Pediatric Preclinical Testing Program (PPTP) Evaluation of the KSP Inhibitor Ispinesib (SB-715992)

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In Vivo Test Results for Ispinesib

A xenograft is a novel small molecule inhibitor of kinesin spindle protein (Eg5), a mitotic kinesin required for separation of the spindle poles. Ispinesib inhibits growth of a broad range of cancer cell lines at low nanomolar concentrations, effectively halting tumor growth and disrupting the tumor microenvironment. Ispinesib was administered intraperitoneally (IP) to a representative subset of xenografts on childhood solid tumors and childhood ALL. Ispinesib was administered IP to a representative subset of xenografts on childhood solid tumors and childhood ALL. Ispinesib was administered IP to a representative subset of xenografts on childhood solid tumors and childhood ALL. Ispinesib was administered IP to a representative subset of xenografts on childhood solid tumors and childhood ALL. Ispinesib was administered IP to a representative subset of xenografts on childhood solid tumors and childhood ALL.

Results

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**Background**

Ispinesib is a novel small molecule inhibitor of kinesin spindle protein (Eg5), a mitotic kinesin required for separation of the spindle poles. Ispinesib inhibits growth of a broad range of cancer cell lines at low nanomolar concentrations, effectively halting tumor growth and disrupting the tumor microenvironment. Ispinesib was administered intraperitoneally (IP) to a representative subset of xenografts on childhood solid tumors and childhood ALL. Ispinesib was administered IP to a representative subset of xenografts on childhood solid tumors and childhood ALL. Ispinesib was administered IP to a representative subset of xenografts on childhood solid tumors and childhood ALL.

**Methods**

The PPTP includes an in vitro panel (23 lines) as well as panels of xenografts (45 lines) representing most of the common types of childhood solid tumors and childhood ALL. Ispinesib was administered IP (10 mg/kg or 5 mg/kg) to a representative subset of xenografts on childhood solid tumors and childhood ALL. Ispinesib was administered IP to a representative subset of xenografts on childhood solid tumors and childhood ALL. Ispinesib was administered IP to a representative subset of xenografts on childhood solid tumors and childhood ALL. Ispinesib was administered IP to a representative subset of xenografts on childhood solid tumors and childhood ALL.

**In Vivo Test Results for Ispinesib**

- **Ispinesib** was active against all but one of the cell lines of the PPTP in vitro panel (1a rhodamine assay, cell lines at all nanomolar concentrations). Ispinesib induced a CR in 1 of 4 GBM. Ispinesib produced 2 CRs and 2 PRs among neuroblastoma. Ispinesib induced maintained CRs in 3 xenografts: 1 of 2 neuroblastomas and 1 of 2 GBM.

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