Deciphera Pharmaceuticals Reports Encouraging Clinical Results with DCC-2618 in Genetically-defined Cancers with Drug Resistant Mutations

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Advanced Kinase Inhibitors with Improved Tumor Targeting Offer Potential for Durable Responses in Difficult-to-Treat Cancers

Late-breaking Oral Presentation of Clinical Data for Pan-KIT Switch Control Inhibitor, DCC-2618, Presented at EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics

Deciphera Pharmaceuticals presented today initial clinical data from an ongoing Phase 1 study of DCC-2618, a pan-KIT and PDGFRα targeted tyrosine kinase inhibitor in development for the treatment of genetically-defined cancers, including gastrointestinal stromal tumors (GIST) as well as other KIT-driven diseases such as systemic mastocytosis. These data support DCC-2618 as a potential treatment option for patients with these difficult-to-treat solid tumor cancers based on encouraging tumor responses and preliminary data showing decreases in circulating tumor DNA that codes for KIT mutations in heavily-pretreated GIST patients with multiple resistance mutations. The clinical results were described in a late-breaking oral presentation at the 28th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics taking place November 29 to December 2, 2016 in Munich, Germany. A poster describing preclinical results with altiratinib (DCC-2701), another candidate in Deciphera's pipeline that is a spectrum-selective MET and TRK-targeted kinase inhibitor for the treatment of solid tumors, was also presented at the meeting.

“DCC-2618 is one of the most active compounds I have seen in the phase I setting in my career. While it is early, we observed signs of benefit in the GIST patients treated whose disease had progressed despite multiple previous treatments.,” said Filip Janku, M.D., Ph.D., Assistant Professor, Department of Investigational Cancer Therapeutics, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center.

“Scientists at Deciphera are at the forefront of advancing kinase inhibitor research, and the development of a new generation of kinase inhibitors, such as DCC-2618, offers potential new therapies for patients with genetically-defined cancers and other diseases including GIST and systemic mastocytosis,” said Oliver Rosen, M.D., Chief Medical Officer of Deciphera Pharmaceuticals. “We are very encouraged by the impressive early clinical results presented on DCC-2618. By inhibiting even difficult to treat drug resistant mutant kinases, DCC-2618 offers the potential for more durable responses in patients with cancer mutations that are resistant to other kinase inhibitor therapies and we look forward to providing further updates in the months to come.”

In a late-breaking oral presentation, titled “DCC-2618, a pan KIT and PDGFR switch control inhibitor, achieves proof-of-concept in a first-in-human study,” Dr. Janku of MD Anderson Cancer Center reported initial data from an ongoing Phase 1, dose escalation study of oral DCC-2618 in advanced solid tumor patients in which objective tumor responses and metabolic PET responses in GIST patients were observed. The data reported on the first 24 patients dosed in an ongoing Phase 1 dose-escalation study of DCC-2618 given orally twice-daily in 28-day cycles at doses ranging from 20-150 mg in advanced solid tumor patients. Highlights from the presentation of the Phase 1 data (as of November 11, 2016) include:

- Partial Metabolic Responses (EORTC criteria) were observed in 14 of 15 patients with KIT-mutant GIST along with initial signs of decreases in circulating tumor DNA that codes for KIT, demonstrating broad spectrum inhibition of KIT mutants in heavily-pretreated GIST patients harboring multiple resistance mutations.
- Two patients achieved partial response (RECIST criteria), including one patient with KIT, PDGFRα and VEGFR2 co-amplified glioblastoma multiforme and a patient with GIST and a KIT Exon 11/17 mutation.

- DNA analyses at baseline revealed established resistance mutations in 9 of 13 patients with KIT-mutant GIST, with up to 5 secondary mutations and 3 established resistance mutations in a single patient confirming extensive tumor heterogeneity in these heavily-pretreated patients. Preliminary evidence of significant decreases in circulating tumor DNA encoding both primary and resistance mutations in KIT demonstrates the broad spectrum inhibition of mutant KIT kinases in heavily-pretreated GIST patients.
- DCC-2618 was well tolerated with an encouraging safety profile. The most common treatment emergent adverse events (>25%) included: fatigue, dyspnea, anemia and decreased appetite. One dose limiting toxicity, a grade 3, asymptomatic lipase elevation in the 100 mg cohort, was reported.
- The maximum tolerated dose for DCC-2618 has not yet been reached in this dose-escalation study.

In a poster presentation, titled “The type II switch control kinase inhibitor, DCC-2701 (altiratinib) effectively inhibits resistant NTRK kinase domain mutants,” Deciphera collaborators at Memorial Sloan Kettering Cancer Center and Oregon Health and Sciences University described preclinical data in which altiratinib with its unique inhibitor binding mode maintained high affinity and inhibitory efficacy for mutant TRK kinase-fusions to circumvent emergent drug resistance.

About DCC-2618 and Altiratinib

DCC-2618 and altiratinib are both currently in Phase 1 clinical trials. DCC-2618 is a pan-KIT and PDGFRα kinase inhibitor in clinical development for the treatment of genetically-defined cancers, including gastrointestinal stromal tumors (GIST) and other KIT-driven diseases such as systemic mastocytosis. Altiratinib is a spectrum selective inhibitor of MET, TRK, TIE2 & VEGFR2 kinases in clinical development for the treatment of solid tumors.

About Deciphera Pharmaceuticals

Deciphera Pharmaceuticals seeks to improve treatment for patients with cancer by designing innovative kinase inhibitor therapies that address key drug resistance mechanisms. Deciphera’s unique approach leverages its deep understanding of kinase biology to develop a robust pipeline of tumor-targeted and immuno-targeted drug

candidates that can improve the rate and durability of response to treatment. Deciphera's innovative switch control platform enables the creation of tumor-targeted agents designed to control therapeutic resistance causing mutations and immuno-targeted agents designed to control activation of immuno-kinases that suppress critical immune system regulators, such as macrophages. This two-pronged approach to kinase inhibition represents an advance over other methods of inhibiting kinases for the treatment of cancer.

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