

## 4MO

### Preclinical evaluation of novel CDK4/6 inhibitor GLR2007 in breast and lung cancer models

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#### Background

Cyclin-dependent kinases (CDKs) such as CDK4/6 are essential in regulating the cell cycle, which is disrupted in many cancers. Currently marketed CDK4/6 inhibitors abemaciclib, palbociclib, and ribociclib have shown preclinical efficacy in solid tumors including breast cancer and non-small cell lung cancer. GLR2007 is an investigational CDK4/6 inhibitor with potential to treat advanced solid tumors. *In vitro* and *in vivo* antitumor effects of GLR2007 were investigated in breast and lung cancer cell line preclinical models.

#### Methods

*In vitro* proliferation inhibition was evaluated through live cell counts in 7 human and murine breast cancer cell lines and 21 human lung cancer cell lines after culture for 72 h with 0.01–10,000 nM GLR2007 or 1.5–10,000 nM abemaciclib, reported as half maximal inhibitory concentration (IC<sub>50</sub>). *In vivo* antitumor efficacy was determined in MCF-7 breast cancer orthotopic xenografts in NOD/SCID mice, and NCI-H1975 and NCI-H2228 lung cancer subcutaneous xenografts in BALB/C nude mice treated with 50 mg/kg GLR2007 by once-daily oral gavage.

#### Results

GLR2007 inhibited proliferation at lower IC<sub>50</sub> values compared to abemaciclib in 5 breast cancer cell lines (IC<sub>50</sub> fold difference range = 0.08–0.92; median = 0.33) and in 20 lung cancer cell lines (IC<sub>50</sub> fold difference range = 0.03–0.99; median = 0.39). In MCF-7 breast cancer orthotopic xenografts, compared to vehicle control, 50 mg/kg GLR2007 induced 49.6% tumor growth inhibition (TGI) ( $P=0.001$ ) in mice treated for 21 days, and 81.4% TGI ( $P=0.037$ ) on day 25 in mice treated for 28 days. In lung cancer subcutaneous xenograft models, compared to vehicle control, 50 mg/kg GLR2007 induced 68.9% TGI ( $P<0.001$ ) on day 16 in mice implanted with NCI-H1975 cells and treated for 22 days, and 33.9% TGI ( $P=0.003$ ) on day 34 in mice implanted with NCI-H2228 cells and treated for 28 days.

#### Conclusions

In a number of tumor cell lines, GLR2007 inhibited proliferation at lower IC<sub>50</sub> values compared to abemaciclib. GLR2007 demonstrated significant antitumor efficacy in xenograft models compared to vehicle controls. These preclinical studies demonstrate the potential of GLR2007 as a novel CDK4/6 inhibitor for the treatment of breast and lung cancer.

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#### Legal entity responsible for the study

Gan & Lee Pharmaceuticals.

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#### Disclosure

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