Aspects of the subject methods include contacting a sample with an ENPP1 inhibitor compound to inhibit the cGAMP hydrolysis activity of ENPP1. In some cases, the ENPP1 inhibitor compound is cell impermeable. ENPP1 inhibitor compounds can act extracellularly to block the degradation of cGAMP. Also provided are pharmaceutical compositions and methods for treating cancer. Aspects of the methods include administering to a subject a therapeutically effective amount of an ENPP1 inhibitor to treat the subject for cancer. In certain cases, the cancer is a solid tumor cancer. Also provided are methods of administering radiation therapy to a subject in conjunction with administering an ENPP1 inhibitor to the subject. The radiation therapy can be administered in the subject methods at a dosage and/or frequency effective to reduce radiation damage to the subject, but still instigate an immune response.

[Continued on next page]

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