DCC-3116 Overview and Preclinical Data

April 15, 2022

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This presentation may contain forward-looking statements that are based on our current expectations, estimates and projections about our industry as well as management's beliefs and assumptions. Words such as "anticipates," "expects," "intends," "plans," "believes," "seeks," "estimates," "may," "will," and variations of these words or similar expressions are intended to identify forward-looking statements. These statements include, without limitation, our expectations and timing regarding our Phase 1 study of DCC-3116 in patients with mutant RAS or RAF cancers, initial data from the dose escalation phase of the Phase 1 study of DCC-3116, expanding the study of DCC-3116 to add a cohort in combination with a mutant KRAS G12C inhibitor in non-small cell lung cancer patients subject to feedback from health authorities, exploration of pre-clinical combinations of DCC-3116 with multiple additional targeted oncology agents, clinical studies including status, progress and results, timing for clinical data readouts, planning efforts for future clinical studies, NDA/MAA (and equivalent) filings and potential additional approvals, research and discovery efforts including the potential of our drug candidates, IND filings, regulatory designations and programs, timing and likelihood of success, plans and objectives of management for future operations, estimated patient populations, the market opportunity for our drug and drug candidates and business guidance, including discovery, clinical and regulatory milestones, cash guidance and the potential impact of COVID-19, and speak only at the time this presentation was prepared. Such statements are based upon the information available to us now and are subject to change. We will not necessarily inform you of such changes. These statements are not guarantees of future performance and are subject to certain risks, uncertainties and assumptions that are difficult to predict. Therefore, actual results could differ materially and adversely from those expressed in any forward-looking statements as a result of various factors, including, among others, the uncertainty around the severity and duration of the impact of COVID-19 on our business and operations, our ability to successfully commercialize QINLOCK, our ability to build in Europe for a potential EU launch, our history of significant losses since inception, our ability to obtain necessary capital when needed on acceptable terms, the timing and results from ongoing or future clinical and non-clinical studies, the possibility preliminary or top-line data may not be indicative of final data, unexpected adverse events, our ability to obtain or expand regulatory approval for our candidates or products, our ability to partner with licensees or distributors, comments, feedback and actions of regulatory agencies, our ability to obtain and maintain reimbursement for any approved products and the extent to which patient assistance programs are utilized, 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 and make QINLOCK and any investigational drugs that may receive approval, available to patients, the fact we may not receive the benefits of regulatory designations, our ability to execute on our marketing plans for any approved drugs, the inherent uncertainty in estimates of patient populations, our ability to comply with healthcare regulations and laws, competition from other products or procedures, our reliance on third-parties to conduct our clinical and non-clinical studies, our reliance on and ability to manage third-party and single source suppliers to manufacture drug supplies and our ability to obtain, maintain and enforce our intellectual property rights. New risk factors and uncertainties may emerge from time to time, and it is not possible to predict all risk factors and uncertainties. There can be no assurance that the opportunity will meet your investment objectives, that you will receive a return of all or part of such investment. Investment results may vary significantly over any given time period. The appropriateness of a particular investment or strategy will depend on an investor's individual circumstances and objectives. Investors should independently evaluate specific investments. For further information regarding these risks, uncertainties and other factors, you should read the "Risk Factors" section of Deciphera's Annual Report on Form 10-K for the year ended December 31, 2021 filed with the Securities and Exchange Commission (the "SEC"), and Deciphera's other SEC filings.

DCC-3116

EXECUTIVE SUMMARY

ULK-MEDIATED AUTOPHAGY AND METABOLIC REWIRING FORM THE FOUNDATION OF A GENERAL TUMOR SURVIVAL PATHWAY

- A broad range of targeted therapeutics that inhibit tumor drivers also activate ULK-mediated tumor survival pathways as a general treatment resistance mechanism
- Addressable market targets ~70% of all human cancers

DCC-3116 COMBINATION WITH RTK INHIBITORS TARGETING MUTANT RTK-DRIVEN CANCERS

- DCC-3116 + osimsertinib combination in mEGFR NSCLC
- DCC-3116 + afatinib combination in mEGFR NSCLC
- Combination exhibits deeper and more durable responses compared to single agent therapy

DCC-3116 COMBINATION WITH KRAS INHIBITORS TARGETING MUTANT RAS-DRIVEN CANCERS

- DCC-3116 + sotorasib combination in mKRAS^{G12C} NSCLC
- DCC-3116 + adagrasib combination in mKRAS^{G12C} NSCLC
- Combination exhibits deeper and more durable regressions compared to single agent therapy

DCC-3116 COMBINATION WITH MAPK INHIBITORS TARGETING MUTANT RAS/RAF-DRIVEN CANCERS

- DCC-3116 + trametinib combination in mKRAS NSCLC, mKRAS PDAC, mKRAS CRC, and mBRAF Melanoma
- Combination exhibits synergy or additivity compared to single agent therapy

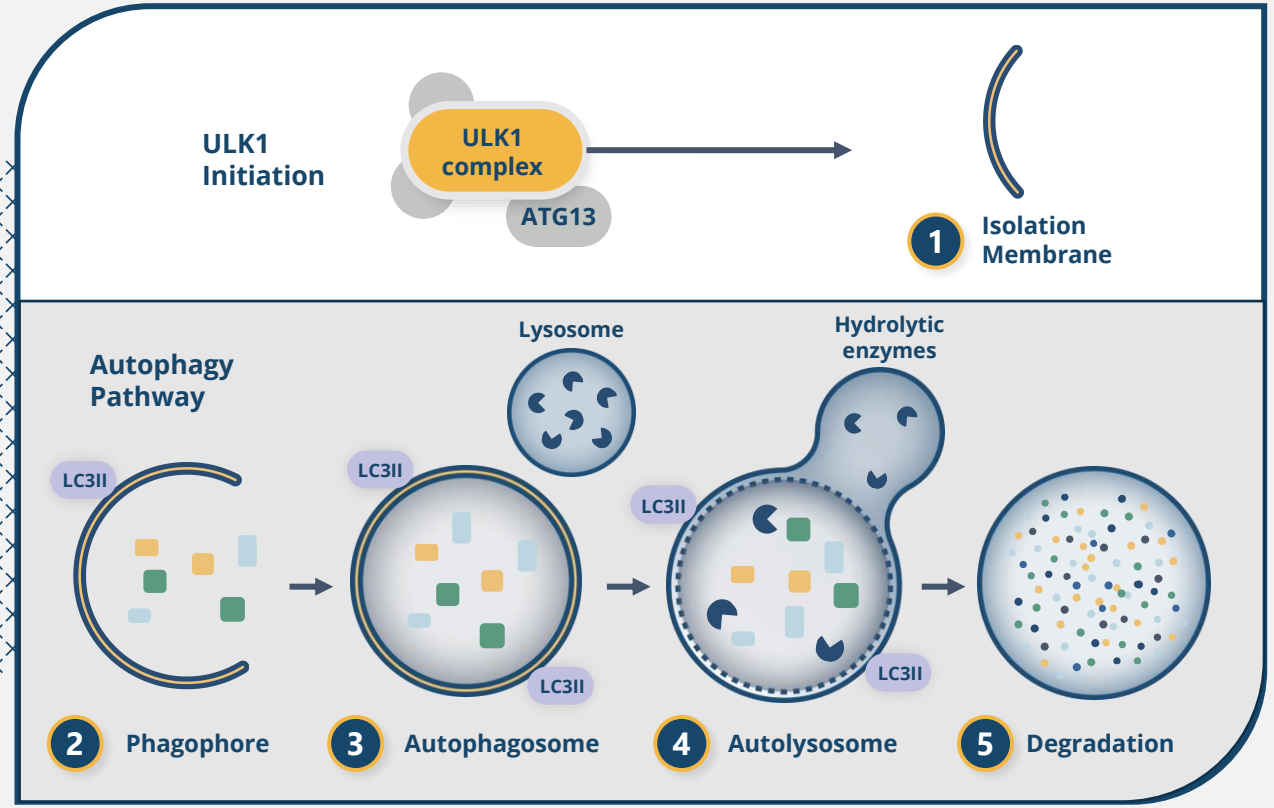
DCC-3116 PHASE 1 TRIAL UNDERWAY

- Single dose escalation underway
- Safety, pharmacokinetic, pharmacodynamic readouts
- Identification of recommended dose for Phase 1b combination studies
- Identification of MTD

Notes: BRAF=proto-oncogene b-RAF; CRC=colorectal cancer; EGFR=epidermal growth factor receptor; G12C=single point mutation with a glycine-to-cysteine substitution at codon 12; KRAS=Kirsten rat sarcoma virus; MTD=maximum tolerated dose; NSCLC=non–small-cell lung cancer; PDAC=pancreatic ductal adenocarcinoma; RAF=rapidly accelerated fibrosarcoma; RAS=rat sarcoma gene; RTK=receptor tyrosine kinase; ULK=unc-51-like kinase.

AUTOPHAGY: A BROAD RESISTANCE MECHANISM IN CANCER

ULK: Initiating Factor for Autophagy



- Autophagy is a catabolic process in which cells recycle components to generate energy
- RTK-, RAS-, and RAF-mutant cancer cells activate autophagy in order to survive stresses or damage **due to anti-cancer therapeutic intervention** with MAPK and PI3K pathway inhibitors
- The **ULK kinase initiates the autophagy pathway** and provides a potential targeted approach to selectively inhibit autophagy in these cancers
- **DCC-3116 is a first-in-class small molecule** designed to inhibit cancer autophagy by inhibiting ULK kinase

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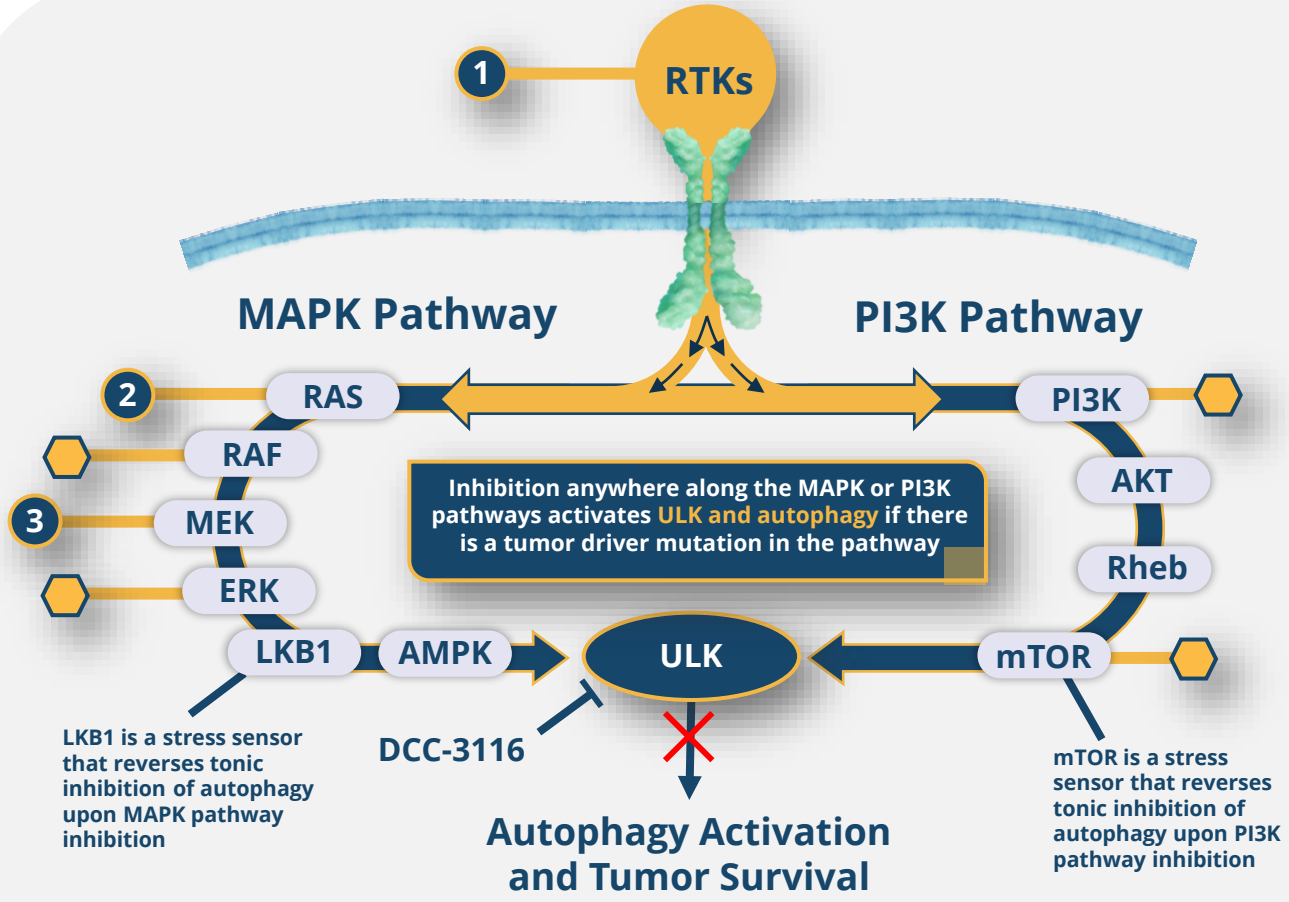
Notes: ATG13=Autophagy-related protein 13; MAPK=mitogen-activated protein kinase; PI3K=phosphatidylinositol-3 kinase; RAF=rapidly accelerated fibrosarcoma; RAS=rat sarcoma gene; RTK=receptor tyrosine kinase; ULK=unc-51-like kinase.

CENTRAL ROLE FOR AUTOPHAGY IN THE RAS/MAPK AND PI3K PATHWAYS



Growing Preclinical Validation for Role of Autophagy in Cancer

1 DCC-3116 In Combination with RTK Inhibition

- DCC-3116 exhibits synergy with osimertinib and afatinib resulting in tumor regression in EGFR-mutant NSCLC *in vivo*

2 DCC-3116 In Combination with KRAS G12C Inhibition

- DCC-3116 exhibits synergy with AMG-510 resulting in tumor regression in KRAS G12C-mutant NSCLC *in vivo*

3 DCC-3116 In Combination with MEK Inhibition

- DCC-3116 exhibits synergy in combination with trametinib and inhibited pancreatic, lung, and melanoma xenograft tumor growth

Other targets where therapeutic intervention activates ULK and autophagy

Notes: AKT=protein kinase B; AMPK=AMP-activated protein kinase; EGFR=epidermal growth factor receptor; ERK=extracellular signal-regulated kinase; G12C=single point mutation with a glycine-to-cysteine substitution at codon 12; KRAS=kirsten rat sarcoma virus; LKB1=liver kinase B1; MAPK=mitogen-activated protein kinase; MEK=mitogen-activated extracellular signal-regulated kinase; mTOR=mammalian target of rapamycin; NSCLC=non–small-cell lung cancer; PI3K=phosphatidylinositol-3 kinase; RAF=rapidly accelerated fibrosarcoma; RAS=rat sarcoma gene; Rheb=ras homolog enriched in brain; RTK=receptor tyrosine kinase; ULK=unc-51-like kinase.

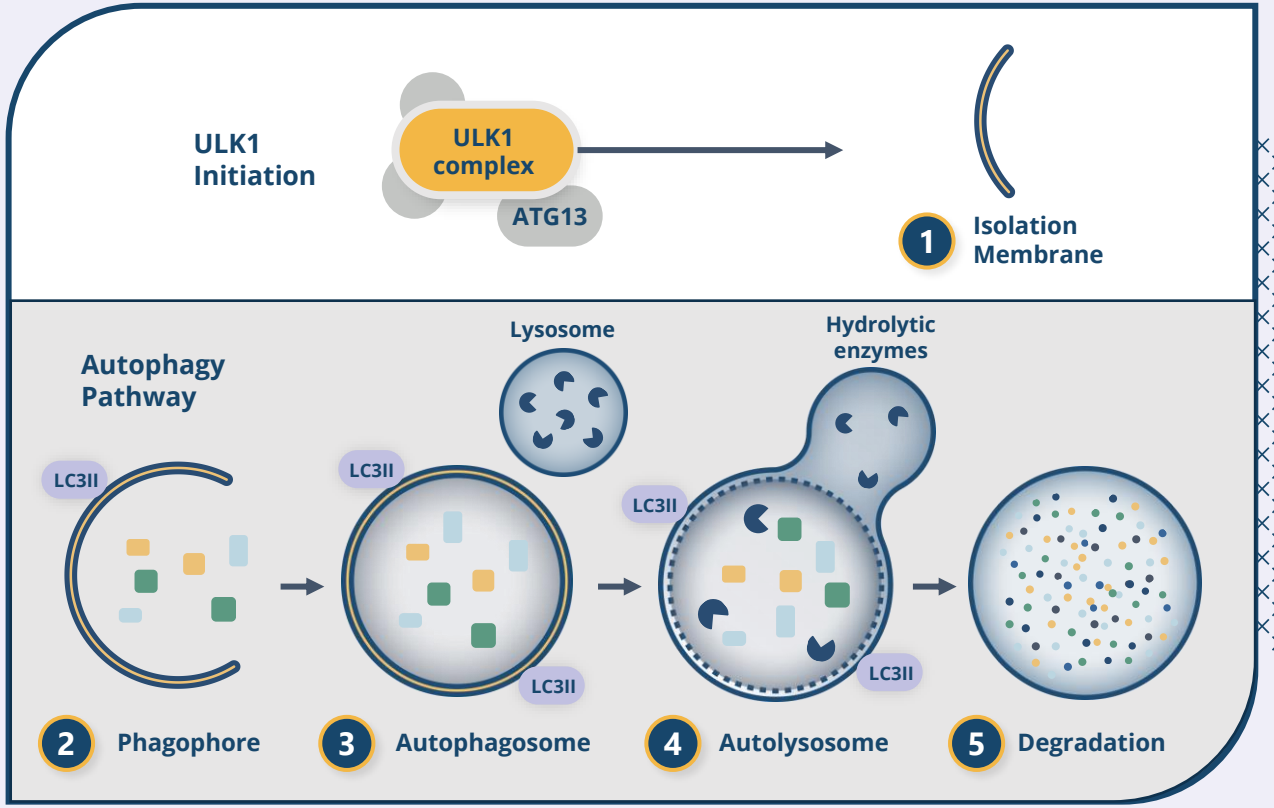
STRATEGIES FOR BLOCKING AUTOPHAGY IN CANCER

ULK Inhibition

- ULK is initiating factor of autophagy
- Druggable serine/threonine kinase
- Receives and processes key input from nutrient and stress sensors

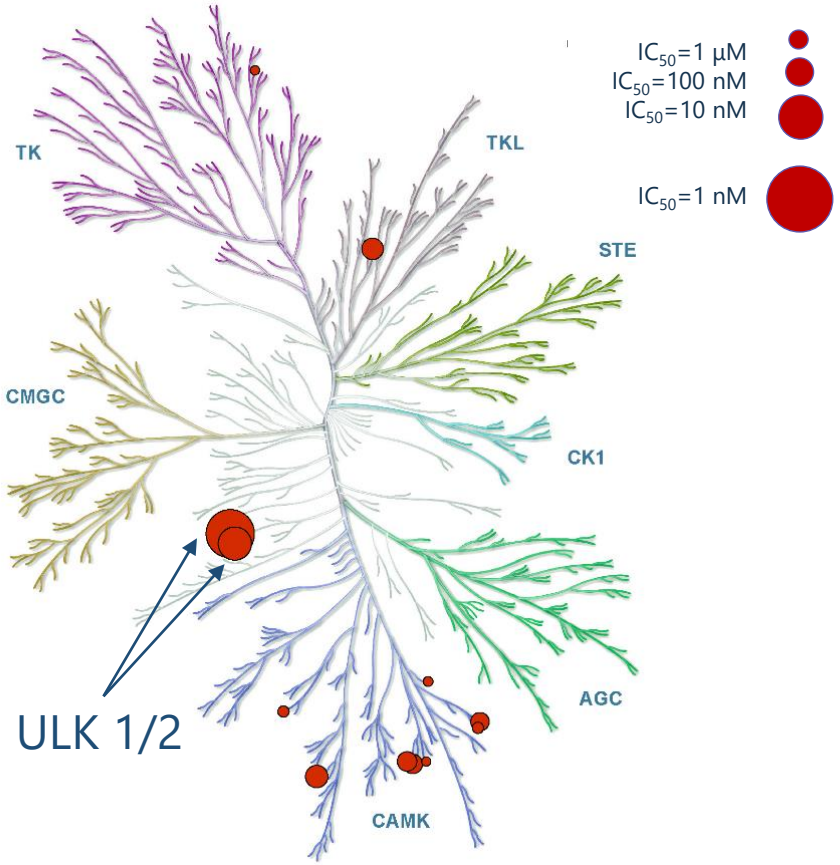
Lysosomal Inhibition

- Indirect and non-selective inhibition by preventing degradation of the contents
- Elevated pH inactivates hydrolases
- Interference with normal lysosomal house-keeping functions



Notes: ATG13=autophagy-related protein 13; ULK=unc-51-like kinase.

POTENT AND SELECTIVE ULK INHIBITOR DESIGNED TO INHIBIT AUTOPHAGY



First-in-Class Switch-Control ULK Kinase Inhibitor

- Potent and selective inhibitor of ULK, the initiating factor in autophagy
- Strong preclinical data in combination with RTK/RAS/MAPK inhibitors
- Potential backbone combination agent across >70% of cancers

Highly Potent (Cellular IC_{50} values for ULK inhibition)

- ULK1 6 nM
- ULK2 9 nM

Highly Selective

- No off-target kinases within 30-fold of ULK1
- Only 5 kinases within 100-fold of ULK1

Designed to Avoid CNS Exposure

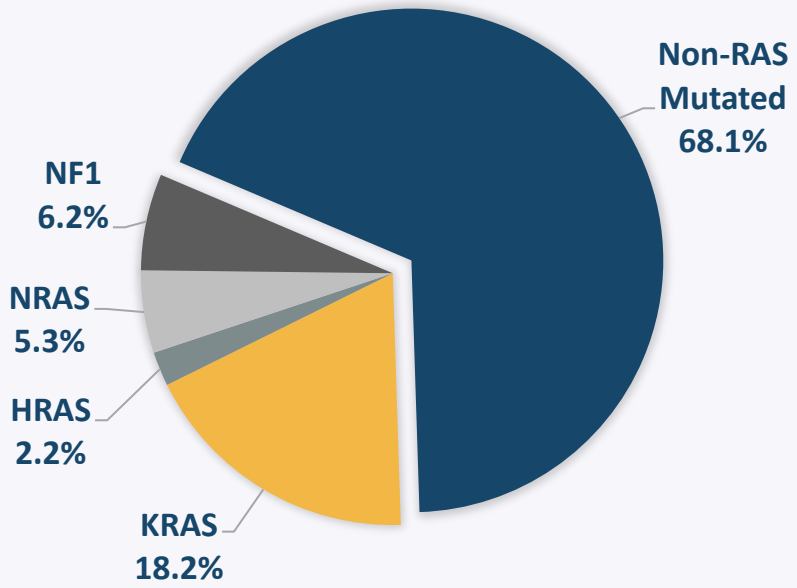
- Low ratio $brain_{ff}/plasma_{ff}$ (4.3%) to avoid CNS autophagy

Notes: MAPK=mitogen-activated protein kinase; RAS=rat sarcoma gene; RTK=receptor tyrosine kinase; ULK=unc-51-like kinase.

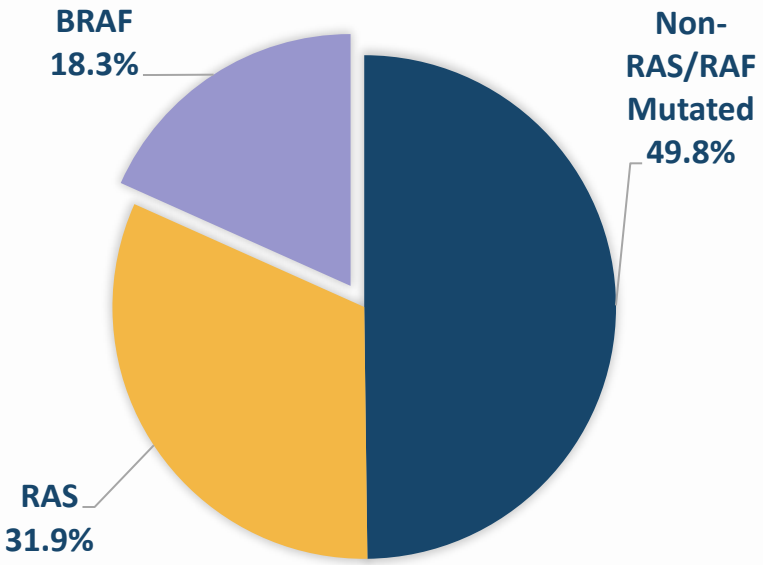
DCC-3116

SIGNIFICANT POTENTIAL OPPORTUNITY EXISTS AS MUTATIONS IN RAS/RAF/RTK SIGNALING OCCURS IN ~70% OF HUMAN CANCERS

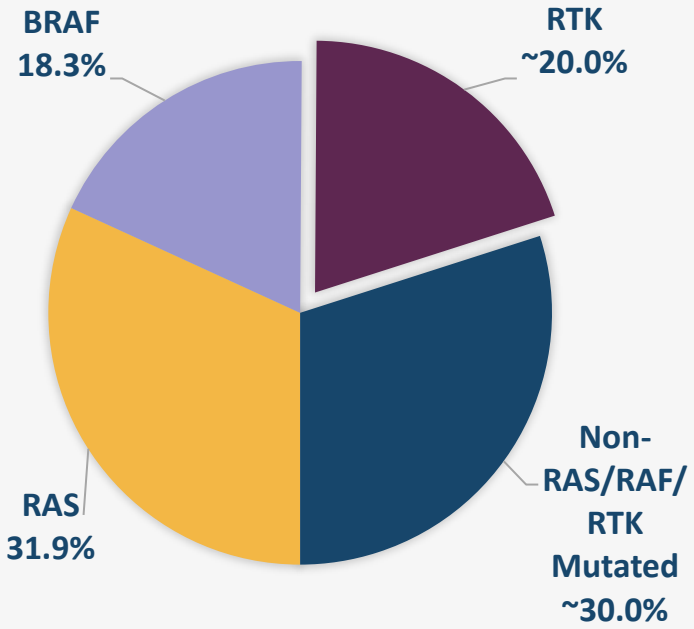
RAS Mutations
~32% of Human Cancers



RAF Mutations
~18% of Human Cancers



RTK Mutations
~20% of Human Cancers



RTK Known Tumor Driver Mutations

- EGFR
- HER2
- HER3
- KIT
- PDGFRa
- FLT3
- TRK A
- TRK B
- TRK C
- ALK
- ROS
- RET
- FGFR 2
- FGFR 3
- FGFR 4
- BCR-ABL
- BTK
- cMET exon 14 skipping

Source: COSMIC (Catalogue of Somatic Mutations in Cancer) Database, v90. **Notes:** RAF=rapidly accelerated fibrosarcoma serine/threonine protein kinase; RAS=rat sarcoma gene; RTK=receptor tyrosine kinase; KRAS=kirsten rat sarcoma virus; BRAF=proto-oncogene b-RAF; HRAS=Harvey rat sarcoma gene; NRAS=neuroblastoma RAS viral oncogene homolog; EGFR=epidermal growth factor receptor; HER2=human epidermal growth factor receptor 2= HER3=human epidermal growth factor receptor 3; PDGFRa=platlet derived growth factor receptor alpha; FLT3=fms-like tyrosine kinase 3; TRK A=Tropomyosin receptor kinase A; TRK B= Tropomyosin receptor kinase B; TRK C= Tropomyosin receptor kinase C; ALK=Anaplastic lymphoma kinase; RET=Rearranged during transfection; FGFR 2=Fibroblast growth factor receptor 2; FGFR 3= Fibroblast growth factor receptor 3; FGFR 4= Fibroblast growth factor receptor 4; BTK= Bruton tyrosine kinase; cMET=tyrosine-protein kinase Met.

GROWING PRECLINICAL DATA SUPPORT MULTIPLE COMBINATION PARTNERS

DCC-3116 Preclinical Combination Data

RTKs

Preclinical Combination Data:
- Osimertinib (EGFRi)
- Afatinib (EGFRi)

RAS

Preclinical Combination Data:
- Sotorasib (KRAS G12Ci)
- Adagrasib (KRAS G12Ci)

MAPK

Preclinical Combination Data:
- Trametinib (MEKi)
- Binimetinib (MEKi)
- Ulixertinib (ERKi)

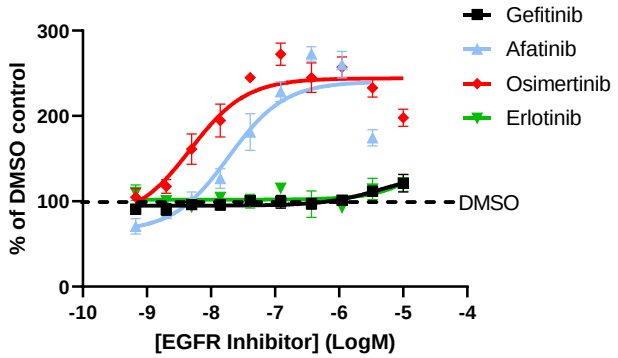
Notes: EGFR=epidermal growth factor receptor; ERK=extracellular signal-regulated kinase; G12C=single point mutation with a glycine-to-cysteine substitution at codon 12; KRAS=kirsten rat sarcoma virus; MAPK=mitogen-activated protein kinase; MEK=mitogen-activated extracellular signal-regulated kinase; RAS=rat sarcoma gene; RTK=receptor tyrosine kinase.

DCC-3116 INHIBITS RTK, RAS, & MAPK PATHWAY INHIBITOR-INDUCED ULK ACTIVITY

DCC-3116 Reverses EGFR Inhibitor-Induced ULK Activation

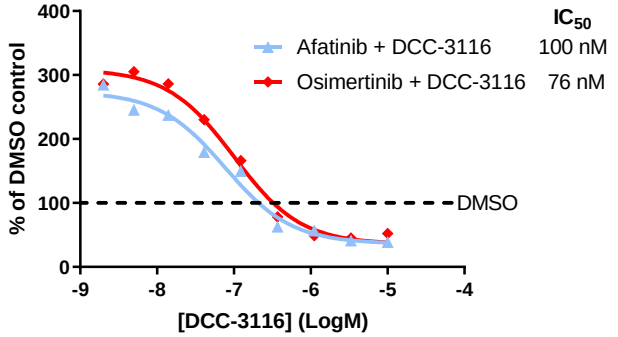
NSCLC: H1975 pATG13 ELISA

EGFR Inhibitors Induce ULK Activity



NSCLC: H1975 pATG13 ELISA

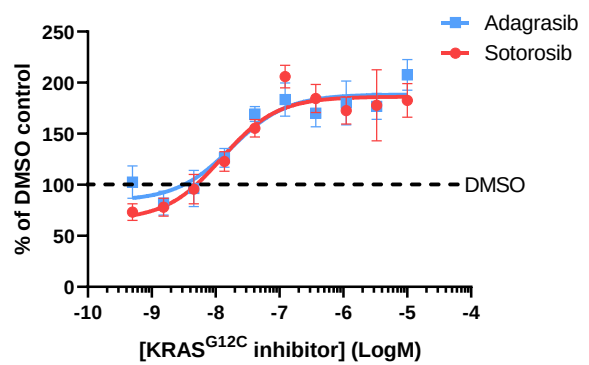
DCC-3116 Inhibits EGFR Family Inhibitor-Induced ULK Activity



DCC-3116 Reverses KRAS^{G12C} Inhibitor-Induced ULK Activation

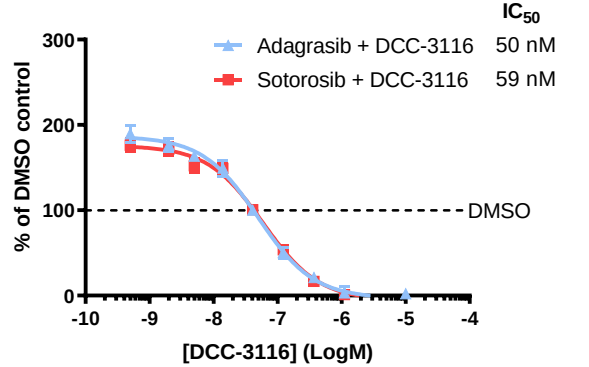
NSCLC: H358 pATG13 ELISA

KRAS^{G12C} Inhibitors Induce ULK Activity



NSCLC: H358 pATG13 ELISA

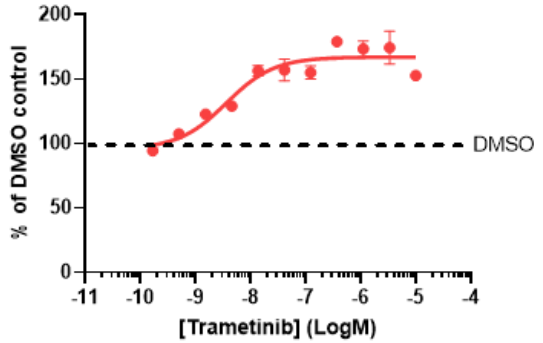
DCC-3116 Inhibits KRAS^{G12C} Inhibitor-Induced ULK Activity



DCC-3116 Reverses MAPK Inhibitor-induced ULK Activation

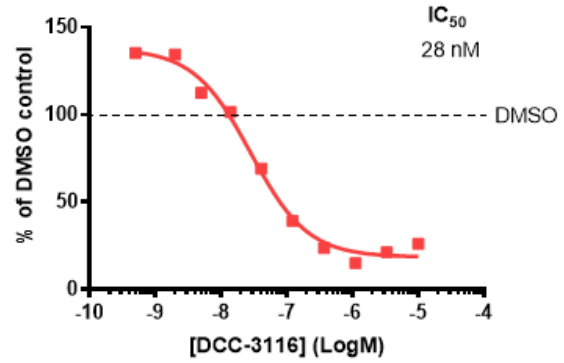
PDAC: MiaPaca-2 pATG13 ELISA

Trametinib Induces ULK Activity



PDAC: MiaPaca-2 pATG13 ELISA

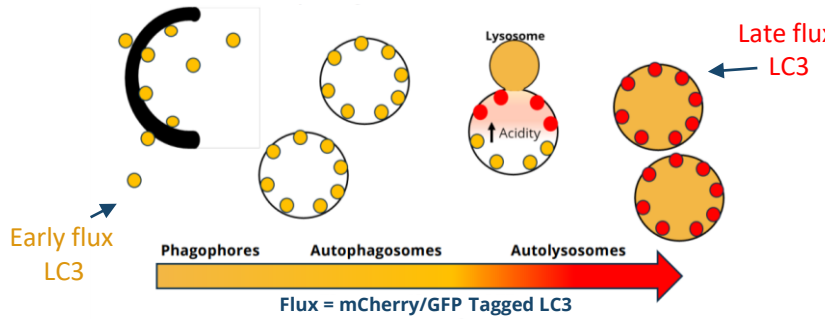
DCC-3116 Inhibits Trametinib-Induced ULK Activity



Notes: EGFR=epidermal growth factor receptor; G12C=single point mutation with a glycine-to-cysteine substitution at codon 12; KRAS=Kirsten rat sarcoma virus; MAPK=mitogen-activated protein kinase; NSCLC=non–small-cell lung cancer; PDAC=pancreatic ductal adenocarcinoma; RAS=rat sarcoma gene; RTK=receptor tyrosine kinase; ULK=unc-51-like kinase.

DCC-3116 OBSERVED PRECLINICALLY TO DURABLY AND POTENTLY INHIBIT AUTOPHAGY INDUCED BY MULTIPLE PATHWAY INHIBITORS

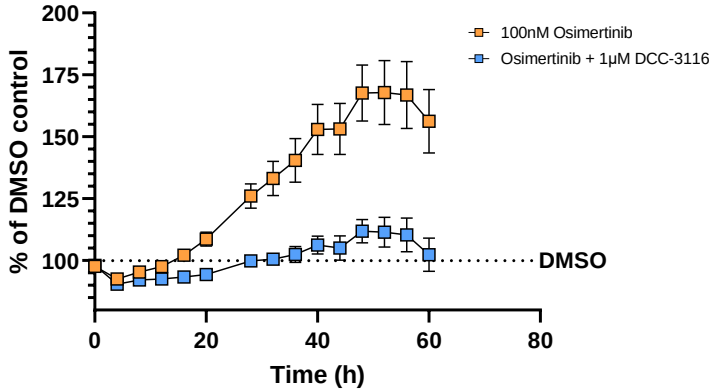
Autophagic Flux Maturation



- RTK/RAS/MAPK induces significant autophagy flux
- DCC-3116 can sustainably inhibit this induction

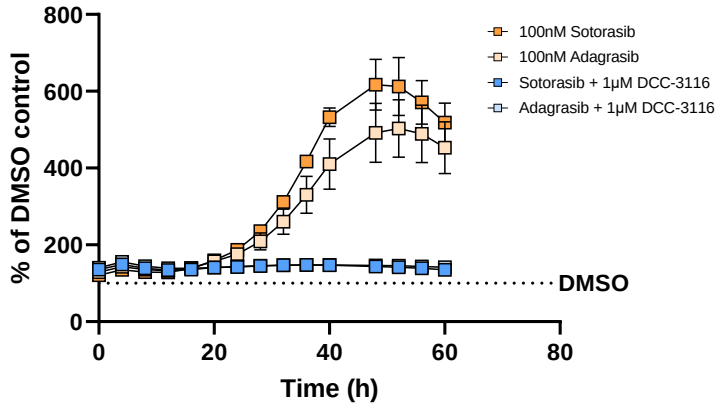
DCC-3116 + EGFR Inhibitor

NSCLC: H1975 Osimertinib-induced Autophagy Induction Over Time (mCherry/GFP Tagged LC3)



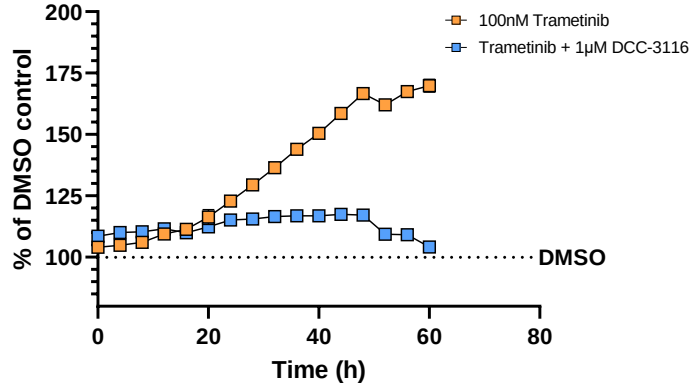
DCC-3116 + KRAS^{G12C} Inhibitor

NSCLC: H358 Sotorasib vs. Adagrasib-induced Autophagy Induction Over Time (mCherry/GFP Tagged LC3)



DCC-3116 + Trametinib (MEK)

PDAC: MiaPaca-2 Trametinib-induced Autophagy Induction Over Time (mCherry/GFP Tagged LC3)

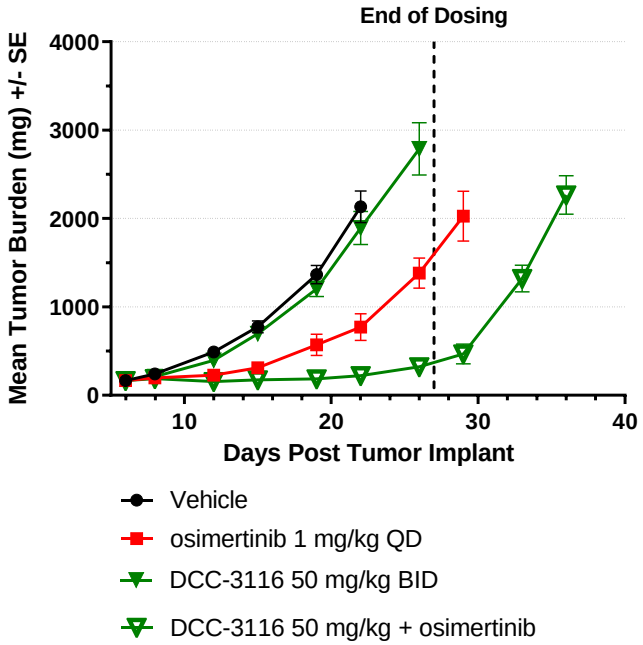


Notes: EGFR=epidermal growth factor receptor; G12C=single point mutation with a glycine-to-cysteine substitution at codon 12; KRAS=Kirsten rat sarcoma virus; MAPK=mitogen-activated protein kinase; NSCLC=non–small-cell lung cancer; PDAC=pancreatic ductal adenocarcinoma; RAS=rat sarcoma gene; RTK=receptor tyrosine kinase.

DCC-3116 EXHIBITED ADDITIVITY OR SYNERGY IN COMBINATION WITH MULTIPLE RTK, RAS, & MAPK PATHWAY INHIBITORS

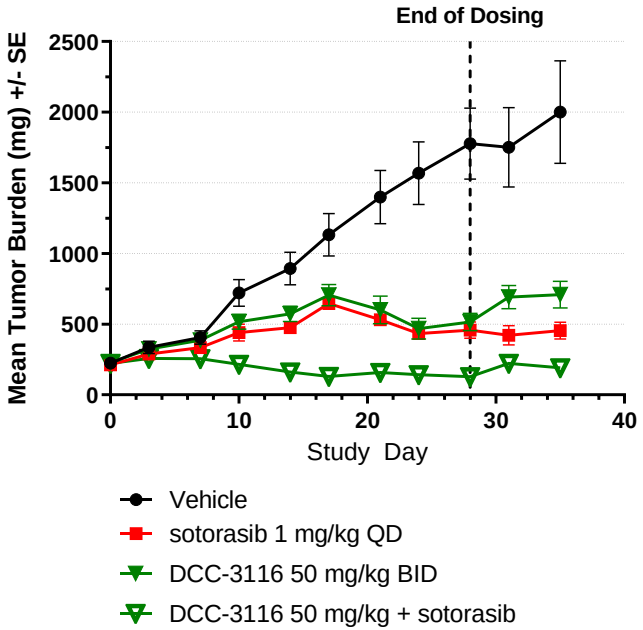
DCC-3116 + Osimertinib (EGFR)

NSCLC: H1975 Tumor Growth



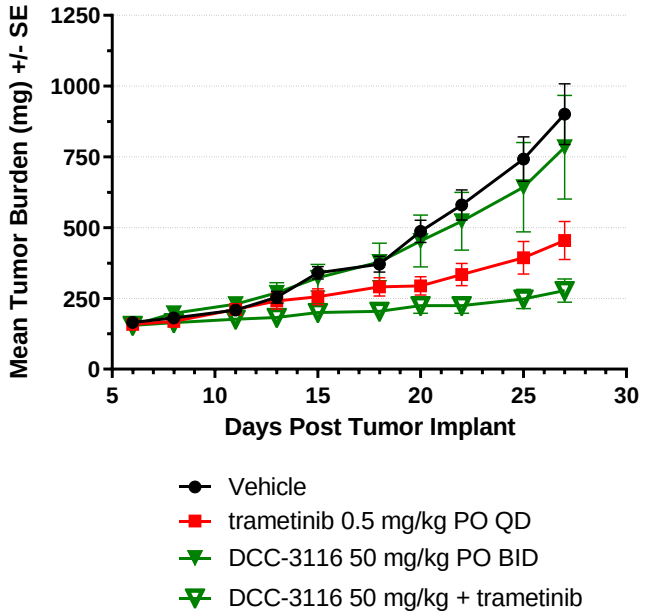
DCC-3116 + Sotorasib (KRAS)

NSCLC: H358 Tumor Growth



DCC-3116 + Trametinib (MEK)

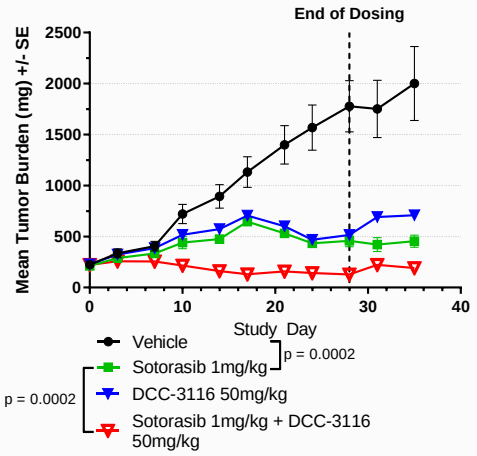
PDAC: MiaPaca-2 Tumor Growth



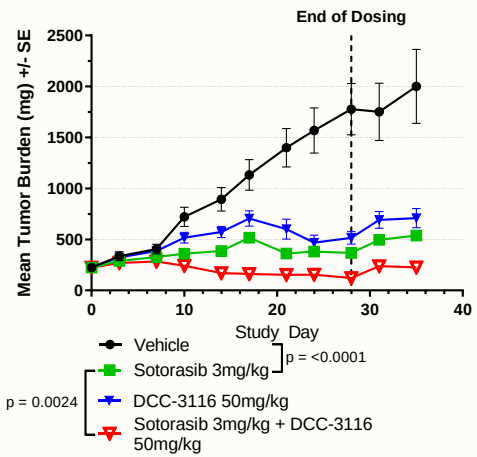
Notes: BID=twice daily; EGFR=epidermal growth factor receptor; KRAS=Kirsten rat sarcoma virus; MAPK=mitogen-activated protein kinase; MEK=mitogen-activated extracellular signal-regulated kinase; NSCLC=non–small-cell lung cancer; PDAC=pancreatic ductal adenocarcinoma; PO=by mouth; QD=once daily; RAS=rat sarcoma gene; RTK=receptor tyrosine kinase.

DCC-3116 DEMONSTRATED DEEPER AND LONGER REGRESSIONS IN COMBINATION WITH SOTORASIB IN KRAS^{G12C} H358 NSCLC

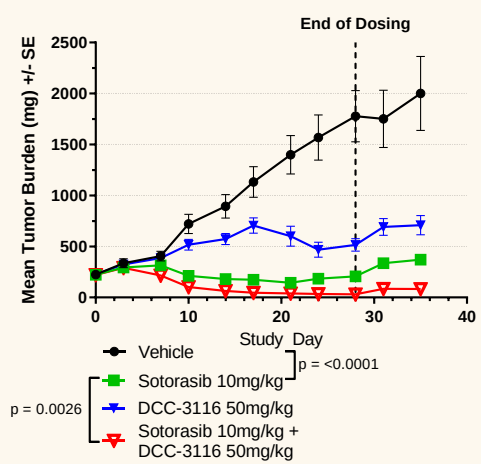
DCC-3116 + Sotorasib 1mg/kg



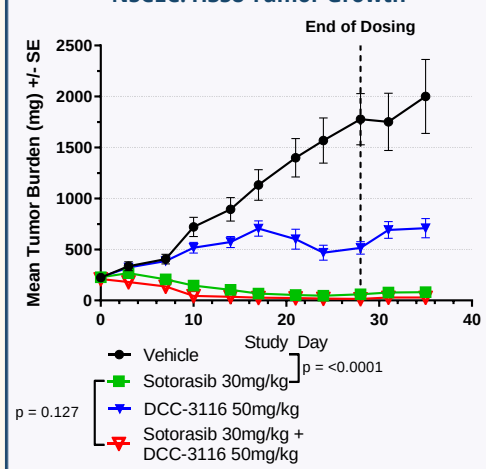
DCC-3116 + Sotorasib 3mg/kg



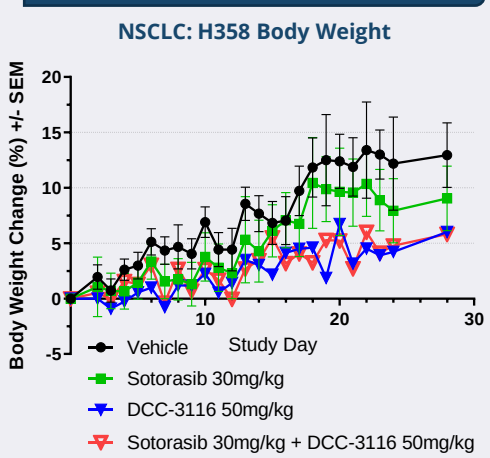
DCC-3116 + Sotorasib 10mg/kg



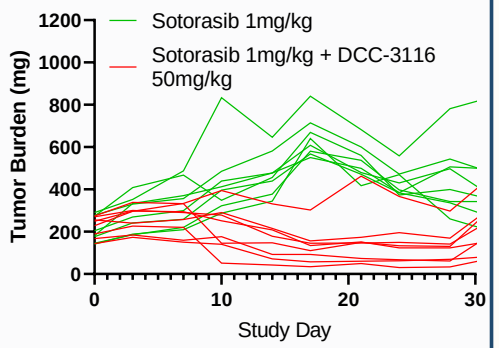
DCC-3116 + Sotorasib 30mg/kg

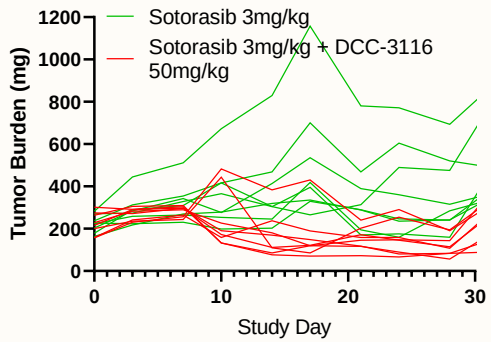


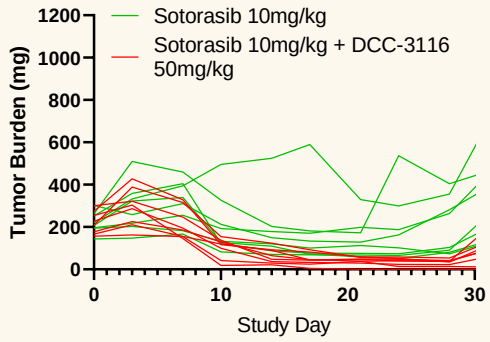
DCC-3116 + Sotorasib 30mg/kg

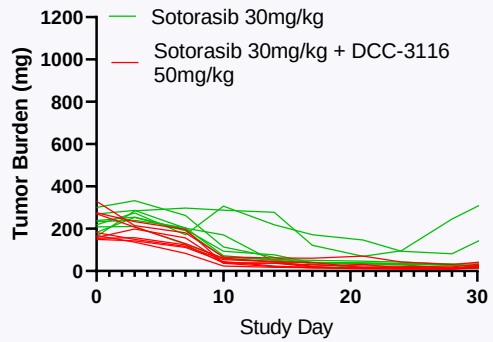


Spaghetti Plots Demonstrating Sustained Regressions In Combination Cohorts









Notes: Data presented at the AACR Meeting 2022; AMG510 was dosed QD and DCC-3116 was dosed BID; G12C=single point mutation with a glycine-to-cysteine substitution at codon 12; KRAS=Kirsten rat sarcoma virus; NSCLC=non–small-cell lung cancer.

MULTICENTER, OPEN-LABEL, FIRST-IN-HUMAN STUDY AS A SINGLE AGENT AND IN COMBINATION WITH A MEK INHIBITOR

Part 1

Dose Escalation Phase (3 + 3 design)

DCC-3116
Single agent dose escalation cohorts

→ **RP2D or MTD** of DCC-3116 as a single agent

DCC-3116 + MEK inhibitor *(trametinib)*
Combination dose escalation cohorts

→ **RP2D** of the combination

Dose Escalation Phase Inclusion Criteria

- Histologically confirmed diagnosis of an advanced or metastatic solid tumor with a documented RAS or RAF mutation

KRAS G12C inhibitor combination in NSCLC planned, subject to feedback from regulatory authorities

Part 2

Dose Expansion Phase

Cohort 1 (n=20)
Pancreatic ductal adenocarcinoma[1]

Cohort 2 (n=20)
Non-small cell lung cancer[2]

Cohort 3 (n=20)
Colorectal cancer[2]

Cohort 4 (n=20)
Melanoma[3]

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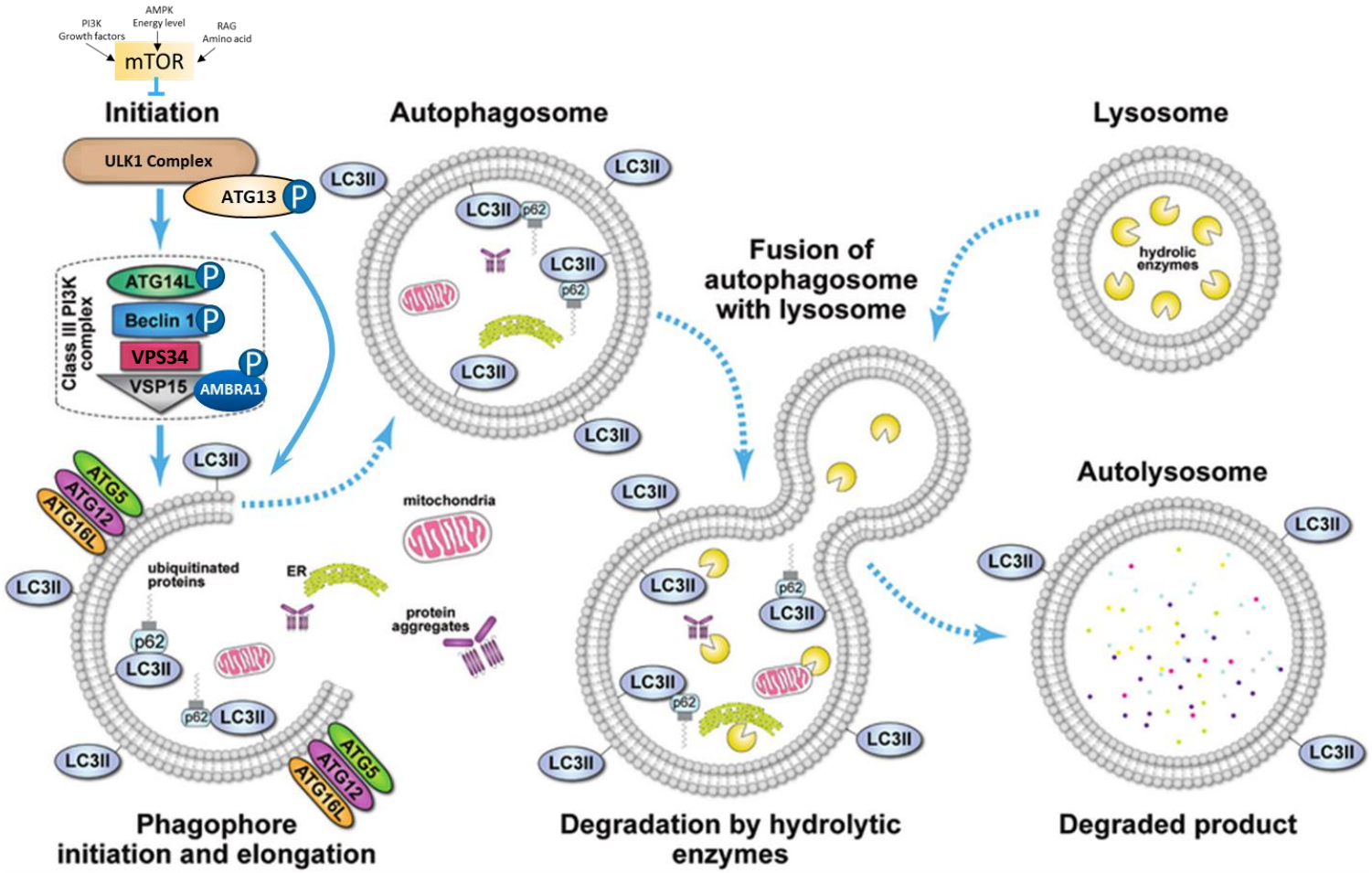
Notes: G12C=single point mutation with a glycine-to-cysteine substitution at codon 12; KRAS=kirsten rat sarcoma virus; MEK=MAPK/ERK kinase; MTD=maximum tolerated dose; NSCLC=non–small-cell lung cancer; RAF=rapidly accelerated fibrosarcoma serine/threonine protein kinase; RAS=rat sarcoma gene; RP2D=recommended Phase 2 dose; (1) with a documented mutation in KRAS or BRAF; (2) with a documented mutation in KRAS, NRAS, or BRAF; (3) with a documented mutation in NRAS or BRAF.

PERIPHERAL BLOOD AUTOPHAGY PD ASSESSMENTS

ULKi **decreases** pATG14 in PBMNCs



Ndoye A and Weeraratna AT. Autophagy- An emerging target for melanoma therapy [version 1]. F1000Research 2016, 5:1888. (doi: 10.12688/f1000research.8347.1)

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PUBLICATIONS AND PRESENTATIONS

SELECTED THIRD-PARTY AUTOPHAGY PUBLICATIONS

A. Reviews

1. Cox, AD et al. Drugging the undruggable RAS: Mission possible? Nat Rev Drug Discov 2014; 13(11):828-51. https://www.ncbi.nlm.nih.gov/pubmed/25323927
2. Dolgin, Elie. Anticancer autophagy inhibitors attract 'resurgent' interest. Nature Reviews Drug Discovery 2019; 18: 408-410. https://www.nature.com/articles/d41573-019-00072-1
3. Papke, B et al. Drugging RAS: Know the enemy. Science 2017; 1158-1163. https://www.ncbi.nlm.nih.gov/pubmed/28302824

B. Mutant RAS cancers

1. Bryant, Kirsten L. et al. Combination of ERK and autophagy inhibition as treatment approach for pancreatic cancer. Nature Medicine 2019; 25: 628-640. https://www.nature.com/articles/s41591-019-0368-8
2. Kinsey, Conan G. et al. Protective autophagy elicited by RAF→MEK→ERK inhibition suggests a treatment strategy for RAS-driven cancers. Nature Medicine 2019; 25: 620-627. https://www.nature.com/articles/s41591-019-0367-9
3. Lee, Chih-Shia et al. MAP kinase and autophagy pathways cooperate to maintain RAS cancer cell survival. PNAS 2019; 16(10): 4508-4517. https://www.pnas.org/content/116/10/4508
4. Yang et al, Pancreatic cancer requires autophagy for tumor growth, Genes and Development, 2011; 25. 717-729. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3070934/
5. Guo, Jessie Yanxiang et al. Activated Ras requires autophagy to maintain oxidative metabolism and tumorigenesis. Genes & Development 2011; 25: 460-470. http://genesdev.cshlp.org/content/25/5/460.abstract

C. RTK mutated cancers

1. Kwon Y, Kim M, Jung HS, Kim Y, Jeoung D. Targeting Autophagy for Overcoming Resistance to Anti-EGFR Treatments. Cancers. 2019; 11(9):1374. https://doi.org/10.3390/cancers11091374

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SELECTED THIRD-PARTY AUTOPHAGY PUBLICATIONS

D. Immuno-oncology

1. Deng, J., Thennavan, A., Dolgalev, I. et al. ULK1 inhibition overcomes compromised antigen presentation and restores antitumor immunity in LKB1-mutant lung cancer. Nat Cancer 2021; 2:503–514. https://doi.org/10.1038/s43018-021-00208-6
2. Poillet-Perez, L. et al. Autophagy promotes growth of tumors with high mutational burden by inhibiting a T-cell immune response. Nat Cancer 2020; 1:923–934. https://doi.org/10.1038/s43018-020-00110-7
3. Yamamoto, K et al. Autophagy promotes immune evasion of pancreatic cancer by degrading MHC-I. Nature 2020; 58:100–105. https://doi.org/10.1038/s41586-020-2229-5
4. Thorburn, A., Towers, C.G. Enhancing anti-tumor immunity by autophagy inhibition. Nat Cancer 2021; 2:484–486. https://doi.org/10.1038/s43018-021-00214-8
5. Kono et al, Cyclic Dinucleotides Trigger ULK1 (ATG1) Phosphorylation of STING to Prevent Sustained Innate Immune Signaling, Cell 155, 2013; 688–698. https://www.cell.com/fulltext/S0092-8674(13)01223-3

E. Non-cancer cell systemic effects of autophagy in oncology

1. Yang, A. et al. Autophagy sustains pancreatic cancer growth through both cell-autonomous and nonautonomous mechanisms. Cancer Discovery 2018; 8: 276-287. http://cancerdiscovery.aacrjournals.org/content/early/2018/01/09/21
59-8290.CD-17-0952.full-text.pdf
2. Poillet-Perez et al, Autophagy maintains tumour growth through circulating arginine, Nature 2018; 563, 569. https://www.nature.com/articles/s41586-018-0697-7

F. Cancer stemness and persistence states

1. Ianniciello A, Zarou MM, Rattigan KM, et al. ULK1 inhibition promotes oxidative stress-induced differentiation and sensitizes leukemic stem cells to targeted therapy. Sci Transl Med. https://pubmed.ncbi.nlm.nih.gov/34586834/
2. Rehman et al, Colorectal Cancer Cells Enter a Diapause-like DTP State to Survive Chemotherapy, Cell 2021; 184, 226–242. https://www.cell.com/cell/pdf/S0092-8674(20)31535-X.pdf

G. Glucose metabolism/regulation of Reactive Oxygen Species (ROS)

1. Ianniciello A, Zarou MM, Rattigan KM, et al. ULK1 inhibition promotes oxidative stress-induced differentiation and sensitizes leukemic stem cells to targeted therapy. Sci Transl Med. 2021;13(613):eabd5016. https://doi.org/10.1126/scitranslmed.abd5016
2. Li et al. ULK1/2 Constitute a Bifurcate Node Controlling Glucose Metabolic Fluxes in Addition to Autophagy, Molecular Cell 2016; 62, 359–370. https://www.cell.com/molecular-cell/pdfExtended/S1097-2765(16)30059-4

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DECIPHERA PRECLINICAL PRESENTATIONS & PUBLICATIONS

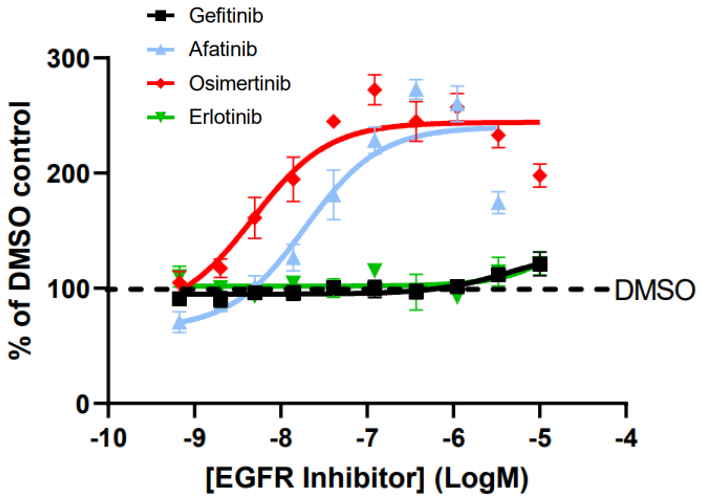
1. Bogdan M. et al. DCC-3116, a first-in-class selective inhibitor of ULK1/2 kinases and autophagy, synergizes with EGFR inhibitors osimertinib and afatinib in NSCLC preclinical models. AACR-NCI-EORTC International Virtual Conference. 2021. (Linked here)
2. Flynn D. Discovery of ULK1/2 inhibitor DCC-3116 for treatment of RAS-driven cancers. Drugging Autophagy Summit. 2020. (Linked here)
3. Smith B. et al. Preclinical studies with DCC-3116, an ULK kinase inhibitor designed to inhibit autophagy as a potential strategy to address mutant RAS cancers. AACR-NCI-EORTC. 2019. (Linked here)
4. Deciphera. DCC-3116: A Selective ULK Kinase Inhibitor; Potential First-in-Class Autophagy Inhibitor to Treat Mutant RAS Cancers. Corporate Presentation. 2019. (Linked here)
5. McMahon M. et al. DCC-3116, a first-in-class selective inhibitor of ULK1/2 kinases and autophagy, synergizes with the KRASG12C inhibitor sotorasib resulting in tumor regression in KRAS mutant NSCLC xenograft models. AACR Annual Meeting. 2022. (Linked here)

APPENDIX

DCC-3116 INHIBITS **OSIMERTINIB** AND **AFATINIB**-INDUCED pATG13 AND AUTOPHAGY

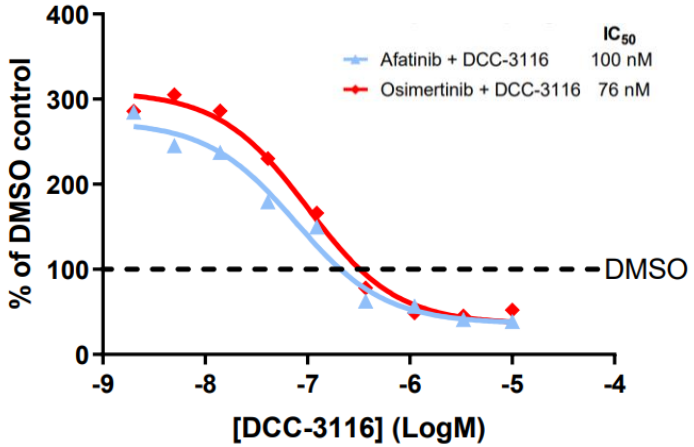
EGFR Inhibitors Induce ULK Activity

NSCLC: H1975 pATG13 ELISA



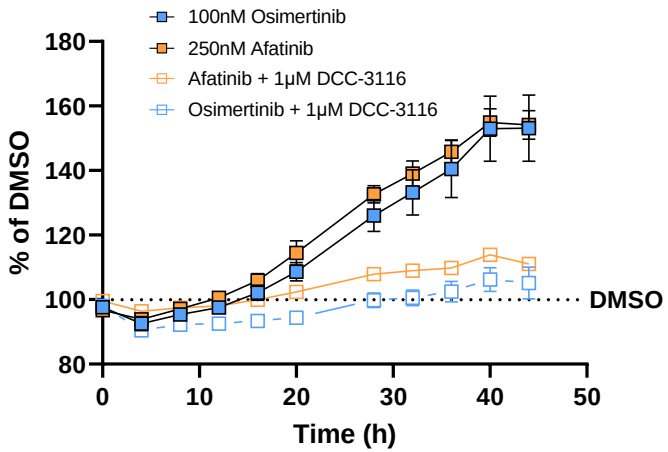
DCC-3116 Inhibits EGFRi Induced ULK Activity

NSCLC: H1975 pATG13 ELISA



DCC-3116 + Osimertinib or Afatinib

NSCLC: Osimertinib-induced Autophagy Induction Over Time (mCherry/GFP Tagged LC3)



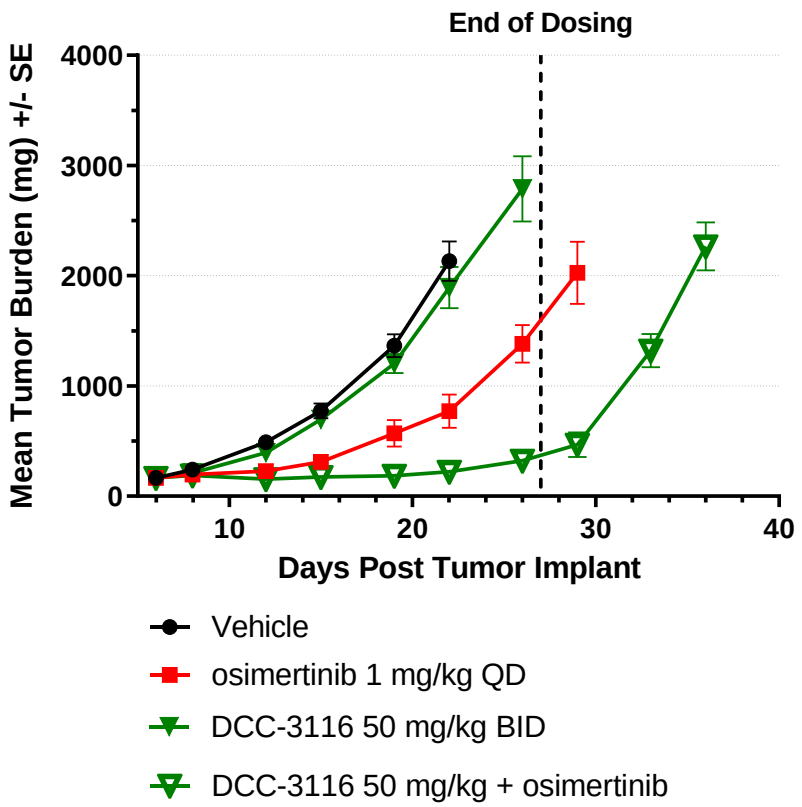
- Osimertinib and afatinib induce autophagy in the H1975 cell line, which is inhibited by DCC-3116.
- EGFR inhibitors (gefitinib and erlotinib) do not induce ULK-mediated ATG13 phosphorylation in the H1975 cell line (with a T790M mutation) as expected since they do not inhibit T790M mutation

Notes: Data presented at the AACR-NCI-EORTC Meeting 2021; ATG13=autophagy-related protein 13; EGFR=epidermal growth factor receptor; G12C=single point mutation with a glycine-to-cysteine substitution at codon 12; KRAS=kirsten rat sarcoma virus; MAPK=mitogen-activated protein kinase; NSCLC=non–small-cell lung cancer; PDAC=pancreatic ductal adenocarcinoma; RAS=rat sarcoma gene; RTK=receptor tyrosine kinase; ULK=unc-51-like kinase.

DCC-3116 EXHIBITS SYNERGY IN COMBINATION WITH **OSIMERTINIB** AND **AFATINIB**

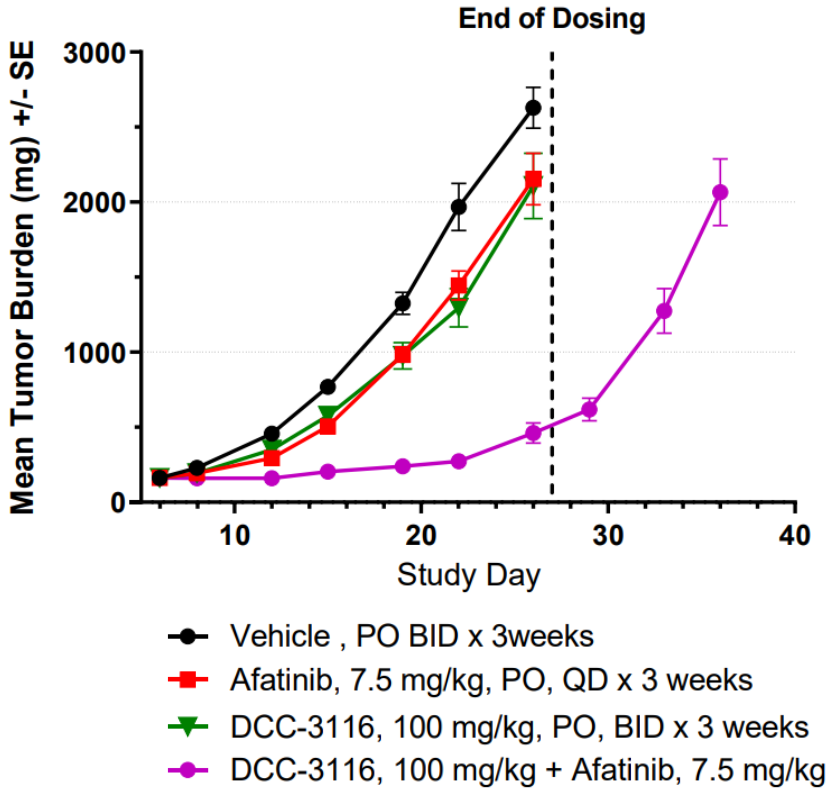
DCC-3116 + Osimertinib

NSCLC: H1975 Tumor Growth



DCC-3116 + Afatinib

NSCLC: H1975 Tumor Growth

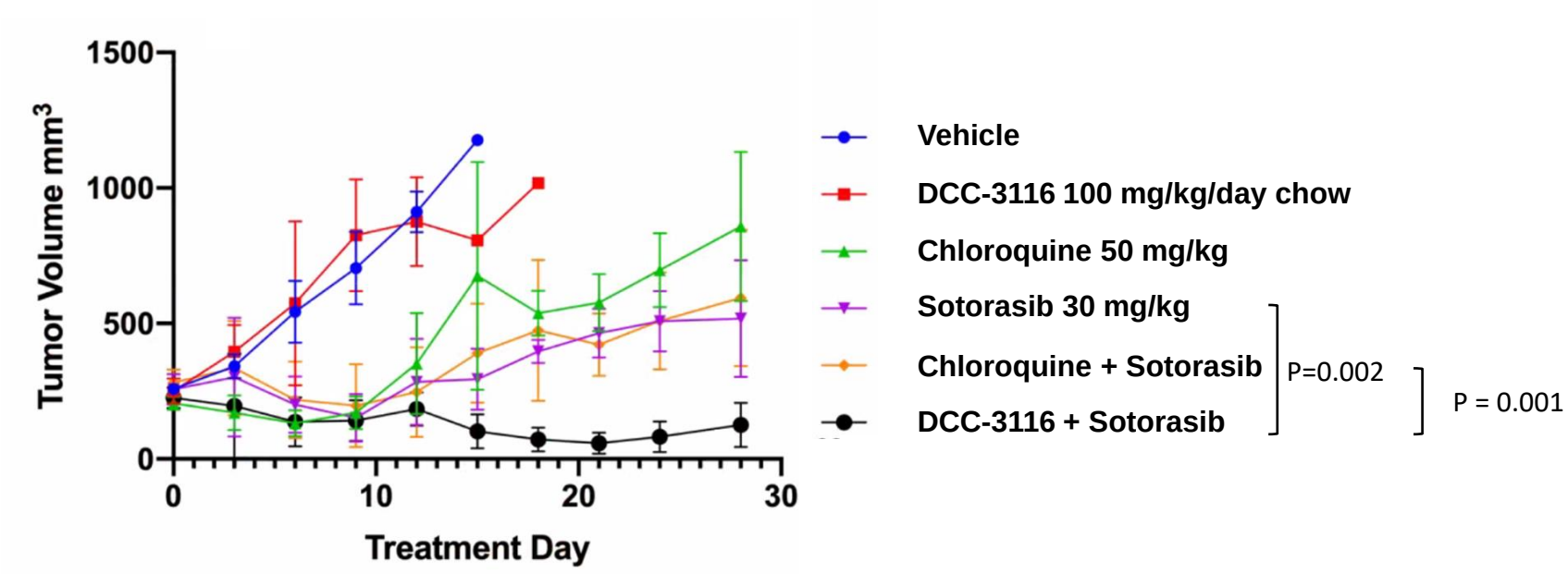


Notes: Data presented at the AACR-NCI-EORTC Meeting 2021; BID=twice daily; NSCLC=non–small-cell lung cancer; PO=by mouth; QD=once daily.

DCC-3116 OUTPERFORMED LYSOSOMAL INHIBITOR CHLOROQUINE AS A COMBINATION PARTNER TO **SOTORASIB** IN A KRAS^{G12C} NSCLC MODEL

DCC-3116 + Sotorasib Exhibits Regressions In a Resistant Calu-1 Model

NSCLC: Calu-1 (KRAS^{G12C}-driven) Xenograft



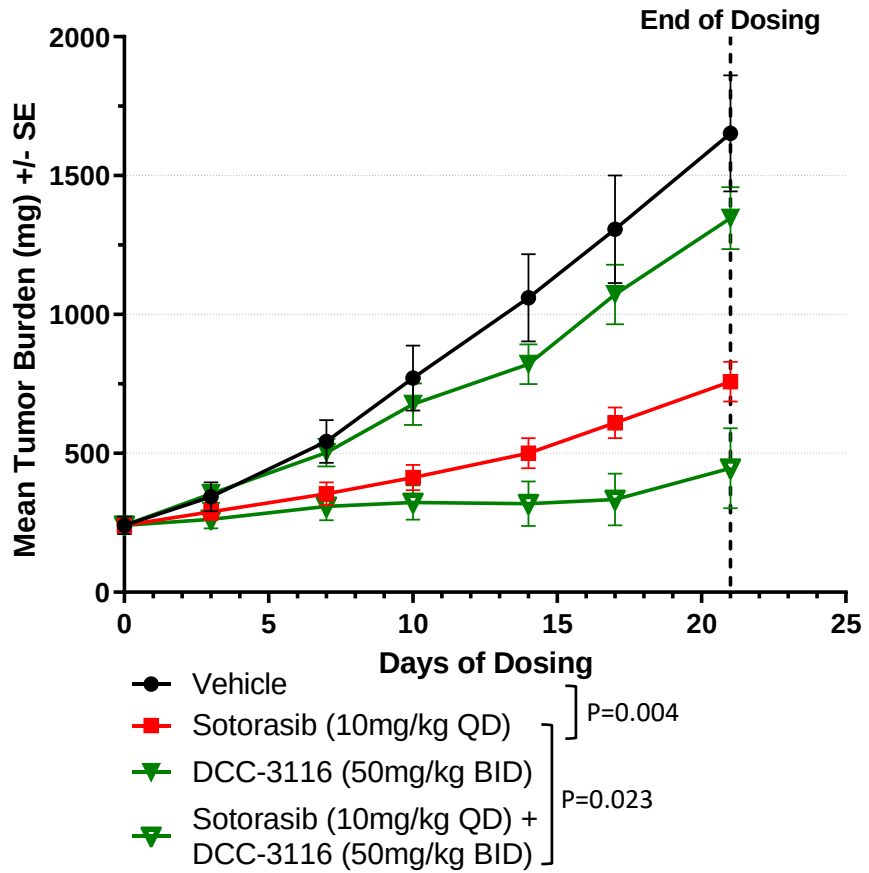
- **DCC-3116 in combination with sotorasib observed to outperform lysosomal in Calu-1 KRAS^{G12C}-driven xenografts**
- **Combination sotorasib plus DCC-3116 elicits tumor regression**

Notes: Data presented at the AACR Meeting 2022; G12C=single point mutation with a glycine-to-cysteine substitution at codon 12; KRAS=Kirsten rat sarcoma virus; NSCLC=non–small-cell lung cancer.

DCC-3116 EXHIBITS COMBINATION EFFICACY WITH **SOTORASIB** AND **ADAGRASIB** IN A PDX LUNG CANCER KRAS^{G12C} MODEL

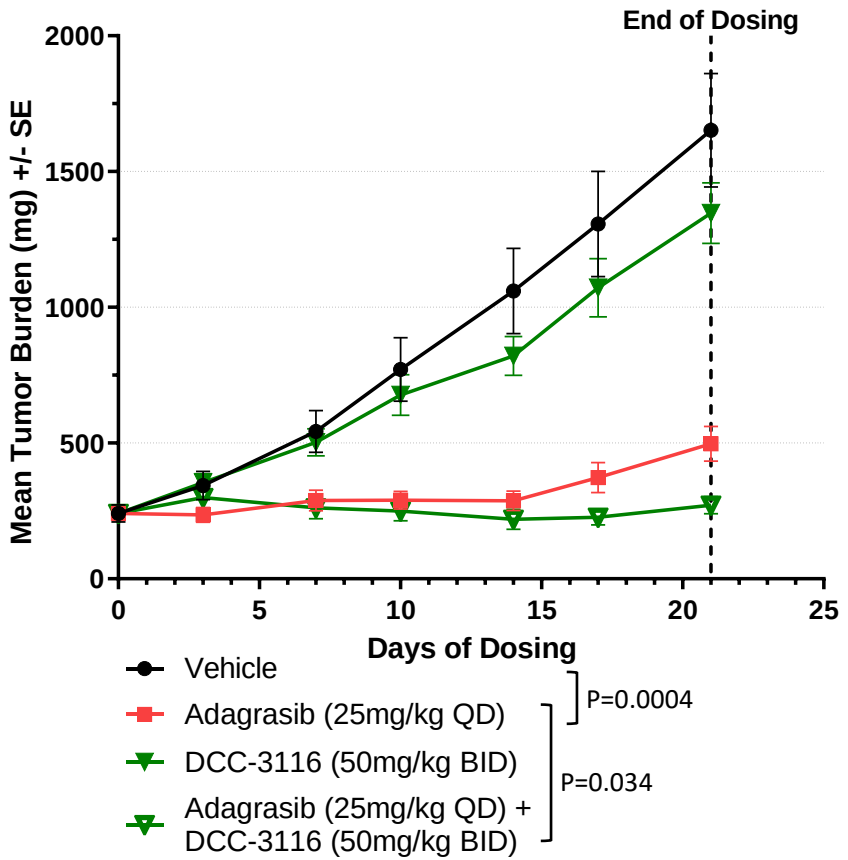
DCC-3116 + Sotorasib

NSCLC: LU11554 PDX Tumor Growth



DCC-3116 + Adagrasib

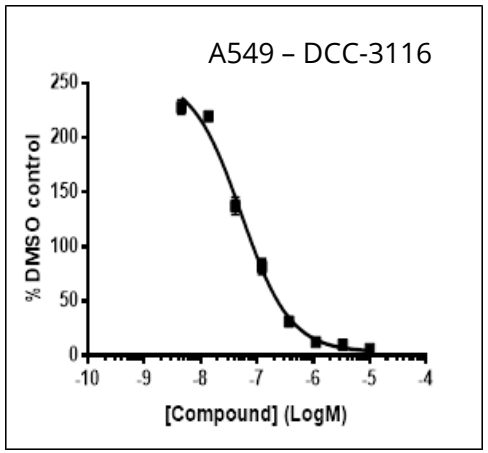
NSCLC: LU11554 PDX Tumor Growth

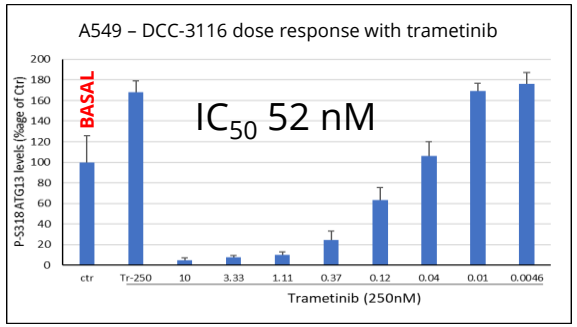


Notes: Data presented at the AACR Meeting 2022; BID=twice daily; G12C=single point mutation with a glycine-to-cysteine substitution at codon 12; KRAS=Kirsten rat sarcoma virus; NSCLC=non–small-cell lung cancer; QD=once daily.

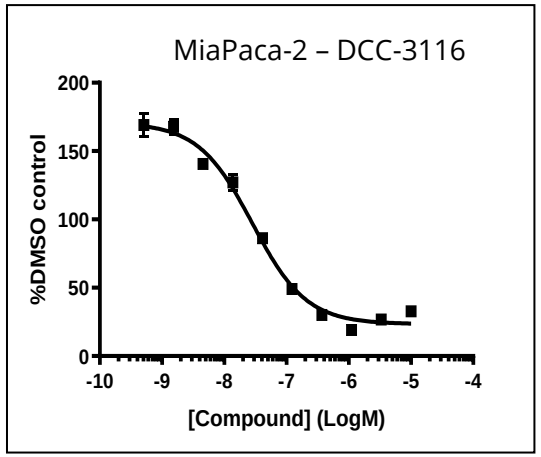
DCC-3116 POTENTLY INHIBITS **TRAMETINIB**-INDUCED ATG13

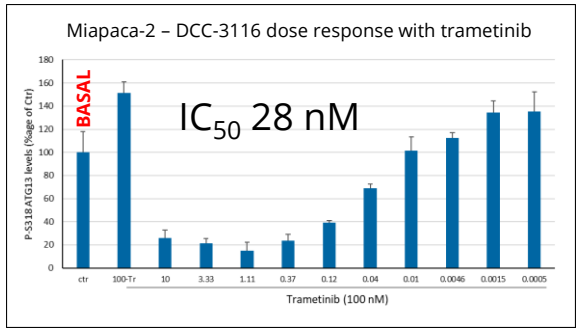
KRAS Lung Cancer



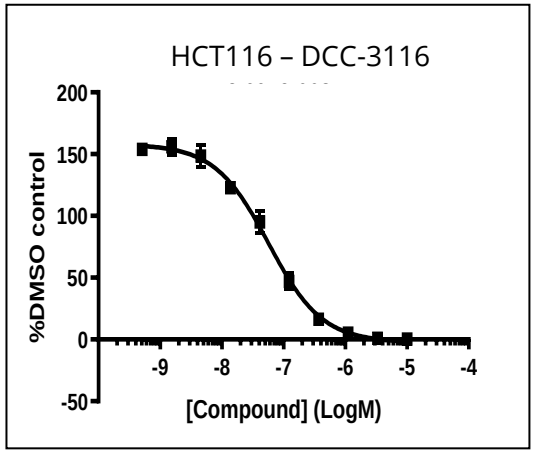


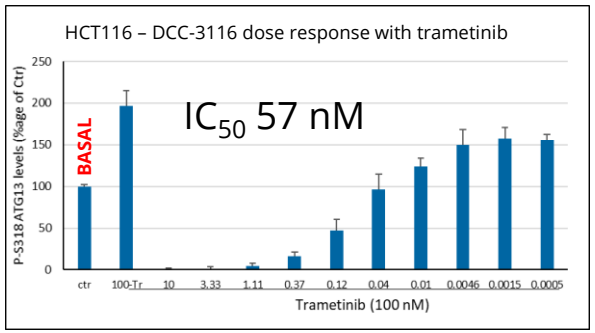
KRAS^{G12C} Pancreatic Cancer



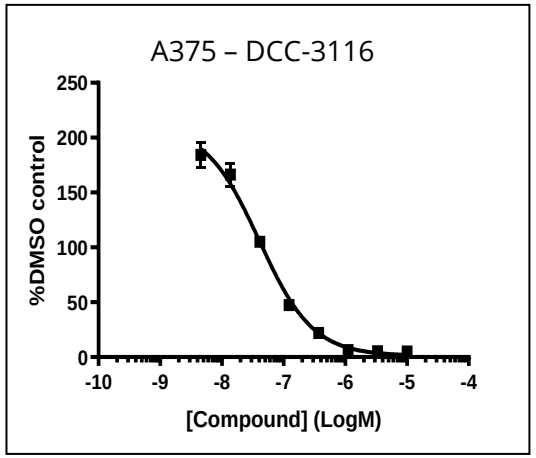


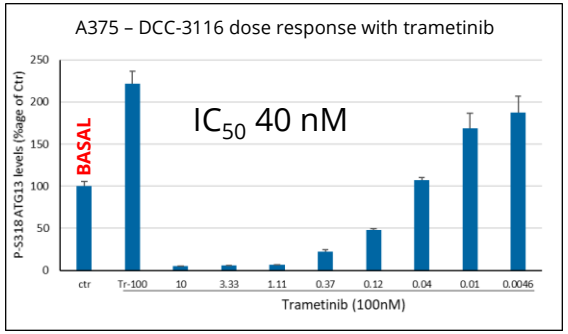
KRAS Colorectal Cancer





BRAF Melanoma Cancer





Basal and MAPK Inhibitor-mediated Compensatory Increased Autophagy are Inhibited

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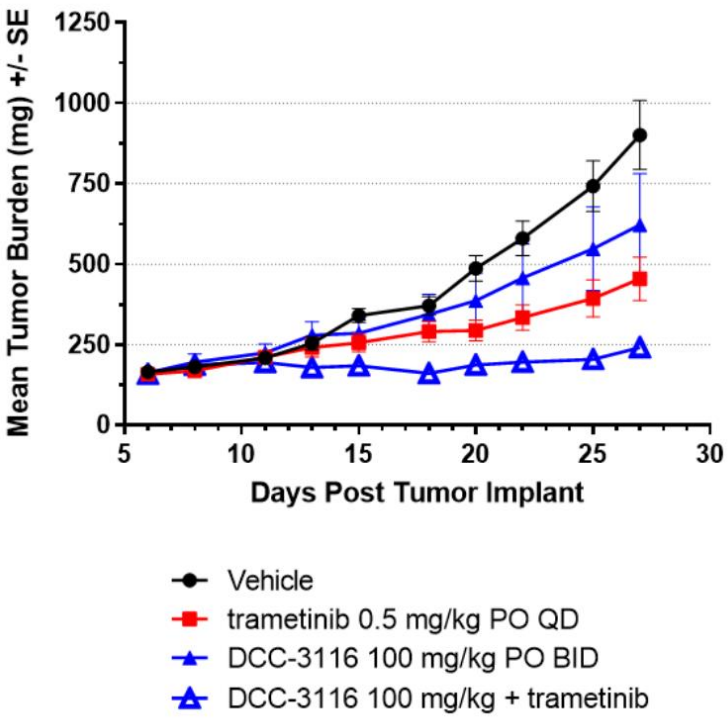
Notes: Data presented at Deciphera's 2019 R&D Day; ATG13=Autophagy-related protein 13; BRAF=proto-oncogene b-RAF; G12C=single point mutation with a glycine-to-cysteine substitution at codon 12; KRAS=Kirsten rat sarcoma virus; MAPK=mitogen-activated protein kinase.

DCC-3116 EXHIBITS ADDITIVITY OR SYNERGY IN COMBINATION WITH **TRAMETINIB**

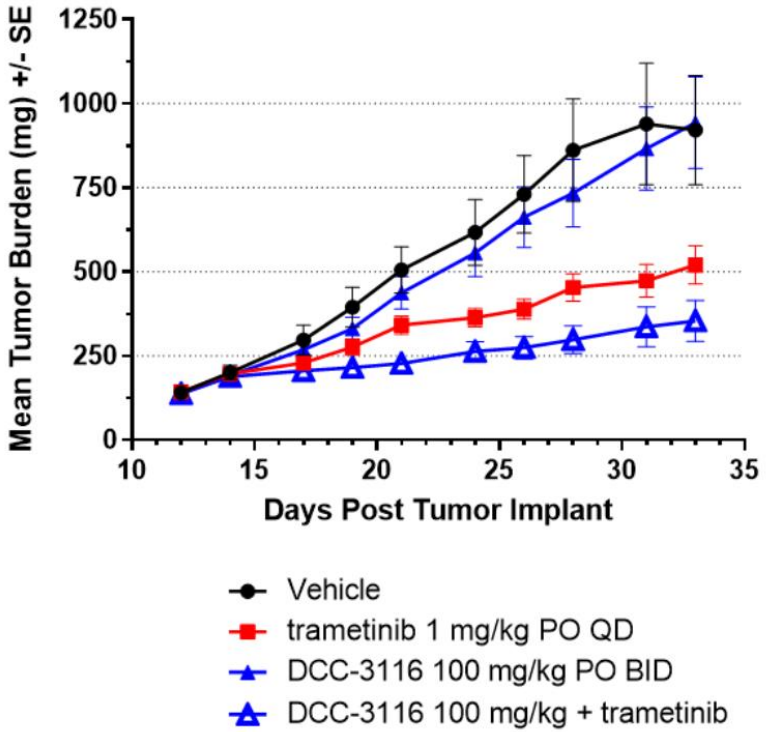
DCC-3116 + Trametinib

PDAC: MiaPaca-2 Tumor Growth



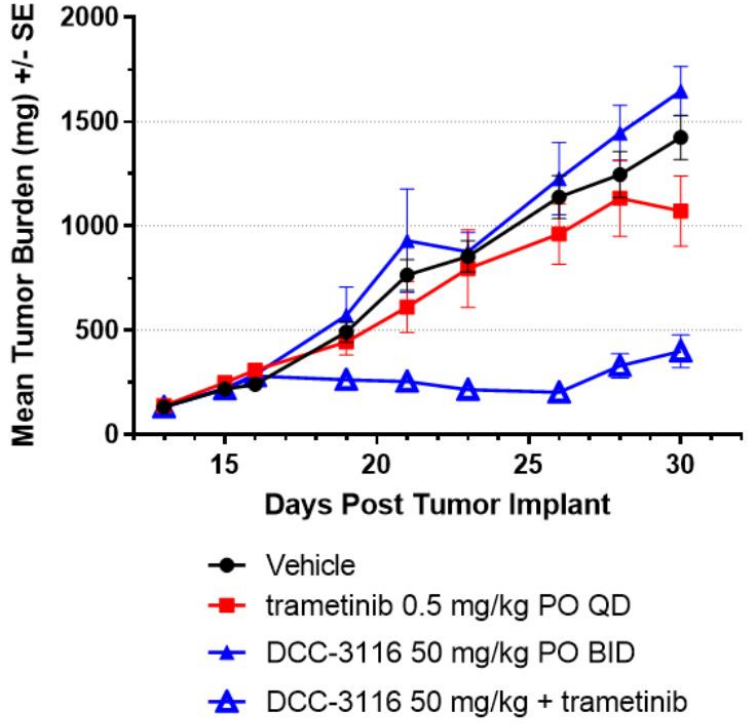
DCC-3116 + Trametinib

NSCLC: A549 Tumor Growth



DCC-3116 + Trametinib

Melanoma: A375 Tumor Growth



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Notes: Data presented at the AACR-NCI-EORTC Meeting 2019; BID=twice daily; NSCLC=non–small-cell lung cancer; PO=by mouth; PDAC=pancreatic ductal adenocarcinoma; QD=once daily.

THANK YOU