Deciphera Pharmaceuticals Announces DCC-2036 research for CML published in Cancer Cell

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Lawrence, KS – April 18, 2011 – Research from Deciphera Pharmaceuticals was published this week disclosing that a novel drug, DCC-2036, shows promise for treating chronic myelogenous leukemia (CML) patients who have few other options because their disease has developed resistance to standard treatments.

Appearing in the April 12th issue of the journal Cancer Cell, the study is the first published report showing that DCC-2036 fights CML in preclinical models of resistant disease and is effective against human leukemia cells, including leukemia cells resistant to all currently approved drugs. DCC-2036 was discovered and developed at Deciphera Pharmaceuticals utilizing its proprietary 'switch control' technology. The drug blocks the human protein, called BCR-ABL, that causes CML. Upon drug binding, the BCR-ABL protein is forced into a shape that blocks its cancer-causing effects.

Notably, DCC-2036 blocks even the most resistant form of BCR-ABL, called the T315I mutation. No currently marketed drug is effective versus the T315I mutant form. DCC-2036 is currently being tested in a phase 1 clinical trial in patients who have failed therapy with two or more previous kinaseblocking drugs. The trial is actively enrolling patients at Tufts Medical Center, MD Anderson Cancer Center, University of Michigan Cancer Center, and the University of Kansas Cancer Center.

"The leukemia-causing BCR-ABL belongs to a class of human proteins known as kinases," said Daniel Flynn, PhD, President & CEO of Deciphera and senior author of the study. "Kinases send messages inside of cells to control cellular functions

including growth and survival. When these proteins are under normal regulation, cells function to promote and maintain health. However, when these proteins are mutated, they lose the ability to 'turn-off', and this can lead to cancer. In the case of BCR-ABL, this leads to chronic myelogenous leukemia."

Other authors of the study include scientists from Tufts Medical Center of Boston, MA, led by Richard Van Etten, MD, PhD and Emerald Biostructures of Bainbridge Island, WA, led by Lance Stewart, PhD. Deciphera Pharmaceuticals used crystal structures of BCR-ABL to custom-design the novel drug to inhibit the mutant enzyme by forcing its molecular switch into the OFF state. The crystal structures were provided by Emerald Biostructures. The published study showed that in human cells taken from treatment-resistant patients who had received the new drug, DCC-2036 blocked the mutant enzyme that led to their relapse. The study also found that the drug killed malignant cells and prolonged survival in a mouse model of CML driven by the highly aggressive T315I mutant form of BCR-ABL. This model was developed by Van Etten's team at Tufts.

The development of kinase blocking drugs such as imatinib has dramatically improved the prognosis for patients with CML, which strikes about 5,000 new patients each year in the United States. But about a third of patients will eventually relapse, principally because of mutations that render the cancer causing BCR-ABL resistant to therapy. Many times, the BCR-ABL mutates to very aggressive forms that conventional drugs like imatinib cannot block, leading to this resistance. Deciphera's technology enables the design of drugs, such as DCC-2036, which turn off even these resistant forms of BCR-ABL. "We call this 'switch control' therapy, because DCC-2036 forces a molecular switch in BCR-ABL to turn this kinase OFF, even in cancer-causing resistant forms where the kinase switch is otherwise aggressively ON," Flynn said. "This new approach will hopefully benefit patients by providing treatments that arrest cancers that are prone to resistance to other types of therapies."