
**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549**

FORM 8-K

**CURRENT REPORT
PURSUANT TO SECTION 13 OR 15(d)
OF THE SECURITIES EXCHANGE ACT OF 1934**

Date of Report (Date of earliest event reported): October 28, 2019

DECIPHERA PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction
of Incorporation)

001-38219
(Commission
File Number)

30-1003521
(IRS Employer
Identification Number)

200 Smith Street
Waltham, MA
(Address of registrant's principal executive office)

02451
(Zip code)

(781) 209-6400
(Registrant's telephone number, including area code)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 203.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Title of each class	Trading Symbol	Name of exchange on which registered
Common Stock, \$0.01 Par Value	DCPH	The Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 or Rule 12b-2 of the Securities Exchange Act of 1934.

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Item 7.01. Regulation FD Disclosure.

On October 28, 2019, Deciphera Pharmaceuticals, Inc. (the “Company”) issued a press release announcing updated data for two of its programs, namely (1) its Phase 1b/2 study of rebastinib (DCC-2036) in combination with paclitaxel: preliminary safety, efficacy, pharmacokinetics and pharmacodynamics in patients with advanced or metastatic solid tumors and (2) preclinical studies with DCC-3116, an ULK kinase inhibitor designed to inhibit autophagy as a potential strategy to address mutant RAS cancers. The data were presented on October 28, 2019 in poster sessions at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics being held October 26-30, 2019 in Boston, MA (the “Triple Meeting”). A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K, and a copy of the presentations are furnished as Exhibit 99.3 and Exhibit 99.4 to this Current Report on Form 8-K.

On October 29, 2019, the Company issued a press release announcing updated data for two of its programs, namely (1) updated results of its phase 1 study of ripretinib (DCC-2618), a broad-spectrum KIT and PDGFRA inhibitor, in patients with gastrointestinal stromal tumor (GIST) by line of therapy (NCT02571036) and (2) its Phase 1 study of DCC-3014, an oral inhibitor of CSF1R, to assess the safety, tolerability, pharmacokinetics, and pharmacodynamics in patients with advanced solid tumors, including diffuse-type tenosynovial giant cell tumor. The data were presented on October 29, 2019 in poster sessions at the Triple Meeting. A copy of the press release is furnished as Exhibit 99.2 to this Current Report on Form 8-K, and a copy of the presentations are furnished as Exhibit 99.5 and Exhibit 99.6 to this Current Report on Form 8-K.

The furnishing of the attached press releases and presentations is not an admission as to the materiality of any information therein. The information contained in the press releases and the presentations is summary information that is intended to be considered in the context of more complete information included in the Company’s filings with the U.S. Securities and Exchange Commission, or the SEC, and other public announcements that the Company has made and may make from time to time by press release or otherwise. The Company undertakes no duty or obligation to update or revise the information contained in this report, although it may do so from time to time as its management believes is appropriate. Any such updating may be made through the filing of other reports or documents with the SEC, through press releases or through other public disclosures. For important information about forward looking statements, see the “Cautionary Note Regarding Forward-Looking Statements” section of the press releases in Exhibit 99.1 and Exhibit 99.2 attached hereto.

The information in this Item 7.01 of this Current Report on Form 8-K and Exhibit 99.1, Exhibit 99.2, Exhibit 99.3, Exhibit 99.4, Exhibit 99.5 and Exhibit 99.6 attached hereto shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liabilities of that section or Sections 11 and 12(a)(2) of the Securities Act of 1933, as amended. The information contained in this Item 7.01 and in the press releases attached as Exhibit 99.1 and Exhibit 99.2 to this Current Report and in the presentations attached as Exhibit 99.3, Exhibit 99.4, Exhibit 99.5, Exhibit 99.6 to this Current Report shall not be incorporated by reference into any filing with the SEC made by the Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing, except as expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.**(d) Exhibits.**

<u>Exhibit No.</u>	<u>Description</u>
99.1	<u>Press Release issued by Deciphera Pharmaceuticals, Inc. on October 28, 2019, furnished herewith.</u>
99.2	<u>Press Release issued by Deciphera Pharmaceuticals, Inc. on October 29, 2019, furnished herewith.</u>
99.3	<u>Presentation from October 28, 2019, furnished herewith.</u>
99.4	<u>Presentation from October 28, 2019, furnished herewith.</u>
99.5	<u>Presentation from October 29, 2019, furnished herewith.</u>
99.6	<u>Presentation from October 29, 2019, furnished herewith.</u>

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: October 29, 2019

DECIPHERA PHARMACEUTICALS, INC.

By: /s/ Steven L. Hoerter
Steven L. Hoerter
President and Chief Executive Officer



Deciphera Pharmaceuticals Presents Data from Rebastinib and DCC-3116 Programs at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics

- *Combination of Rebastinib and Paclitaxel Exhibited Encouraging Preliminary Anti-tumor Activity Across Treatment Arms in the Ongoing Phase 1b/2 Clinical Study -*
- *DCC-3116 Represents a Differentiated Approach to Autophagy Inhibition and a First-in-Class Opportunity for a New Therapeutic Modality in Mutant RAS Cancers -*

Waltham, MA – October 28, 2019 – Deciphera Pharmaceuticals, Inc. (Nasdaq:DCPH), a clinical-stage biopharmaceutical company addressing key mechanisms of tumor drug resistance, today presented data from its ongoing Phase 1b/2 clinical study of rebastinib, an oral TIE2 kinase inhibitor, in combination with paclitaxel at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics in Boston. In addition, the Company also presented data from preclinical studies of DCC-3116, a potential first-in-class autophagy inhibitor to treat mutant RAS cancers.

“Both of these datasets highlight the broad applicability of Deciphera’s kinase switch control platform and our potential to address unmet needs in oncology,” said Matthew L. Sherman, M.D., Executive Vice President and Chief Medical Officer of Deciphera. “We look forward to continuing Part 2 of our Phase 1b/2 study of rebastinib in combination with paclitaxel with the insights garnered from Part 1 of the study. We also look forward to advancing the IND-enabling studies for DCC-3116.”

Rebastinib

The Phase 1b/2 study of rebastinib in combination with paclitaxel is a two-part, open-label, multicenter study assessing the safety, tolerability, anti-tumor activity and pharmacokinetics of multiple doses of rebastinib in patients with advanced or metastatic solid tumors. Data presented today are from 43 patients from Part 1 of the study, including 24 patients from the rebastinib 50 mg oral twice a day (BID) with paclitaxel 80 mg/m² IV cohort and 19 patients from the rebastinib 100 mg oral BID with paclitaxel 80 mg/m² IV cohort. Preliminary results from Part 1 included:

- Encouraging preliminary anti-tumor activity was observed in both dose cohorts, with objective responses seen across a heavily pre-treated patient population, including patients with prior exposure to paclitaxel. Objective responses were seen in eight patients including ovarian (3), breast (2), carcinosarcoma (2), and peritoneal mesothelioma (1), seven of whom had prior therapy with paclitaxel or docetaxel. A best response of partial response (PR) was observed in 5 of 24 patients in the 50 mg BID dose cohort and 3 of 19 patients in the 100 mg BID dose.
- Exposure to rebastinib was dose-proportional at the 50 mg BID and 100 mg BID doses when given in combination with paclitaxel.
- Mean circulating Ang-2 levels increased with exposure to higher doses of rebastinib in combination with paclitaxel, indicating TIE2 inhibition.
- Rebastinib in combination with paclitaxel was generally well-tolerated, with similar frequency of treatment-emergent adverse events (TEAEs) between the two dose cohorts, and most TEAEs were consistent with first-in-human studies of rebastinib or known to be associated with treatment with paclitaxel.



- Based on the observed frequency of muscular weakness in preliminary data from the ongoing Part 2 portion of the study with the 100 mg BID dose, the recommended phase 2 dose (RP2D) was changed to 50 mg BID.

DCC-3116

DCC-3116 is designed as a potential autophagy inhibitor by selectively targeting 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 application, 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 (MAPK inhibitors) as well as with direct inhibitors of mutant RAS. Preclinical data presented today included the following:

- DCC-3116 was shown to be a potent, selective, and tight-binding inhibitor of ULK kinase.
- DCC-3116 inhibited phosphorylation of the ULK substrate ATG13 in cancer cells and exhibited synergy *in vitro* in combination with MAPK inhibitors in inhibiting cancer cell growth.
- Oral doses of DCC-3116 led to sustained inhibition of ULK activity as shown by the inhibited phosphorylation of the ULK substrate ATG13 *in vivo*.
- DCC-3116 exhibited synergy with MAPK inhibitors in tumor growth inhibition in mouse models.

A copy of each poster presentation is available at www.deciphera.com.

About Rebastinib

Rebastinib is an investigational, orally administered, potent and selective inhibitor of the TIE2 kinase, the receptor for angiopoietins, an important family of vascular growth factors in the tumor microenvironment that also activate pro-tumoral TIE2 expressing macrophages. In a Phase 1 clinical study, biomarker data have demonstrated rebastinib-induced increases in the TIE2 ligand angiopoietin 2, providing evidence of TIE2 inhibition. Rebastinib is currently being evaluated in a Phase 1b/2 clinical study in combination with paclitaxel ([NCT03601897](https://clinicaltrials.gov/ct2/show/study/NCT03601897)) and in a Phase 1b/2 clinical study in combination with carboplatin ([NCT03717415](https://clinicaltrials.gov/ct2/show/study/NCT03717415)).

About DCC-3116

DCC-3116 is a potential first-in-class small molecule designed to inhibit cancer autophagy, a key tumor survival mechanism, by inhibiting the ULK kinase. Subject to favorable investigational new drug (IND)-enabling studies and filing and activation of an IND application, expected in mid-2020, Deciphera intends to develop DCC-3116 for the potential treatment of mutant RAS cancers in combination with inhibitors of downstream RAS effector targets including RAF, MEK, or ERK inhibitors as well as with direct inhibitors of mutant RAS.

About Deciphera Pharmaceuticals

Deciphera Pharmaceuticals is a clinical-stage biopharmaceutical company focused on improving the lives of cancer patients by addressing 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, immuno-targeted agents designed to control the activation of immunokinases that suppress critical immune system regulators, and agents designed to inhibit reprogramming of cancer cell



metabolism. We have used our platform to develop a diverse pipeline of tumor-targeted, immuno-targeted, and metabolism-targeted drug candidates designed to improve outcomes for patients with cancer by improving the quality, rate and/or durability of their responses to treatment.

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 expectations regarding the broad applicability of our kinase switch control platform, the potential of our drug candidates to address unmet needs in oncology, continuation of Part 2 of our Phase 1b/2 study of rebastinib in combination with paclitaxel, advancing DCC-3116 through IND-enabling studies, and the timing of the potential filing of an IND for DCC-3116, subject to favorable IND enabling studies. 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 delay of any current or planned clinical studies or the development of our drug candidates, including ripretinib, 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, actions of regulatory agencies, any or all of which may affect the initiation, timing and progress of clinical studies and regulatory development and other risks identified in our SEC filings, including our Quarterly Report on Form 10-Q for the quarter ended June 30, 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.

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Deciphera Pharmaceuticals Presents Updated Data from Ripretinib and DCC-3014 Programs at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics

- Median Progression Free Survival (mPFS) of 46 Weeks for the Second-Line Gastrointestinal Stromal Tumors (GIST) Cohort from the Phase 1 Study of Ripretinib in Patients Receiving 150 mg QD as Starting Dose -

- DCC-3014 Phase 1 Data Demonstrated Tolerability, Pharmacokinetics and Biomarker Mechanistic Proof-of-Concept in Patients with Advanced Malignancies -

Waltham, MA – October 29, 2019 – Deciphera Pharmaceuticals, Inc. (Nasdaq:DCPH), a clinical-stage biopharmaceutical company addressing key mechanisms of tumor drug resistance, today announced the presentation of updated results from its ongoing Phase 1 study of ripretinib, a broad-spectrum KIT and PDGFR α inhibitor, in patients with second-line through fourth-line plus GIST, as well as its Phase 1 study of DCC-3014, an oral inhibitor of CSF1R, in patients with advanced solid tumors. The data are being presented today at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics in Boston.

“These updated results continue to underscore the potential of our diverse pipeline of product candidates, all generated using our proprietary kinase switch control inhibitor platform, to improve the lives of cancer patients,” said Matthew L. Sherman, M.D., Executive Vice President and Chief Medical Officer of Deciphera. “Of note, we believe ripretinib continues to demonstrate strong clinical benefit in post-imatinib GIST patients, particularly in the second-line setting. These results bolster our confidence in the ongoing INTRIGUE pivotal Phase 3 clinical study, which is designed to support potential regulatory approvals in patients with second-line GIST.”

Ripretinib

Updated results from the Company’s ongoing Phase 1 study of ripretinib in patients with second-line through fourth-line plus GIST included data from 142 GIST patients receiving 150 mg of ripretinib once daily (QD) as the starting dose, which is the dose being utilized in the Company’s INVICTUS and INTRIGUE registration-enabling studies, as of an August 10, 2019 data cutoff date. The table below includes local, investigator-assessed objective response rate (ORR) by best response as determined by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1, median duration of response, median progression free survival (mPFS) and mean treatment duration.

<u>Line of Therapy</u>	<u>2nd Line (n=31)</u>	<u>3rd Line (n=28)</u>	<u>≥4th Line (n=83)</u>
ORR (confirmed responses only)	19%	14%	7%
Median Duration of Response	80 weeks	NE ⁽¹⁾	76 weeks
mPFS	46 weeks	36 weeks	24 weeks
Mean Treatment Duration ⁽²⁾	56 weeks	58 weeks	45 weeks

(1) NE = not estimable; (2) Includes 64 patients who elected for intra-patient dose escalation from 150 mg QD to 150 mg twice daily (BID).

Data from GIST patients receiving \geq 100 mg of ripretinib daily (n=178) in the ongoing Phase 1 study, as of an August 10, 2019 cutoff date, including 2nd line (n=37), 3rd line (n=31), and \geq 4th line (n=110) patients were (a) ORR (confirmed responses only): 2nd line (22%), 3rd line (13%), \geq 4th line (7%); (b) median duration of response: 2nd line (80 weeks), 3rd line (NE), \geq 4th line (48 weeks); (c) mPFS: 2nd line (46 weeks), 3rd line (40 weeks), \geq 4th line (24 weeks); (d) mean treatment duration (includes 72 patients who elected for intra-patient dose escalation to 150 mg BID): 2nd line (53 weeks), 3rd line (54 weeks), \geq 4th line (48 weeks).



Ripretinib was generally well tolerated and the updated adverse events were consistent with previously presented Phase 1 data in patients with GIST. Grade 3 or 4 treatment-emergent adverse events (TEAEs) in >5% of patients were increase in lipase level (n=25; 18%), anemia (n=11; 8%), and abdominal pain (n=11; 8%).

DCC-3014

The Company's Phase 1 study of DCC-3014 was designed to evaluate the safety, pharmacokinetics and pharmacodynamics of multiple doses of DCC-3014 in patients with advanced solid tumors. The Company expects to present preliminary data from initial tenosynovial giant cell tumor (TGCT) patients at the 2019 Connective Tissue Oncology Society (CTOS) Annual Meeting being held November 13-16 in Tokyo, Japan.

- As of the data cut-off date of September 10, 2019, increasing doses of DCC-3014 were assessed in seven dose cohorts across 36 patients with advanced solid tumor tumors. This included one dose cohort that received 10 mg once daily and six dose cohorts that received a three to five day loading dose regimen at doses of up to 50 mg followed by a schedule of daily, once-weekly or twice-weekly maintenance dosing with DCC-3014.
- Data demonstrated dose-proportional exposure for DCC-3014 and exposure to DCC-3014 was associated with an increase in plasma CSF1 and IL-34, rapid and sustained reduction of CD16+ monocytes in peripheral blood, and substantial decreases in CD163+ macrophages in tumor.
- DCC-3014 was generally well-tolerated, with most treatment-emergent adverse events (TEAEs) Grade 1 or 2. Most common related TEAEs $\geq 10\%$ were fatigue (n=6; 17%), diarrhea (n=4; 11%), and nausea (n=4; 11%). Grade 3 or 4 related TEAEs occurred in 4 patients, which were grade 3 aspartate aminotransferase (AST) increase, grade 4 lipase increase, grade 3 amylase increase, and grade 3 colitis. Serious adverse events were reported in 17 patients; none of which were related to DCC-3014.
- The dose escalation evaluation is ongoing to determine a recommended phase 2 dose for advanced solid tumors and diffuse-type TGCT.

A copy of each presentation is available at www.deciphera.com/science/presentation-publications/.

About Ripretinib

Ripretinib is an investigational tyrosine kinase switch control inhibitor that was engineered to broadly inhibit KIT and PDGFR α mutated kinases by using a unique dual mechanism of action that regulates the kinase switch pocket and activation loop. Ripretinib is currently in clinical development for the treatment of KIT and/or PDGFR α -driven cancers, including gastrointestinal stromal tumors, or GIST, systemic mastocytosis, or SM, and other cancers. Ripretinib inhibits initiating and secondary KIT mutations in exons 9, 11, 13, 14, 17, and 18, involved in GIST, as well as the primary D816V exon 17 mutation involved in SM. Ripretinib also inhibits primary PDGFR α mutations in exons 12, 14 and 18, including the exon 18 D842V mutation, involved in a subset of GIST. In June 2019, the U.S. FDA granted Fast Track Designation to ripretinib for the treatment of patients with advanced GIST who have received prior treatment with imatinib, sunitinib and regorafenib. For more information about the Company's clinical trials with ripretinib, please visit www.clinicaltrials.gov.



Deciphera Pharmaceuticals has an exclusive license agreement with Zai Lab (Shanghai) Co., Ltd. for the development and commercialization of ripretinib in Greater China (Mainland China, Hong Kong, Macau and Taiwan). Deciphera Pharmaceuticals retains development and commercial rights for ripretinib in the rest of the world.

About DCC-3014

DCC-3014 is an investigational, orally administered, potent and highly selective inhibitor of CSF1R. DCC-3014 was designed using the Company's proprietary switch control kinase inhibitor platform to selectively bind to the CSF1R switch pocket. DCC-3014 has greater than 100-fold selectivity for CSF1R over other closely related kinases and has an even greater selectivity for CSF1R over approximately 300 other human kinases. CSF1R controls the differentiation and function of macrophages including Tumor Associated Macrophages (TAMs) whose density within certain tumors including cancers of the breast, cervix, pancreas, bladder and brain correlates with poor prognosis. Tumors induce TAMs to suppress a natural immune response mediated by cytotoxic T-cells, a type of lymphocyte that would otherwise eradicate the tumor; a process known as macrophage checkpoints. Through inhibition of CSF1R, DCC-3014 has in preclinical studies demonstrated potent macrophage checkpoint inhibition as both a single agent and in combination with PD1 inhibitors. DCC-3014 is currently being evaluated in a Phase 1 clinical study. For more information about the clinical trial design please visit www.clinicaltrials.gov ([NCT03069469](https://clinicaltrials.gov/ct2/show/study/NCT03069469)).

About Deciphera Pharmaceuticals

Deciphera Pharmaceuticals is a clinical-stage biopharmaceutical company focused on improving the lives of cancer patients by addressing 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, and agents designed to inhibit reprogramming of cancer cell metabolism. We have used our platform to develop a diverse pipeline of tumor-targeted, immuno-targeted, and metabolism-targeted drug candidates designed to improve outcomes for patients with cancer by improving the quality, rate and/or durability of their responses to treatment.

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 expectations regarding our updated Phase 1 study of ripretinib in patients with GIST to support our pivotal Phase 3 INTRIGUE study in second-line GIST patients, the potential of our pipeline drug candidates to improve the lives of patients with cancer, and the expectation to present additional data from our Phase 1 study of DCC-3014 in patients with diffuse-type tenosynovial giant cell tumor at an upcoming medical meeting. 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 delay of any current or planned clinical studies or the development of our drug candidates, including ripretinib, 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 ability to timely complete and prepare the information



required for and file an NDA for ripretinib, our ability to manage and our reliance on third parties such as our third party drug substance and drug product contract manufacturers, actions of regulatory agencies, any or all of which may affect the initiation, timing and progress of clinical studies and the timing of and our ability to obtain regulatory approval, if at all, and make our investigational drugs available to patients, and other risks identified in our SEC filings, including our Quarterly Report on Form 10-Q for the quarter ended June 30, 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.

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Phase 1b/2 study of rebastinib (DCC-2036) in combination with paclitaxel: Preliminary safety, efficacy, pharmacokinetics, and pharmacodynamics in patients with advanced or metastatic solid tumors

Filip Janku,¹ Michael Birrer,² Debra Richardson,³ Christina Chu,⁴ Sanjay Goel,⁵ Gege Tan,⁶ Bahar Matin,⁷ Kelsuke Kuida,⁸ Rodrigo Ruiz-Soto,⁹ Erika Paige Hamilton¹⁰

¹University of Texas MD Anderson Cancer Center, Houston, TX; ²University of Alabama at Birmingham Comprehensive Cancer Center, Birmingham, AL; ³Washington Cancer Center/Bethesda Cancer Research Institute of the University of Oklahoma Health Sciences Center, Oklahoma City, OK; ⁴Yon Cancer Center, Haverhill, PA; ⁵Albert Einstein College of Medicine, Bronx, NY; ⁶Topivera Pharmaceuticals, LLC, Watford, MA; ⁷Novartis Cancer Research Institute and ⁸Tennessee Oncology, P.L.L.C., Nashville, TN

Abstract: B055

INTRODUCTION

- Tumor necrosis factor- α (TNF- α) is a cell surface receptor transmits tumor necrosis factor from an activated T-helper cell and a subset of macrophages. Inhibiting TNF- α signaling leads to immunomodulatory effects.
- TNF- α is an essential cell, the angiogenic/lymphatic signaling as a key regulator of angiogenesis and tumor progression.¹
- TNF- α is an essential cell, the angiogenic/lymphatic signaling as a key regulator of angiogenesis and tumor progression.
- Inhibition of TNF- α signaling leads to immunomodulatory effects.
- Rebastinib (DCC-2036) is a novel TNF- α inhibitor that is a potent and selective inhibitor of TNF- α signaling.
- Phase 1b/2 study of rebastinib (DCC-2036) in combination with paclitaxel (PTX) in patients with advanced or metastatic solid tumors.

Figure 1. Metastasis-related tumor cell invasion

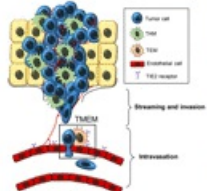


Figure 2. Overall study design

METHODS



Table 1. Key inclusion and exclusion criteria for Part 1

Criteria	Inclusion	Exclusion
Age	≥ 18 years	≤ 75 years
Performance	ECOG 0-1	ECOG ≥ 2
Organ function	Normal	Abnormal

Table 2. Study objectives for Part 1

Objective	Primary	Secondary
Safety and toxicity	Identify	Characterize
Pharmacokinetics	Describe	Describe
Pharmacodynamics	Describe	Describe

RESULTS

Patient demographics and disposition

As of August 1, 2015, 43 patients with advanced solid tumors were enrolled and treated with rebastinib (50 mg BID or 100 mg BID) in combination with paclitaxel, of which 32 (74%) are still on treatment (Figure 3).

Figure 3. Patient disposition

Disposition	50 mg BID (n=22)	100 mg BID (n=21)
Enrolled	22	21
Completed	15	17
Discontinued	7	4
Withdrawn	0	0
Still on treatment	15	17

Table 3. Patient demographics and clinical characteristics

Characteristic	50 mg BID (n=22)	100 mg BID (n=21)	Total (n=43)
Age, median (range), years	61 (25-74)	61 (25-74)	61 (25-74)
Female (%)	9.1	14.3	11.6
Cancer Type (%)			
Lung adenocarcinoma	9.1	14.3	11.6
Breast cancer	9.1	14.3	11.6
Colorectal adenocarcinoma	9.1	14.3	11.6
Pancreatic adenocarcinoma	9.1	14.3	11.6
Squamous cell carcinoma	9.1	14.3	11.6
Sarcoma	9.1	14.3	11.6
Other	9.1	14.3	11.6

Table 4. Prior therapy

Therapy	50 mg BID (n=22)	100 mg BID (n=21)	Total (n=43)
Any prior therapy (%)	90.9	95.2	93.0
Chemotherapy	86.4	90.5	88.4
Surgery	9.1	14.3	11.6
Radiation	9.1	14.3	11.6
Targeted therapy	9.1	14.3	11.6
Immunotherapy	9.1	14.3	11.6

Safety

- Commonly reported treatment-emergent adverse events (TEAEs) ≥ 10% of total population of patients are shown in Table 5.
- Frequency of TEAEs was similar between 50 mg and 100 mg BID.
- The most frequent TEAEs were diarrhea, nausea, and vomiting.
- Grade 3-4 TEAEs were reported in 10.5% of patients in the 50 mg BID group and 14.3% in the 100 mg BID group.
- No patients died as a result of treatment.
- No patients were hospitalized as a result of treatment.
- No patients were discontinued as a result of treatment.

Table 5. Common (≥10%) TEAEs regardless of relationship

TEAE	50 mg BID (n=22)	100 mg BID (n=21)	Total (n=43)
Fatigue	9.1	14.3	11.6
Diarrhea	9.1	14.3	11.6
Nausea	9.1	14.3	11.6
Vomiting	9.1	14.3	11.6
Headache	9.1	14.3	11.6
Constipation	9.1	14.3	11.6
Abdominal pain	9.1	14.3	11.6
Weight decreased	9.1	14.3	11.6
Other	9.1	14.3	11.6

Pharmacokinetics and pharmacodynamics

- Rebastinib exposure was dose-proportional from 50 mg BID to 100 mg BID (Figure 4).
- Rebastinib exposure was dose-proportional from 50 mg BID to 100 mg BID.
- Rebastinib exposure was dose-proportional from 50 mg BID to 100 mg BID.
- Rebastinib exposure was dose-proportional from 50 mg BID to 100 mg BID.
- Rebastinib exposure was dose-proportional from 50 mg BID to 100 mg BID.

Figure 4. Time on treatment and best response for the (A) 50 mg BID and (B) 100 mg BID dose cohorts

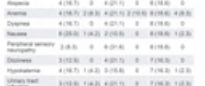


Figure 5. Rebastinib concentration vs time profiles for the 50 mg BID and 100 mg BID three cohorts



CONCLUSIONS

- Rebastinib in combination with paclitaxel was generally well-tolerated.
- There were no significant differences in safety between the 50 mg and 100 mg BID dose cohorts in Part 1.
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Preclinical studies with DCC-3116, an ULK kinase inhibitor designed to inhibit autophagy as a potential strategy to address mutant RAS cancers

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Abstract B129

INTRODUCTION

- Cancer cells activate autophagy, a catabolic process to recycle damaged organelles, in order to survive stresses such as limited nutrients and hypoxia, or chemotherapy treatments.
- RAS mutant cancers, in particular, have been found to require autophagy for tumor growth and survival.^{1,2} Treating RAS mutant tumors with inhibitors of the downstream MAPK pathway has been largely unsuccessful, as these drugs have been shown to further stimulate autophagy, allowing for tumor cell survival.³ Inhibiting autophagy in combination with MAPK pathway inhibition may represent a possible new treatment paradigm for RAS mutant cancers.
- Proof-of-concept for this strategy was obtained in cancer models and in a RAS mutant pancreatic cancer patient by blocking autophagy with derivatives of chloroquine, in combination with MAPK inhibitors.⁴
- ULK1/2 kinases initiate autophagy and provide the potential for a targeted approach for selectively inhibiting autophagy in RAS mutant cancers. Herein, we describe preclinical studies with the ULK kinase inhibitor DCC-3116, designed as a potential inhibitor of autophagy in RAS mutant cancers.

METHODS

In vitro kinase assays were performed using cellular levels of AT7 (1 nM) and a peptide substrate. In cell assays, ULK activity was assessed using an ELISA for phosphorylated ATG13 (a cellular ULK substrate). Autophagosome formation was measured using the dye, Cyto-ID. Autophagic flux was assessed using cells expressing the autophagy protein LC3 fused to luciferase. The synergy of DCC-3116 in combination with MAPK inhibitors was assessed in 2D or 3D cell growth assays. Xenograft models were used to assess pharmacokinetics (PK) and pharmacodynamics (PD), as well as efficacy in vivo.

ULK KINASE: INITIATING FACTOR FOR AUTOPHAGY

Figure 1. Autophagy Pathway

- ULK1/2 kinases initiate autophagy by phosphorylating and activating other autophagy proteins (e.g. ATG13, BECLIN1, and ATG14)
- Damaged proteins, organelles, and other cargo are targeted to, and enveloped by, autophagosomes
- Fusion of autophagosomes and lysosomes allows for breakdown and recycling of metabolic precursors and nutrients

RESULTS

Autophagy is a Compensatory Survival Mechanism in MAPK Pathway Inhibited RAS Mutant Cancers

- Treatment of a RAS mutant cancer cell line with inhibitors of the MAPK pathway (i.e. RAS, RAF, MEK, or ERK inhibitors) leads to activation of ULK kinase and phosphorylation of downstream autophagy protein substrates



DCC-3116 is a Potent & Selective ULK Kinase Inhibitor Designed to Inhibit Autophagy

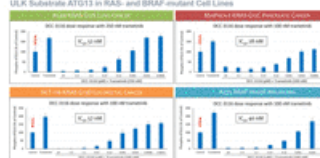
- Potent (IC_{50} at 1 nM AT7)
- ULK1 & 2, ULK2 26 nM
- Tight binding inhibitor with residency time > 7 hours

Figure 3. DCC-3116 Kinome Tree

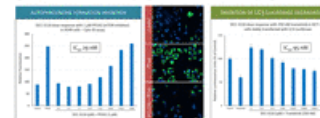
- Highly Selective
 - No off-target kinases within 30-fold of ULK1
 - Only 6 kinases within 100-fold, inclusive of ULK2
- Designed to Avoid CNS Exposure
 - Low Brain Plasma ratio (4%) to avoid inhibition of CNS autophagy
- Optimized Pharmaceutical Properties
 - High solubility and oral bioavailability
 - Plasma Free Fraction > 10%
 - CP1142: 209, 20116, 206, 344 and NERF IC_{50} values >20 μ M

DCC-3116 is a Potent Inhibitor of ULK Kinase and Autophagy in Cellular Assays

Figure 4. DCC-3116 Inhibits Both Basal and Trametinib-induced Phosphorylation of ULK Substrate ATG13 in RAS- and BRAF-mutant Cell Lines

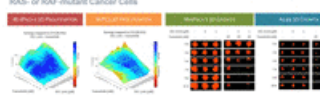


DCC-3116 Inhibits Autophagosome Formation and Autophagic Flux of LC3



DCC-3116 Synergizes with MAPK Inhibitors in 2D and 3D Cellular Growth Assays

Figure 6. DCC-3116 Exhibits Synergy with Trametinib in Inhibiting Cell Growth of RAS- or BRAF-mutant Cancer Cells



DCC-3116 Inhibited ULK Kinase in PKPD Models and Inhibited Tumor Growth in Combination with MAPK Inhibitors in Mouse Xenograft Models

Figure 7. DCC-3116 Inhibited ATG13 Phosphorylation in vivo in a PKPD Model



Figure 8. DCC-3116, in Combination with Trametinib, Inhibited Pancreatic, Lung, and Melanoma Xenograft Tumor Growth

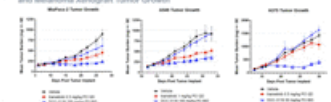
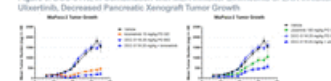


Figure 9. DCC-3116, in Combination with MEK Inhibitor Binimetinib or ERK Inhibitor Ulfetinib, Decreased Pancreatic Xenograft Tumor Growth



CONCLUSIONS

- RAS cancers have high basal autophagy, and induce greater autophagy in response to drug treatments
- ULK kinase inhibitors represent a differentiated approach to autophagy inhibition, and a first-in-class opportunity for a new therapeutic modality in RAS- and BRAF-mutant cancers
- DCC-3116 is a potent, selective and tight-binding inhibitor of ULK kinases
- DCC-3116 inhibits phosphorylation of the ULK substrate ATG13 in cancer cells, and inhibited synergy in vivo in combination with MAPK inhibitors in inhibiting cancer cell growth
- One dose of DCC-3116 acts as sustained inhibitor of ATG13 dephosphorylation in vivo
- In combination with MAPK inhibitors, DCC-3116 exhibited synergy in tumor growth inhibition in mouse models
- Selectively inhibiting autophagy via inhibition of ULK1/2 kinases, in combination with MAPK pathway inhibition, is a promising therapeutic approach for RAS-mutant cancers
- DCC-3116 warrants further study as an inhibitor of autophagy, and has been selected as a candidate for potential clinical development in the treatment of RAS mutant cancers

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Phase 1 study of DCC-3014, an oral inhibitor of CSF1R, to assess the safety, tolerability, pharmacokinetics, and pharmacodynamics in patients with advanced solid tumors, including diffuse-type tenosynovial giant cell tumor

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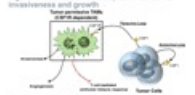
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Abstract: C087

INTRODUCTION

- CSF1R is a tyrosine kinase receptor that is essential for the survival and proliferation of myeloid cells in the bone marrow.
- CSF1R inhibition with DCC-3014 is a novel approach to inhibit CSF1R signaling and reduce CSF1R-dependent myeloid cell populations in solid tumors.
- CSF1R inhibition is being evaluated in phase 1 studies in patients with advanced solid tumors.

Figure 1. Role of CSF1R receptor in the tumor microenvironment and growth.



- DCC-3014 is an oral, selective CSF1R inhibitor that is being evaluated in phase 1 studies in patients with advanced solid tumors.
- DCC-3014 is a potent CSF1R inhibitor that is being evaluated in phase 1 studies in patients with advanced solid tumors.
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METHODS

- This is a phase 1, multicenter, open-label study of DCC-3014 in patients with advanced solid tumors.
- The study is designed to determine the recommended phase 2 dose (RP2D) and to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of DCC-3014.
- The study is designed to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of DCC-3014.

Table 1. Dose cohorts in Part 1 (2+3 dose escalation)

Cohort	Dose (mg)	Frequency	Duration
1	100	QD	28 days
2	200	QD	28 days
3	400	QD	28 days
4	800	QD	28 days
5	1600	QD	28 days
6	3200	QD	28 days

Table 2. Key inclusion and exclusion criteria for Part 1

- Inclusion criteria:
 - Age ≥ 18 years
 - Eastern Cooperative Oncology Group performance grade 0-2
 - Adequate organ function
 - No prior CSF1R inhibitor treatment
- Exclusion criteria:
 - Prior CSF1R inhibitor treatment
 - Active infection
 - Pregnancy or breastfeeding
 - Uncontrolled hypertension
 - Uncontrolled diabetes
 - Uncontrolled hyperlipidemia
 - Uncontrolled hypothyroidism
 - Uncontrolled hypoparathyroidism
 - Uncontrolled hypokalemia
 - Uncontrolled hyponatremia
 - Uncontrolled hypocalcemia
 - Uncontrolled hypomagnesemia
 - Uncontrolled hypophosphatemia
 - Uncontrolled hypocalcemia
 - Uncontrolled hypomagnesemia
 - Uncontrolled hypophosphatemia

Table 3. Study endpoints

- Primary endpoint: Safety and tolerability, defined as the number of patients with grade 3 or higher adverse events.
- Secondary endpoints:
 - Pharmacokinetics (PK): C_{max}, AUC, t_{1/2}, t_{1/2β}
 - Pharmacodynamics (PD): CSF1R inhibition, myeloid cell populations
 - Clinical efficacy: Objective response rate (ORR), progression-free survival (PFS), overall survival (OS)

RESULTS

Patient demographics and disposition

- Total number of patients: 100
- Median age: 65 years
- Male: 60 (60%)
- Female: 40 (40%)
- Eastern Cooperative Oncology Group performance grade: 0 (0%), 1 (10%), 2 (90%)

Table 4. Patient disposition

Disposition	Number of Patients
Completed	10
Discontinued	90
Adverse events	15
Progression	25
Death	5

Table 5. Baseline demographics and clinical characteristics

Characteristic	Number of Patients
Age (years)	65
Male (%)	60
Female (%)	40
ECOG performance grade (%)	0 (0%), 1 (10%), 2 (90%)
Primary tumor type	Various
Number of prior lines of therapy	1-4

Table 6. Types of cancers

Cancer Type	Number of Patients
Adenocarcinoma	45
Squamous cell carcinoma	25
Neuroendocrine tumor	10
Other	20

Table 7. Common (≥10%) TEAEs regardless of relationship

TEAE	Grade 1	Grade 2	Grade 3	Grade 4
Headache	15	5	0	0
Nausea	10	5	0	0
Fatigue	12	3	0	0
Diarrhea	8	2	0	0

Table 8. Safety

- No deaths were reported.
- No grade 4 adverse events were reported.
- No grade 3 adverse events were reported.
- No grade 2 adverse events were reported.
- No grade 1 adverse events were reported.

Table 9. Pharmacokinetics and pharmacodynamics

- DCC-3014 exposure increases proportionally with increasing dose (Table 10).
- DCC-3014 exposure increases proportionally with increasing dose (Table 10).
- DCC-3014 exposure increases proportionally with increasing dose (Table 10).

Table 10. DCC-3014 geometric mean PK parameters on CD11b by cohort

Parameter	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6
C _{max} (ng/mL)	100	200	400	800	1600	3200
AUC _{0-24h} (ng·h/mL)	1000	2000	4000	8000	16000	32000
t _{1/2} (h)	12	12	12	12	12	12

Table 11. CSF1R inhibition and myeloid cell populations

- CSF1R inhibition was observed in all patients.
- Myeloid cell populations (CD11b⁺ cells) were significantly reduced in patients receiving DCC-3014.
- Myeloid cell populations (CD11b⁺ cells) were significantly reduced in patients receiving DCC-3014.

Table 12. Preliminary antitumor activity

- No objective responses were observed.
- No partial responses were observed.
- No stable diseases were observed.
- No progressive diseases were observed.

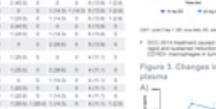
Table 13. Changes in levels of whole blood CD11b⁺ monocytes



Table 14. Changes in levels of CD11b⁺ macrophages in tumors



Table 15. Changes in levels of circulating A) CSF1 and B) IL-34 in patients



CONCLUSIONS

- DCC-3014 was generally well tolerated in patients with advanced solid tumors and diffuse-type TGCT.
- Exposure to DCC-3014 was dose proportional and was associated with an increase in CSF1 and IL-34 in plasma and a rapid, sustained reduction of CSF1R⁺ monocytes in peripheral blood, and a reduction in CD11b⁺ macrophages in tumor.
- These results support further evaluation of DCC-3014 in advanced solid tumors as single agent or in combination, as well as in diffuse-type TGCT.
- The preliminary results from solid diffuse-type TGCT patients will be presented at American Society of Hematology Annual Meeting (Abstract 4201734, November 15-16, 2019, Tokyo, Japan).