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(54) **Title**: CANCER TREATMENT USING ANTIBODIES THAT BING CELL SURFACE GRP78

(57) **Abstract**: This application provides, inter alia, antibodies or antigen-binding fragments thereof, targeting cell surface GRP78 expressed on tumor cells, tumor endothelial cells, and tumor initiating cancer cells. These anti-GRP78 antibodies, or antigen-binding fragments thereof, have a high affinity for GRP78 and are less immunogenic compared to their unmodified parent antibodies in a given species, e.g., a human, and function to inhibit GRP78. Importantly, these isolated novel antibodies and antigen-binding fragments thereof, attenuate PI3K signaling and promote apoptosis in tumor cells, while leaving normal cells unaffected. The antibodies and antigen-binding fragments are useful for UPR- targeted cancer therapeutic treatments.