Deciphera Pharmaceuticals Presents Data on Altiratinib (DCC-2701), an Advanced Multi-targeted Kinase Inhibitor, at 26th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics

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Preclinical Data with Altiratinib Showed Promising Profile for Robust Tumor Inhibition and Potential to Block Tumor and Tumor Microenvironment Resistance Mechanisms

Deciphera Pharmaceuticals, a clinical stage biotechnology company focused on advanced kinase inhibitor treatments targeting the tumor cell and the tumor microenvironment, today announced the presentation of preclinical data which demonstrated that altiratinib (DCC-2701) provided balanced inhibition of MET, TRK, TIE2 and VEGFR2 kinases. Altiratinib exhibited potency against both wild-type and mutant forms of MET and TRK kinases. In in vivo studies, altiratinib was shown to inhibit tumor growth, evasive vascularization, invasion and/or metastasis. In one model an increased overall survival was observed. Altiratinib exhibited anti-tumor activity in a variety of xenograft or allograft tumor models, including melanoma, gastric, lung, colorectal, breast, ovarian and glioblastoma. These data were presented today at the 26th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics in Barcelona, Spain. Altiratinib is currently in a Phase 1 clinical study in cancer patients with solid tumors.

“In this preclinical data set, the profile observed with altiratinib demonstrated robust and durable inhibition of kinases related to multiple hallmarks of cancer., Our data demonstrate blocking of tumor progression and growth and tumor microenvironment related mechanisms, including evasive vascularization and metastasis in a variety of cancer models,” said Michael D. Taylor, PhD, Deciphera’s President and Chief Executive Officer. “We look forward to further evaluation of altiratinib’s anti-cancer activity, including top-line data from our ongoing Phase 1 clinical study in patients with advanced solid tumors which is expected in mid-2015.”

In a poster presentation titled “Altiratinib: a balanced inhibitor of MET, TRK, TIE2, and VEGFR2 kinases that exhibits broad anti-tumor and anti-angiogenic activities,” Deciphera researchers described data which demonstrated that altiratinib inhibited tumors driven by MET amplification, overexpression, or mutation and also provided the potential for blocking tumor microenvironment angiogenic resistance mechanisms and pro-tumoral effects. Findings from the data include:

- Altiratinib potently inhibited MET, TIE2, VEGFR2, and TRK kinases in functional cellular assays, including activity against proliferation, migration, and capillary tube formation, and with sufficient single-digit nanomolar potency such that all of these targets could be effectively inhibited simultaneously in vivo.
- Altiratinib exhibited efficacy at preventing tumor growth, as well as inhibiting evasive vascularization, pro-tumoral macrophages, epithelial-to-mesenchymal transition (EMT) and metastasis in a variety of cancer models.
- Altiratinib inhibited MET kinase for more than 24 hours after a single 10 mg/kg dose in a gastric cancer xenograft model leading to significant inhibition of tumor growth.
- Altiratinib blocked bevacizumab-induced evasive vascularization and EMT in an aggressive, invasive glioblastoma model.
- Altiratinib inhibited primary tumor growth and showed additive activity with paclitaxel; in addition, it reduced TIE2-expressing macrophages in the tumor stroma and significantly reduced lung metastases in a metastatic breast cancer model.
- Altiratinib exhibited a long off-rate from kinases (greater than 24 hours from TIE2 and TRKA) in a variety of cell-based assays, based on its binding mode.

- Altiratinib inhibited microvessel density and tumor growth in a xenograft model where both TIE2 and VEGFR2 kinases contribute to vessel growth.
- Altiratinib compared favorably with other multi-targeted MET inhibitors, and had additional activity in inhibiting oncogenic MET mutants found in papillary renal cell carcinoma (PRCC), while other MET inhibitors have not been shown to inhibit activated MET mutants.

About Altiratinib (DCC-2701)

Altiratinib is a MET/TIE2/VEGFR2/TRK (A,B,C) kinase inhibitor in Phase 1 clinical development for the treatment of invasive solid tumors including glioblastoma. The U.S. Food and Drug Administration has granted altiratinib Orphan Drug Designation for glioblastoma. Altiratinib has pharmaceutical properties amenable to oral administration and also exhibits substantial blood-brain-barrier penetration, making altiratinib a promising candidate for the treatment of glioblastoma. The discovery and development of altiratinib was based on the rationale of inhibiting MET and TRK kinases as cancer driver mutations while also incorporating balanced inhibition of the tumor microenvironment via MET, TIE2, and VEGFR2 kinases within a single therapeutic. With its balanced potency, altiratinib can inhibit three major tumor angiogenesis pathways (HGF, VEGF, ANG), thus overcoming the problem of tumor evasive vascularization, allowing for durable MET or TRK inhibition in tumors and overcoming HGF/MET mediated drug resistance. Other potential indications in which altiratinib may be active include MET-driven cancers, such as melanoma, pancreatic cancer, gastric tumors, renal cell carcinoma and BRAF-mutated melanoma as well as TRK-driven cancers such as non-small cell lung cancer, acute myeloid leukemia, colorectal cancer, ovarian cancer and thyroid cancer.

About Deciphera Pharmaceuticals

Deciphera Pharmaceuticals is inspired to improve treatment for patients with cancer by designing kinase inhibitor therapies that target the hallmarks of cancer biology. Our small-molecule drugs are specifically engineered to simultaneously block multiple cancer signaling mechanisms in the tumor cell and the tumor microenvironment to prevent growth and spread. Deciphera's unique approach represents an important advance over current therapies in the durability of kinase inhibition and resiliency to genetic mutations to provide greater benefit across a range of cancers. Deciphera's

business strategy is to advance its drug candidates for genetically-defined cancers and cancers that target the tumor microenvironment through both proprietary and partnered programs.

Deciphera's internal product pipeline includes altiratinib (DCC-2701) a MET/TIE2 /VEGFR2/TRK kinase inhibitor currently in Phase 1 clinical development, DCC-2618, a pan-KIT inhibitor currently in preclinical development and rebastinib, a TIE2/VEGFR1 kinase inhibitor currently in Phase 1 clinical development. Partnered programs include LY3009120 (DP-4978), a pan-RAF inhibitor developed in collaboration with Eli Lilly. Additional research-stage programs are also in development.

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