Deciphera Pharmaceuticals, Inc. Expands Pipeline with Potential First-in-Class Autophagy Inhibitor to Treat Mutant RAS Cancers

June 10, 2019

-DCC-3116 Selectively Targets ULK Kinase, an Initiating Protein that Activates Autophagy -

- Company to Host a Webcast on Tuesday, June 18, 2019 at 8 a.m. ET to Discuss Autophagy Inhibition and the Treatment of Mutant RAS Cancers -

WALTHAM, Mass.--(BUSINESS WIRE)--Jun. 10, 2019-- Deciphera Pharmaceuticals, Inc. (NASDAQ:DCPH) today announced the addition of a new candidate to its pipeline, DCC-3116, a potential first-in-class small molecule designed to inhibit cancer autophagy, a key tumor survival mechanism. DCC-3116, discovered using the Company's novel switch control inhibitor platform, is designed to inhibit autophagy by inhibiting the ULK kinase. Autophagy is a cellular pathway that has been shown to be upregulated in mutant RAS cancers and that also mediates resistance to inhibitors of the RAS signaling pathway. Subject to favorable investigational new drug (IND)-enabling studies and filing and activation of an IND, Deciphera intends to develop DCC-3116 for the potential treatment of mutant RAS cancers in combination with inhibitors of downstream effector targets including RAF, MEK, or ERK inhibitors as well as with direct inhibitors of mutant RAS.

Based on pre-clinical studies, DCC-3116 selectively inhibits ULK kinase, believed to be the initiating factor that activates autophagy. Autophagy is a cell survival pathway in which cells respond to stress by recycling their own components and/or clearing damaged organelles and proteins from the cell. Mutant RAS cancers, including KRAS, NRAS, and HRAS cancers, are reported to have high basal levels of autophagy, which they use to maintain nutrient supply, regulate cancer cell metabolism, and mitochondria surveillance.[1] In multiple *in vitro* and *in vivo* models of mutant RAS cancers, autophagy inhibition combined with inhibition of MAPK signaling using MEK inhibitors or ERK inhibitors has demonstrated synergistic anti-tumor effects.[2,3] When used in pre-clinical *in vitro* and *in vivo* studies in combination with inhibitors of the MAPK pathway, DCC-3116 synergized with these inhibitors to inhibit mutant RAS cancer growth. Cellular studies in mutant RAS cancers have demonstrated that MAPK pathway inhibitors further activate autophagy as a compensatory survival mechanism. Such activation of autophagy is seen with RAF, MEK, and ERK inhibitors as well as with direct inhibitors of mutant KRAS G12C. As an inhibitor of ULK, DCC-3116 is designed to address mutant RAS cancers by inhibiting the basal and compensatory autophagy that mutant RAS cancer cells use for their survival.

"We are very excited to announce our new development candidate, DCC-3116, a potential first-in-class agent aimed at treating mutant RAS cancers through the inhibition of autophagy," said Steve Hoerter, President and Chief Executive Officer of Deciphera. "Recent efforts in the fight against cancer have focused on direct approaches targeting mutant RAS, which comprise approximately 30% of all cancers and that we believe represents one of largest unmet medical needs in oncology. We believe that as a highly selective inhibitor of ULK kinase, DCC-3116 may offer a new and complementary approach to targeting mutant RAS cancer through suppression of autophagy."

"Our new clinical candidate, DCC-3116, is a potent and selective inhibitor of ULK kinase generated using our proprietary switch control inhibitor platform. Inhibition of ULK has potential application in a very wide range of cancers and is an exciting addition to our pipeline," said Daniel Flynn, Executive Vice President, Chief Scientific Officer and Founder of Deciphera.

Deciphera is currently conducting IND-enabling studies for DCC-3116 and, pending favorable results, expects to file an IND in mid-2020.

DCC-3116 Event and Webcast Information

Deciphera will host a live event and webcast to discuss the new program on Tuesday, June 18, 2019 at 8 a.m. ET. The event will feature members of the Deciphera management team and Channing Der, Ph.D., Sarah Graham Kenan Distinguished Professor, Department of Pharmacology, UNC School of Medicine, who is a leading expert in mutant RAS cancers and autophagy.

A live audio webcast of the event and accompanying slides may be accessed through the Investors section of Deciphera's website at www.deciphera.com. A replay of the webcast will be available for 30 days following the event.

About Deciphera Pharmaceuticals

Deciphera Pharmaceuticals is a clinical-stage biopharmaceutical company focused on improving the lives of cancer patients by tackling key mechanisms of drug resistance that limit the rate and/or durability of response to existing cancer therapies. Our small molecule drug candidates are directed against an important family of enzymes called kinases, known to be directly involved in the growth and spread of many cancers. We use our deep understanding of kinase biology together with a proprietary chemistry library to purposefully design compounds that maintain kinases in a "switched off" or inactivated conformation. These investigational therapies comprise tumor-targeted agents designed to address therapeutic resistance causing mutations and immuno-targeted agents designed to control the activation of immunokinases that suppress critical immune system regulators, such as macrophages. We have used our platform to develop a diverse pipeline of tumor-targeted and immuno-targeted drug candidates designed to improve outcomes for patients with cancer by improving the quality, rate and/or durability of their responses to treatment.

Availability of Other Information About Deciphera Pharmaceuticals

Investors and others should note that Deciphera Pharmaceuticals communicates with its investors and the public using its company website (www.deciphera.com), including but not limited to investor presentations and scientific presentations, Securities and Exchange Commission filings, press releases, public conference calls and webcasts. The information that Deciphera Pharmaceuticals posts on these channels and websites could be deemed to be material information. As a result, Deciphera Pharmaceuticals encourages investors, the media and others interested in Deciphera Pharmaceuticals to review the information that it posts on these channels, including Deciphera Pharmaceuticals' investor relations website, on a regular basis. This list of channels may be updated from time to time on Deciphera Pharmaceuticals' investor relations website and may include other social media channels than the ones described above. The contents of Deciphera Pharmaceuticals' website or these channels, or any other website that may be accessed from its website or these channels, shall not be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding our DCC-3116 program, our expectations for and the possibility of our DCC-3116 candidate to inhibit ULK and autophagy and possibly treat or provide therapeutic benefit for a wide range of cancers, and the timing of and our plans to conduct IND-enabling studies, file an IND and develop DCC-3116 for mutant RAS cancers. The words “may,” “will,” “could,” “would,” “should,” “expect,” “plan,” “anticipate,” “intend,” “believe,” “estimate,” “predict,” “project,” “potential,” “continue,” “target” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this press release are based on management’s current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, risks and uncertainties related to the designation of DCC-3116 as a new clinical candidate, the expected benefits and development of DCC-3116, delay of any current or planned pre-clinical, IND-enabling and/or clinical studies or the development of our drug candidates, including ripretinib, rebastinib, DCC-3014 and DCC-3116, our advancement of multiple early-stage and later-stage efforts, our ability to successfully demonstrate the efficacy and safety of our drug candidates including in later-stage studies, the preclinical and clinical results for our drug candidates, which may not support further development of such drug candidates, our efforts to scale up and manage drug product manufacturing, our ability to implement commercial readiness, actions of regulatory agencies, any or all of which may affect the initiation, timing and progress of clinical studies and other risks identified in our SEC filings, including our Quarterly Report on Form 10-Q for the quarter ended March 31, 2019, and subsequent filings with the SEC. We caution you not to place undue reliance on any forward-looking statements, which speak only as of the date they are made. We disclaim any obligation to publicly update or revise any such statements to reflect any change in expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements. Any forward-looking statements contained in this press release represent our views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date. We explicitly disclaim any obligation to update any forward-looking statements.

References:

1.Guo, Jessie Yanxiang et al. “Activated Ras requires autophagy to maintain oxidative metabolism and tumorigenesis.” *Genes & Development* 2011; 25: 460-470.
2. Bryant, Kirsten L. et al. “Combination of ERK and autophagy inhibition as treatment approach for pancreatic cancer.” *Nature Medicine* 2019; 25: 628-640.
3. Kinsey, Conan G. et al. “Protective autophagy elicted by RAF → MEK → ERK inhibition suggests a treatment strategy for RAS-driven cancers.” *Nature Medicine* 2019; 25: 620-627.

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