

# DEFEATING CANCER: The Challenge. Our Mission.

May 2020



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clinical trials, our reliance on single-source thirdparty suppliers to manufacture clinical, nonclinical and any future commercial supplies of our drug substance and drug product candidates 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. Deciphera recommends that investors independently evaluate specific investments and strategies. For further information regarding these risks, uncertainties and other factors, you should read the "Risk Factors" section of Deciphera's Quarterly Report on Form 10-Q for the quarter ended March 31, 2020 filed with the Securities and Exchange Commission (the "SEC"), and Deciphera's other SEC filings.

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#### **Executing on Our Mission**

At Deciphera,
we are focused
on discovering,
developing, and
bringing important
new medicines to
patients for the
treatment of cancer.



Successfully **launch** QINLOCK™ (ripretinib) in the U.S.



Continued development of QINLOCK in additional indications



Rapidly advancing wholly-owned clinical-stage portfolio(1)



Novel switch control kinase inhibitor discovery platform fuels the pipeline

#### Robust Clinical Stage Oncology Pipeline of Novel Kinase Inhibitors







2020

#### **Expected Milestones for the Year Ahead**



- ✓ FDA approval and U.S. commercial launch in 4<sup>th</sup> line GIST
- Submit EU Marketing Authorisation Application to EMA
- Complete enrollment in the INTRIGUE Phase 3 study in 2<sup>nd</sup> line GIST
- Present Phase 1 study expansion data

**DCC-3014** 

- Select Phase 2 dose for tenosynovial giant cell tumor (TGCT) and initiate the expansion portion of study
- Update Phase 1 data in TGCT patients

Rebastinib

- Selected Phase 2 dose and activate Part 2 of Phase 1b/2 study in combination with carboplatin
- ✓ Present Phase 1b/2 data in combination with paclitaxel
- Present Phase 1b/2 data in combination with carboplatin

Submit IND application to FDA

**DCC-3116** 

#### QINLOCK™: Potential to Change Practice in Advanced GIST



Novel TKI designed to inhibit broad range of mutations in KIT and PDGFRα



Strong efficacy and safety data from randomized Phase 3 INVICTUS study



FDA approved for 4th line GIST



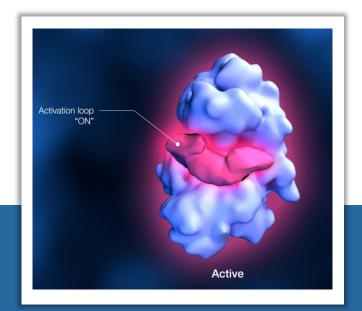
- Received approval ~3 months early
- Breakthrough Therapy Designation
- Reviewed under FDA Real-Time Oncology Review (pilot program)



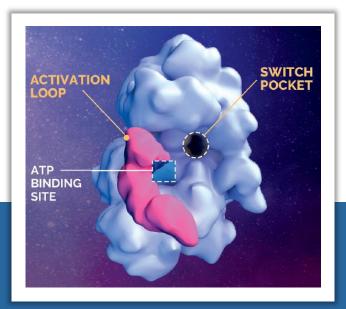
Marketing applications submitted to Health Canada and Australian Therapeutic Goods Administration for advanced GIST and are being reviewed under FDA Project Orbis (initiative)

#### QINLOCK™: A Novel Kinase Switch Control Inhibitor

**Switched on:** Kinase active



Switched off: Kinase inactive



Achieving switch control prevents downstream signaling and cell proliferation to potentially overcome the mechanisms of resistance associated with progressing GIST

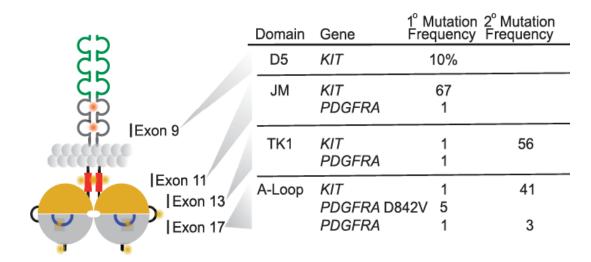
## A unique dual mechanism of action that regulates the kinase switch pocket and activation loop

- Prevents the activation loop from binding to the switch pocket
- Locks the kinase in the inactive ("off") state



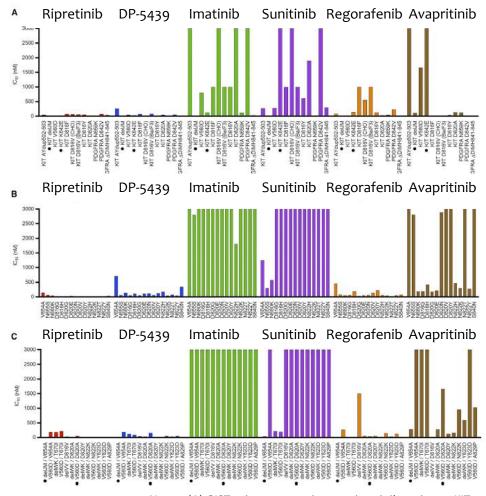
#### QINLOCK™: Designed to Address a Broad Range of Mutations in GIST

#### KIT Mutations Drive ~80% of GIST



Source: Hemming M et al. Translational insights into gastrointestinal stromal tumors and current clinical advances. Annals of Oncology; 29: 2037-2045, 2018.

#### Ripretinib: Broad Mutational Coverage in KIT and PDGFRα



Notes: (A) GIST primary mutations; or imatinib-resistant KIT mutations with (B) exon 9 or (C) exon 11 primary mutations.



#### QINLOCK™: U.S. Prescribing Information Overview



#### **INDICATION**

QINLOCK is a kinase inhibitor indicated for the treatment of adult patients with advanced gastrointestinal stromal tumor (GIST) who have received prior treatment with 3 or more kinase inhibitors, including imatinib.

#### RECOMMENDED DOSE

150 mg orally once daily with or without food.

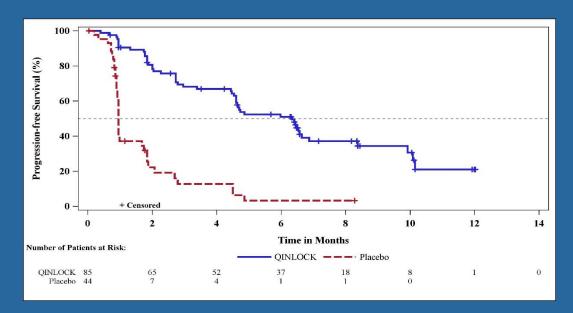
QINLOCK is the first approved TKI designed specifically for GIST regardless of patients' mutational status



#### QINLOCK™: A Potential Best-In-Class Treatment for Advanced GIST

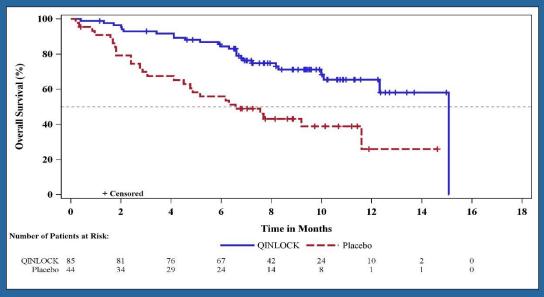
QINLOCK significantly improved **progression free survival** vs. placebo, reducing the risk of progression or death by 85%

(median PFS of 6.3 months vs. 1.0 month; HR=0.15, 95% CI (0.09-0.25), *P*<0.0001)



QINLOCK showed a clinically meaningful benefit in **overall survival** vs. placebo, reducing the risk of death by <u>64%</u>

(median OS of 15.1 months vs. 6.6 months; HR=0.36, 95% CI (0.21-0.62))



Key secondary endpoint of objective response rate was 9.4% compared with 0% for placebo (*P*=0.0504)



#### QINLOCK™: Safety Highlights from the Prescribing Information

#### **Most Common Adverse Reactions (≥20%; Any Grade)**

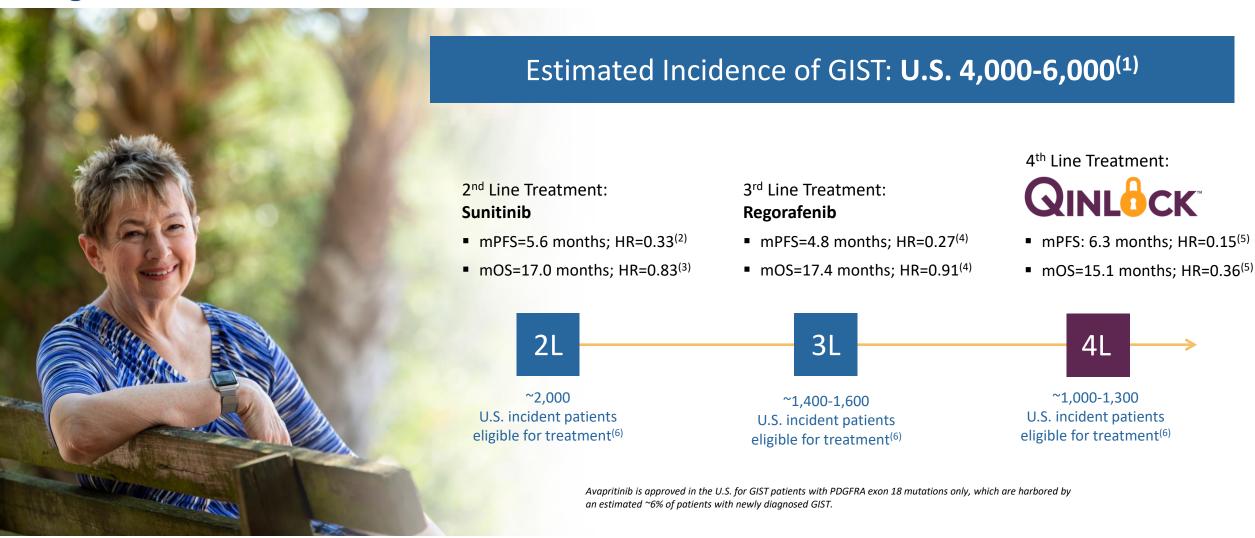
 Alopecia, fatigue, nausea, abdominal pain, constipation, myalgia, diarrhea, decreased appetite, palmar-plantar erythrodysesthesia syndrome, and vomiting

#### **Warnings and Precautions**

- Palmar-plantar erythrodysesthesia syndrome
- New primary cutaneous malignancies
- Hypertension
- Cardiac dysfunction
- Risk of impaired wound healing
- Embryo-fetal toxicity

Dose Modifications from INVICTUS Phase 3 Study <sup>(1)</sup>					
Any adverse reaction leading to	RIPRETINIB (n=85)	<b>PLACEBO</b> (n=43) <sup>(2)</sup>			
Treatment discontinuation	7 (8%)	5 (12%)			
Dose interruption	20 (24%)	9 (21%)			
Dose reduction	6 (7%)	1 (2%)			

#### Significant Unmet Medical Need Post-Imatinib





Notes: mPFS=median progression free survival; mOS=median overall survival; HR=hazard ratio; (1) American Cancer Society, Key Statistics for Gastrointestinal Stromal Tumors, Accessed December 13, 2019; (2) Sutent [package insert]. New York, NY: Pfizer; 2011, mPFS and mOS converted from weeks to months; (3) Garrett CR, et al. Poster presented at: Connective Tissue Oncology Society: November 13-15, 2008; London, UK. Abstract 35049;. (4) Stivarga [package insert]. Germany: Bayer Healthcare; 2013; (5) QINLOCK [package insert]. Waltham, MA: Deciphera Pharmaceuticals; 2020; (6) Internal Deciphera estimates of annual new treatment-eligible patients are based on analyses of U.S. claims data; eligible patients for 3<sup>rd</sup> and 4<sup>th</sup> lines exclude the estimated proportion of patients across lines that die, discontinue oncology treatment, or enter clinical trial and, therefore, are not eligible for treatment. Estimates are inherently uncertain.

## QINL&CK: 4 Strategic Objectives For Launch

1	Educate and raise awareness	<ul> <li>Extensive mutational heterogeneity drives resistance to established therapies</li> </ul>
2	Differentiate QINLOCK™	<ul> <li>Novel switch control mechanism of action</li> <li>Potent inhibition of broad spectrum of mutations in vitro</li> <li>Potentially practice-changing efficacy</li> <li>Favorable tolerability with low dose modifications due to AEs</li> </ul>
3	Reach and impact GIST prescribers	<ul> <li>Academic centers of excellence</li> <li>Community practices</li> </ul>
4	Optimize patient access	<ul> <li>Deciphera AccessPoint™</li> <li>Comprehensive patient support programs and resources</li> </ul>



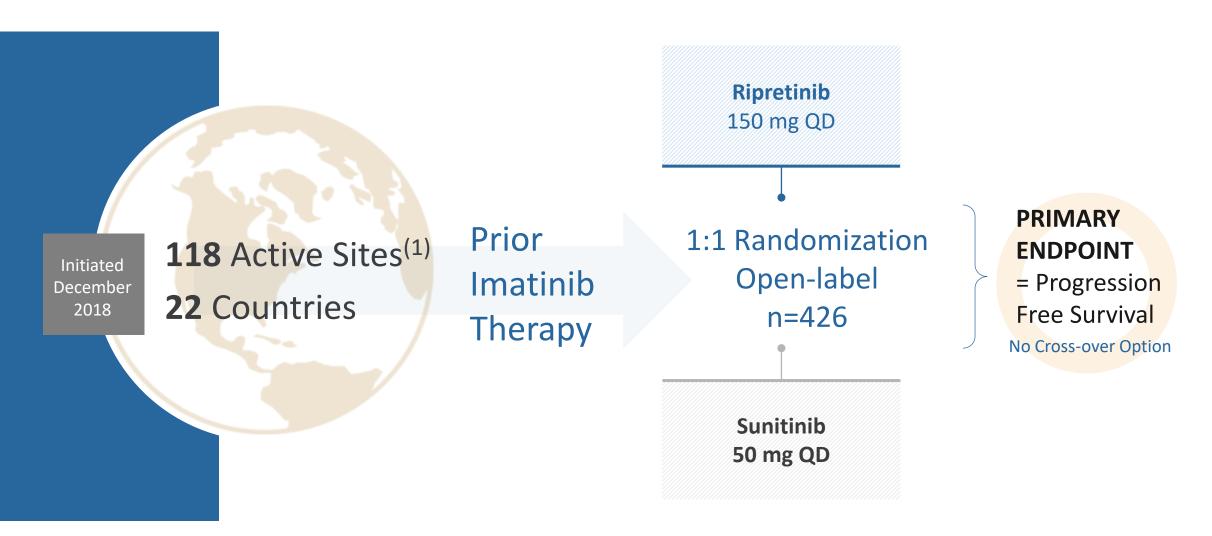
## QINLOCK™: Phase 1 GIST Cohorts Positive Updated Results Across All Lines of Treatment

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

#### Ripretinib 150 mg QD (n=142)

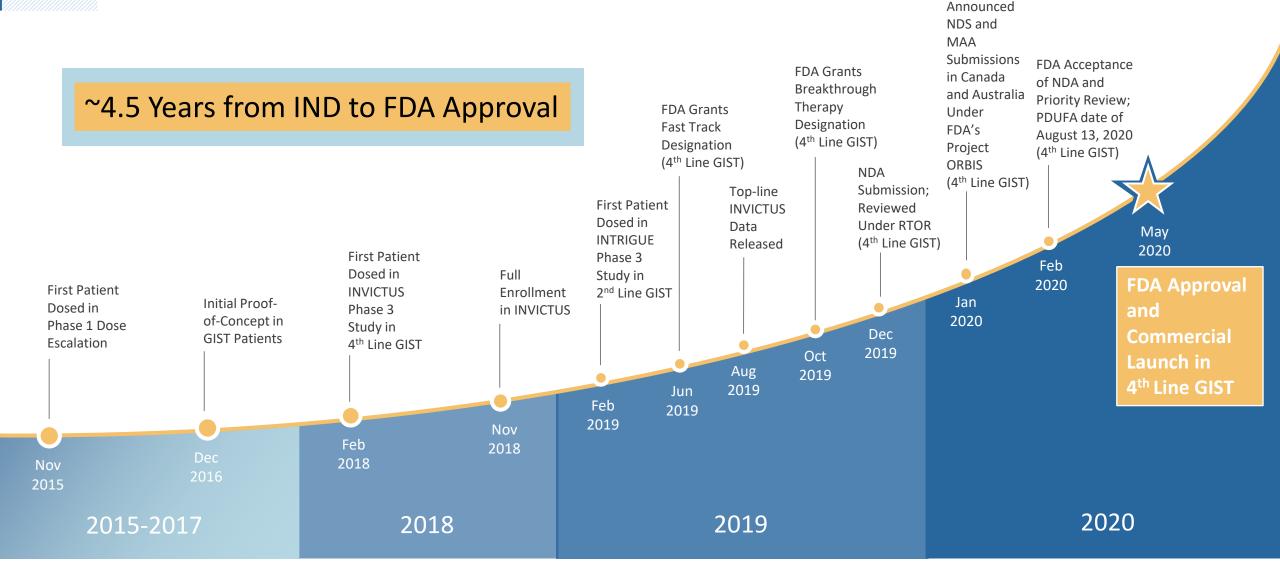


#### intrigue > Ongoing Global Pivotal Phase 3 Study in 2<sup>nd</sup> Line GIST



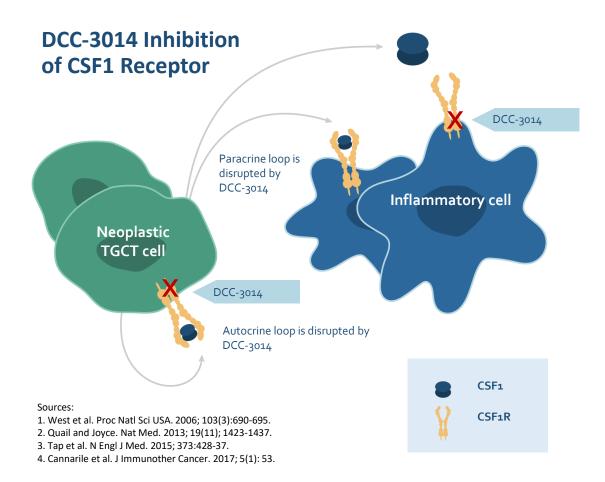


#### QINLOCK™: Rapid Clinical Development to Approval





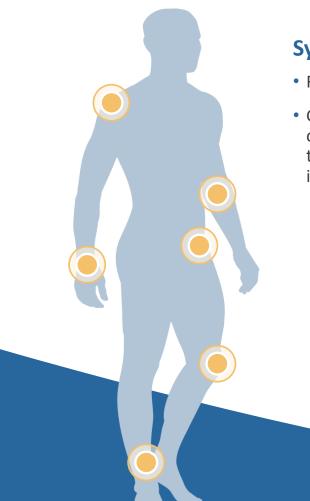
#### DCC-3014: A Highly Selective and Potent CSF1R Inhibitor



- Phase 1 dose escalation study ongoing
- Generally well tolerated in patients at doses of up to 50 mg receiving three-day loading, followed by 20 mg QD maintenance regimen
- Initial proof-of-concept in three patients with diffuse-type tenosynovial giant cell tumor (TGCT) with preliminary anti-tumor activity
  - Potential for favorable tolerability profile when considering challenges of existing approved therapy



#### Unmet Medical Need in Tenosynovial Giant Cell Tumor (TGCT)



#### **Symptoms**

- Rare, locally aggressive tumors
- Genetic translocation causes overproduction of CSF-1, triggering migration of inflammatory cells to tumor sites

#### **Two Types of TGCT**

#### 1. Localized TGCT

- Affects fingers, toes, knee, wrist and ankle
- Annual incidence of new cases in the U.S.: ~13,000<sup>(1)</sup>

#### 2. Diffuse TGCT

- Most commonly affects the knee, as well as hip, ankle, elbow and shoulder
- Annual incidence of new cases in the U.S.: ~1,300<sup>(1)</sup>

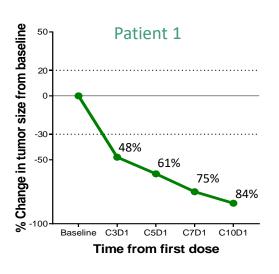
#### **Unmet Medical Need**

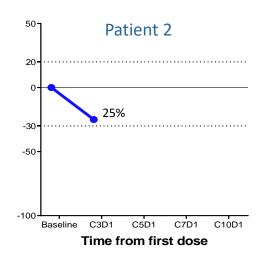
- Surgical resection is standard treatment
- · High rate of recurrence in diffuse TGCT
- CSF1R inhibition has demonstrated clinical benefit in diffuse TGCT
- Pexidartinib received FDA approval in August 2019
  - REMS and intensive monitoring required due to hepatotoxicity concerns (off-target)
- Unmet medical need for effective CSF1R inhibitor with favorable safety/tolerability profile for TGCT patients

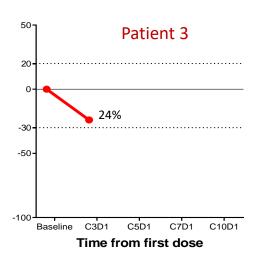


#### DCC-3014: Preliminary Phase 1 Data in Initial TGCT Patients

Clinical Proof-of-Concept in TGCT Patients







Changes from baseline in tumor size assessed by investigator per RECIST version 1.1

DCC-3014 was generally well tolerated in initial three patients with diffuse-type TGCT

No grade ≥3 TEAEs observed

Preliminary anti-tumor activity and symptomatic improvement

Symptomatic improvements in mobility and reduced pain were observed in all three patients based on investigator notes

Dose-escalation
evaluation is ongoing
to determine the
recommended
Phase 2 dose



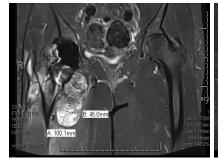
#### DCC-3014: TGCT Case Studies from the Phase 1

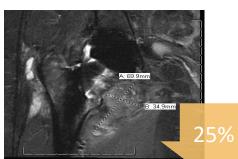
## Patient 1 C3D1 C10D1 Baseline 48%

- 24-year-old female patient diagnosed with diffuse-type TGCT (right posterior knee) in June 2016, three prior surgeries, and recurrence/progression on MRI by December 2018
- Active in Cycle 10 as of data cut-off

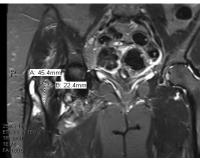
#### Patient 2

Baseline C3D1









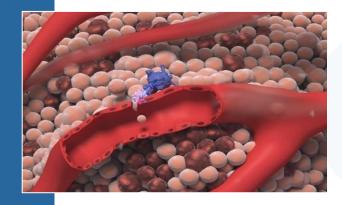
- 57-year-old female patient diagnosed with diffuse-type TGCT (right hip) in 2014, six prior surgeries, and recurrent disease on MRI by February 2019
- Active in Cycle 5 as of data cut-off



#### Rebastinib: A Highly Potent and Selective TIE2 Inhibitor

## Potential Benefits in Combination with Chemotherapy

- Chemotherapy leads to recruitment of pro-tumoral M2 macrophages from the bone marrow
- Rebastinib is designed to inhibit chemotherapyinduced recruitment of M2 macrophages to tumors
- M2 macrophages serve as pumps for tumor cell intravasation and metastasis
- Rebastinib is designed to block rebound angiogenesis and inhibit M2 macrophages



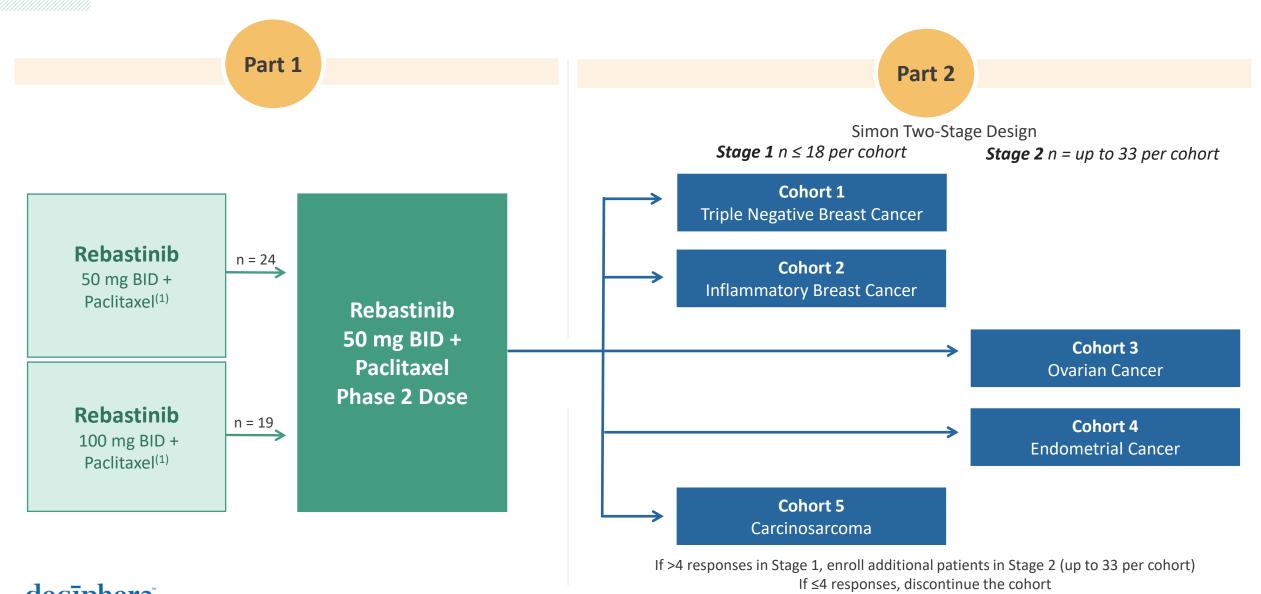
- Potent, small molecule inhibitor of TIE2
- Targets TIE2 expressing macrophages (TEMs) and endothelial cells in tumor environment
- Combination of rebastinib with chemotherapy may increase tumor killing through multiple mechanisms
  - Tumor vascularization, dissemination, metastasis, immunotolerance

#### **Development status**

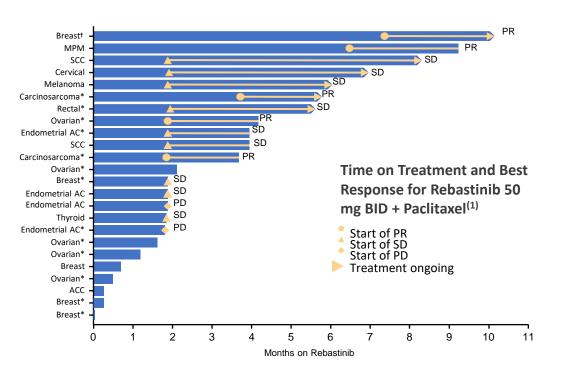
- Two ongoing studies in combination with paclitaxel or carboplatin
- Encouraging preliminary results from Part 1 of the Phase 1b/2 study in combination with paclitaxel presented in October 2019
- Selected Phase 2 dose and activated Part 2 of the Phase 1b/2 study in combination with carboplatin in January 2020

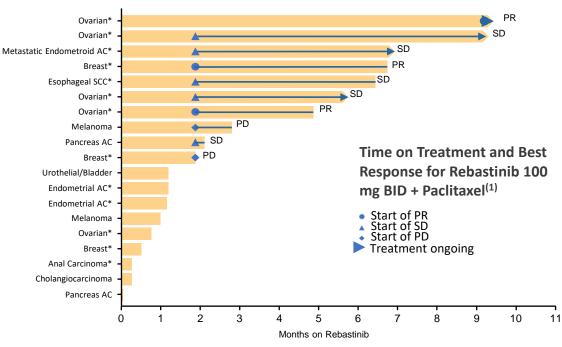


#### Rebastinib: Phase 1b/2 Study in Combination with Paclitaxel



## **Rebastinib:** Part 1 of Phase 1b/2 Study in Combination with Paclitaxel Shows Encouraging Preliminary Anti-tumor Activity





CARCINOSARCOMA -

Objective responses





**OVARIAN** 





**BREAST** 









**PERITONEAL** 



Notes: Data presented at AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics 2019; AC=adenocarcinoma; ACC=adrenocortical carcinoma; MPM=malignant peritoneal mesothelioma; PD=progressive disease; PR=partial response; SCC=squamous cell carcinoma; SD=stable disease; (1) Tumor responses were evaluated by the investigator according to Response Evaluation Criteria in Solid Tumors 1.1 criteria; as per study protocol, includes confirmed and unconfirmed responses; \*prior paclitaxel therapy; †patient did not receive prior paclitaxel, but did receive prior docetaxel.

## **Rebastinib:** Part 1 Data of the Phase 1b/2 Study Showed the Combination with Paclitaxel Was Generally Well Tolerated

TEAEs ≥ 10% regardless of relatedness

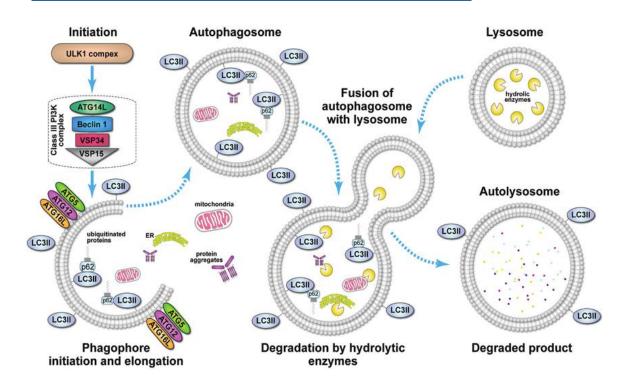
	50 mg BID (n=24)		100 mg BID (n= 19)		Total (n=43)	
Preferred Term	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3
Fatigue	8 (33%)	1 (4%)	5 (26%)	0	13 (30%)	1 (2%)
Constipation	3 (13%)	0	6 (32%)	0	9 (21%)	0
Diarrhea	2 (8%)	0	7 (37%)	0	9 (21%)	0
Dry mouth	6 (25%)	0	3 (16%)	0	9 (21%)	0
Alopecia	4 (17%)	0	4 (21%)	0	8 (19%)	0
Anemia	4 (17%)	2 (8%)	4 (21%)	2 (11%)	8 (19%)	4 (9%)
Dyspnea	4 (17%)	0	4 (21%)	0	8 (19%)	0
Nausea	6 (25%)	1 (4%)	2 (11%)	0	8 (19%)	1 (2%)
Peripheral sensory neuropathy	2 (8%)	0	6 (32%)	0	8 (19%)	0
Dizziness	3 (13%)	0	4 (21%)	0	7 (16%)	0
Hypokalemia	4 (17%)	1 (4%)	3 (16%)	0	7 (16%)	1 (2%)
Urinary tract infection	3 (13%)	1 (4%)	4 (21%)	0	7 (16%)	1 (2%)
Hypomagnesemia	3 (13%)	0	3 (16%)	0	6 (14%)	0
Onychomadesis	3 (13%)	0	3 (16%)	0	6 (14%)	0
Sepsis	2 (8%)	2 (8%)	4 (21%)	4 (21%)	6 (14%)	6 (14%)
ALT increased	5 (21%)	0	0	0	5 (12%)	0
Decreased appetite	3 (13%)	0	2 (11%)	0	5 (12%)	0
Dysgeusia	3 (13%)	0	2 (11%)	0	5 (12%)	0
Headache	1 (4%)	1 (4%)	4 (21%)	0	5 (12%)	1 (2%)
Rash	3 (13%)	0	2 (11%)	0	5 (12%)	0
Stomatitis	4 (17%)	1 (4%)	1 (5%)	0	5 (12%)	1 (2%)
Vomiting	4 (17%)	1 (4%)	1 (5%)	0	5 (12%)	1 (2%)

- Frequencies of TEAEs were similar between 50 mg and 100 mg BID
- One patient experienced a rebastinib-related SAE (grade 2 muscular weakness) and 4 patients had an SAE related to paclitaxel and rebastinib (5 events: grade 3 pneumonia [n=2], grade 3 nausea [n=1], grade 3 vomiting [n=1], and grade 2 myocardial ischemia [n=1])
- Two patients experienced muscular weakness (one grade 1 at 50 mg BID and remains on treatment, and one grade 2 at 100 mg BID and discontinued treatment)



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

#### **ULK:** Initiating Factor for Autophagy



Adapted from: Ndoye A and Weeraratna AT. Autophagy- An emerging target for melanoma therapy [version 1]. F1000Research 2016, 5:1888.



### First-in-class opportunity for new therapeutic in RAS mutant cancers

- RAS mutant cancers have high basal levels of autophagy
- DCC-3116 observed preclinically to durably and potently inhibit autophagy in RAS mutant cancer cell lines through the inhibition of ULK kinase
- Combination of DCC-3116 and MAPK pathway inhibitors have been observed to synergize to block RAS mutant cancers in vivo



#### Highly potent and selective ( $IC_{50}$ at 1 mM ATP)

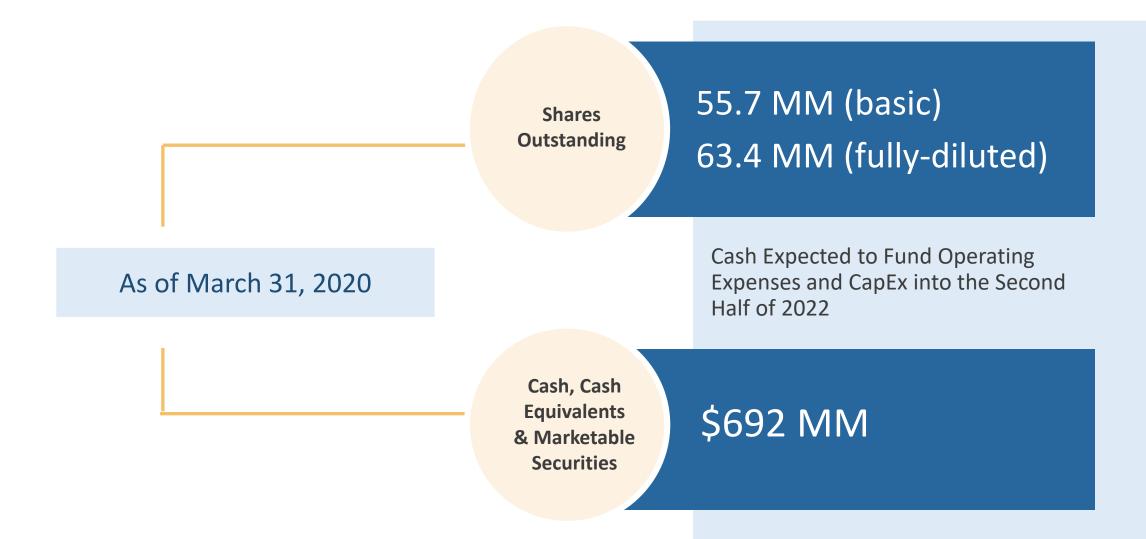
- ULK1 4.7 nM and ULK2 35 nM
- No off-target kinases within 30-fold of ULK1/5 kinases within 100-fold of ULK1

Designed to avoid CNS exposure

IND submission expected in 2H 2020

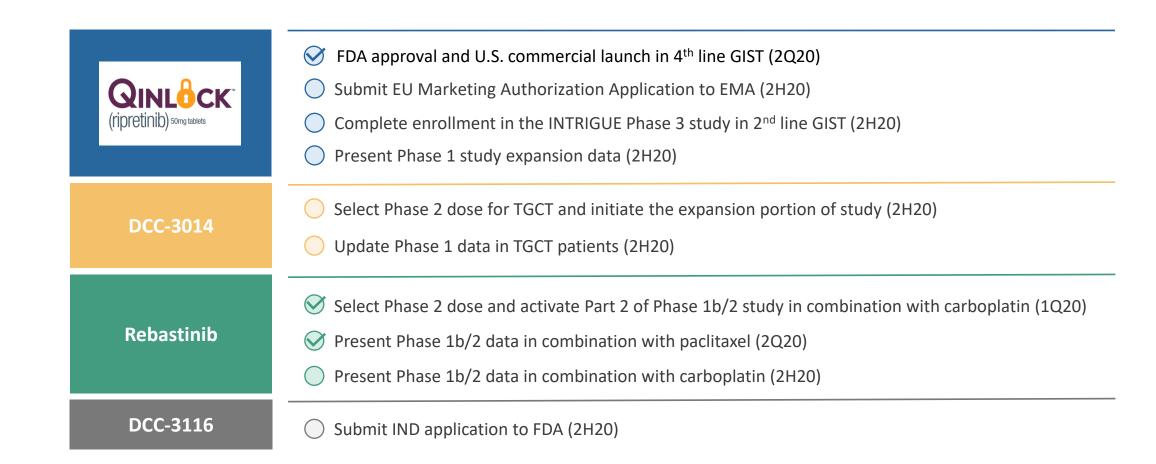


#### Financial Highlights





#### Significant Expected 2020 Milestones Across the Pipeline





## **THANK YOU**



