Deciphera Pharmaceuticals Presents Preclinical Data from DCC-3116 Program at the AACR Annual Meeting

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– ULK Inhibitor DCC-3116 Shown to Inhibit KRAS^{G12C} Inhibitor-induced Autophagy in Mutant KRAS^{G12C} NSCLC Cell Lines –

– DCC-3116 in Combination with KRAS^{G12C} Inhibitors Translated to Deeper and Longer Tumor Regressions than KRAS^{G12C} Inhibitors Alone In Vivo –

WALTHAM, Mass.--(BUSINESS WIRE)--Apr. 12, 2022-- Deciphera Pharmaceuticals, Inc. (NASDAQ: DCPH), a commercial-stage biopharmaceutical company developing innovative medicines to improve the lives of people with cancer, announced the presentation of preclinical data for DCC-3116, the Company's first-in-class ULK kinase inhibitor, in combination with KRAS ^{G12C} inhibitors in non-small cell lung cancer (NSCLC) models at the American Association for Cancer Research (AACR) Annual Meeting 2022 in New Orleans, Louisiana.

"Autophagy is recognized as a mechanism of drug resistance in cancer and an exciting target for drug development. The combination of a KRAS ^{G12C} inhibitor with DCC-3116, a selective and potent inhibitor of the ULK1/2 protein kinases that are key autophagy regulators, has the potential to promote deeper and more durable clinical responses than a KRAS^{G12C} inhibitor alone," said Martin McMahon, Ph.D., Cumming-Presidential Chair of Cancer Biology in the Dept. of Dermatology, Senior Director for Preclinical Translation and Co-Leader of the Experimental Therapeutics Program in the Huntsman Cancer Institute. "The data I presented today provides strong preclinical rationale for this approach and underscores the importance of autophagy inhibition in the treatment of cancer, demonstrating a compelling rationale to study DCC-3116 in combination with KRAS^{G12C} inhibitors in clinical trials in non-small cell lung cancer patients."

Results from the preclinical studies, presented in an oral presentation titled "DCC-3116, a first-in-class selective inhibitor of ULK1/2 kinases and autophagy, combines with the KRAS^{G12C} inhibitor sotorasib resulting in tumor regression in NSCLC xenograft models" are summarized below. The presentation is available on-demand via the meeting's website and on the Company's website at www.deciphera.com/presentations-publications.

Summary of Preclinical Data and Findings

Results from the preclinical studies showed that KRAS^{G12C} inhibitors, sotorasib and adagrasib, activate ULK-mediated autophagy as an adaptive treatment resistance mechanism. DCC-3116 in combination with sotorasib and with adagrasib inhibited ULK kinase activation and the resulting autophagic flux in a KRAS^{G12C} mutated NSCLC cell line. Results demonstrated that DCC-3116 in combination with sotorasib and with adagrasib translated to deeper and longer tumor regressions *in vivo.* The study also demonstrated that DCC-3116 in combination with sotorasib outperformed both single agent sotorasib and the combination of sotorasib and chloroquine, a nonspecific lysosomal inhibitor of autophagy.

Results of the preclinical studies were as follows:

- Treatment of mutant KRAS^{G12C} NSCLC cell lines with KRAS^{G12C} inhibitors, sotorasib and adagrasib, induced autophagy via activation of ULK1/2 kinases as measured by an increase in ULK-mediated phosphorylation of the key ULK autophagy substrate ATG13 and resulting increase in autophagic flux.
- In mutant KRAS^{G12C} NSCLC cell lines, DCC-3116 inhibited ULK kinase activation by both sotorasib and adagrasib, as measured by a decrease in phosphorylated ATG13 and resulting autophagic flux.
- In the H358 KRAS^{G12C} NSCLC xenograft model, the combination of DCC-3116 and sotorasib resulted in deeper and longer tumor regressions compared to all single agent sotorasib cohorts.
- In the Calu-1 KRAS^{G12C} NSCLC xenograft model, the combination of DCC-3116 and sotorasib resulted in tumor regressions and outperformed both single agent sotorasib and the combination of sotorasib and chloroquine.
- In the LU11554 KRAS^{G12C} NSCLC patient derived xenograft model, the efficacy for the combination of DCC-3116 with sotorasib or with adagrasib increased tumor growth inhibition compared to sotorasib or adagrasib alone.

DCC-3116 is currently being investigated in a Phase 1, multicenter, open-label, first-in-human study designed to evaluate the safety, tolerability, clinical activity, pharmacokinetics, and pharmacodynamics of DCC-3116 as a single agent and in combination with trametinib, an FDA approved MEK inhibitor, in patients with advanced or metastatic tumors with a mutant RAS or RAF gene. Initial data from the single agent dose escalation portion of the Phase 1 study is expected in the second half of 2022. The Company expects to initiate Phase 1 study dose escalation cohorts in the second half of 2022 in combination with trametinib in patients with selected mutations in advanced or metastatic pancreatic ductal adenocarcinoma, NSCLC, colorectal cancer, and melanoma. Planning is underway to add a combination with a KRAS^{G12C} inhibitor in NSCLC to the ongoing Phase 1 study, subject to feedback from regulatory authorities.

About DCC-3116

DCC-3116 is an investigational, orally administered, potent, and highly selective switch-control inhibitor designed to inhibit cancer autophagy, a key tumor survival mechanism in cancer cells, by inhibiting the ULK1/2 kinases, which have been shown to be the initiating factors that activates

autophagy. DCC-3116 is currently being studied in a Phase 1, multicenter, open-label, first-in-human study as a single agent and in combination with trametinib, an FDA approved MEK inhibitor, in patients with advanced or metastatic tumors with a mutant RAS or RAF gene (NCT04892017).

About Deciphera Pharmaceuticals

Deciphera is a biopharmaceutical company focused on discovering, developing, and commercializing important new medicines to improve the lives of people with cancer. We are leveraging our proprietary switch-control kinase inhibitor platform and deep expertise in kinase biology to develop a broad portfolio of innovative medicines. In addition to advancing multiple product candidates from our platform in clinical studies, QINLOCK® is Deciphera's switch control inhibitor for the treatment of fourth-line GIST. QINLOCK is approved in Australia, Canada, China, the European Union, Hong Kong, Switzerland, Taiwan, the United Kingdom, and the United States. For more information, visit www.deciphera.com and follow us on LinkedIn and Twitter (@Deciphera).

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, our expectations and timing regarding the potential of a combination of a $KRAS^{G12C}$ inhibitor with the selective and potent inhibitor of ULK 1/2, DCC-3116, to promote deeper and more durable clinical responses than a $KRAS^{G12C}$ inhibitor alone, the rationale to study DCC-3116 in combination with $KRAS^{G12C}$ inhibitors in non-small cell lung cancer patients, initial data from the dose escalation phase of the Phase 1 study of DCC-3116, plans to initiate the trametinib combination dose escalation portion of the Phase 1 study of DCC-3116, and plans to expand the ongoing Phase 1 study of DCC-3116 to add a combination with a mutant KRAS G12C inhibitor in NSCLC patients subject to feedback from regulatory authorities. The words "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "seek," "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 our ability to provide access to QINLOCK in European countries other than Germany and France through other channels, the severity and duration of the impact of COVID-19 on our business and operations, our ability to successfully demonstrate the efficacy and safety of our drug or drug candidates, the preclinical or clinical results for our product candidates, which may not support further development of such product candidates, comments, feedback and actions of regulatory agencies, our ability to commercialize QINLOCK and execute on our marketing plans for any drugs or indications that may be approved in the future, the inherent uncertainty in estimates of patient populations, competition from other products, our ability to obtain and maintain reimbursement for any approved product and the extent to which patient assistance programs are utilized and other risks identified in our Securities and Exchange Commission (SEC) filings, including our Annual Report on Form 10-K for the year ended December 31, 2021, 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.

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