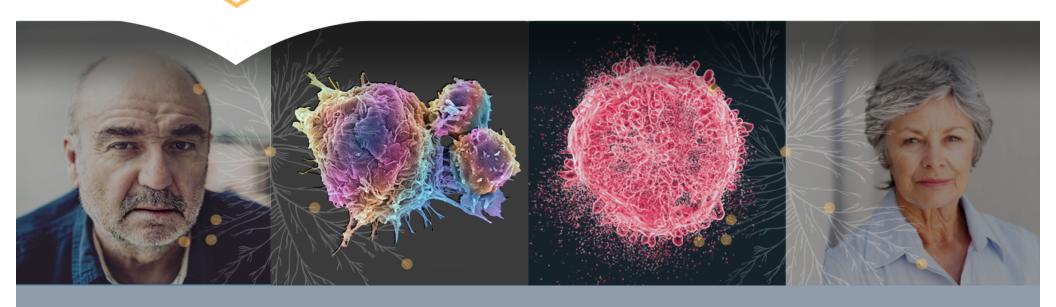


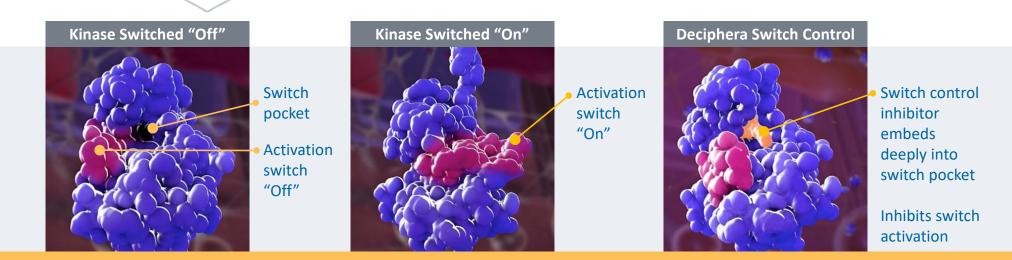
# Addressing Key Mechanisms of Tumor Drug Resistance

July 2018



Kinase switch control inhibitors for tumortargeted and immune-targeted cancer therapies

## **Our Proprietary Kinase Switch Control Platform**

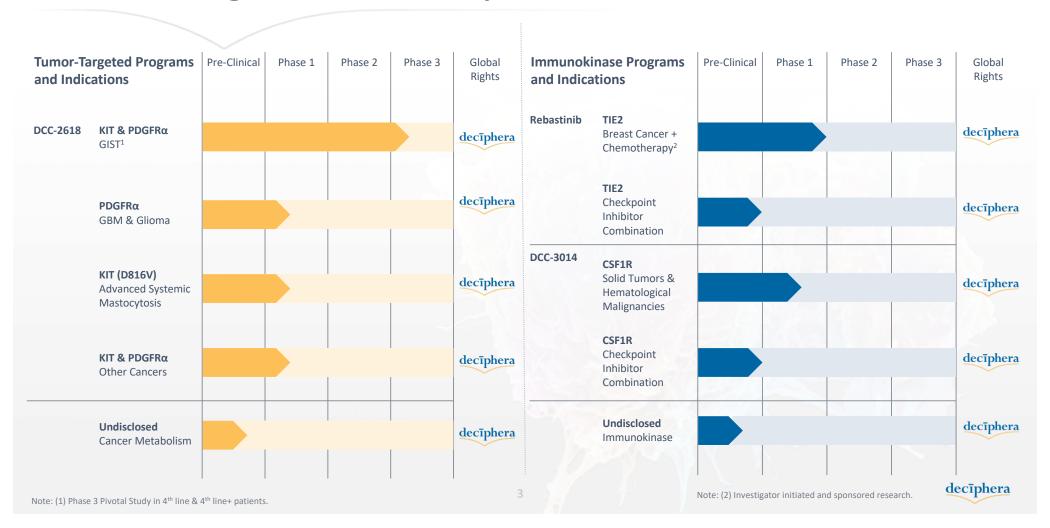


#### **Advantages of Switch Control Inhibitors**

Tumor-Targeted Programs	Broader Activity Enhanced Durability	Inhibit wild-type and many or all mutant forms of targeted kinases Resilient to gain-of-function mutations and drug resistance
Immunokinase Programs (Macrophage Checkpoints)	Engineered Profiles Superior Binding	Highly selective or target multiple kinases at desired potency  More potent and more durable; resilient to ATP concentration



### **Clinical-Stage Small Molecule Pipeline**



#### DCC-2618 Phase 1 Trial

#### Part 1: Dose Escalation

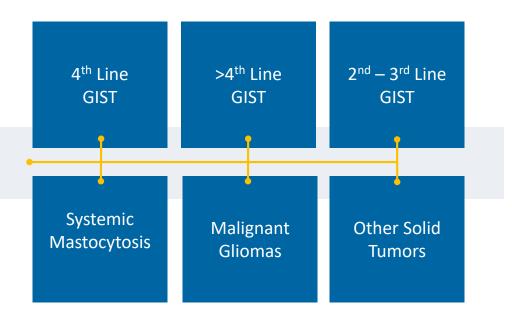
- Key Objectives: MTD, recommended Phase 2 dose, safety, tolerability, pharmacokinetics and anti-tumor activity
- Design: 3+3 design with enrichment of targeted patients
- Dose Levels: 20, 30, 50, 100, 150, and 200 mg BID; and 100, 150 and 250 mg QD
- MTD: not determined

Advanced Malignancies (n=68)

Recommended Dose 150 mg QD

#### Part 2: Dose Expansion

• 6 cohorts enrolling 200 pts





ASCO 2018: Phase 1 Demographics and Baseline Characteristics GIST Patients at ≥100 mg/d

GIST Patients ≥100 mg /d	n=150 <sup>(1)</sup>	
Age (years), median (range)	62 (27-87)	
GIST Subtype	n (%)	
KIT-driven	141 (94%)	
PDGFRα-driven	8 (5%)	
SDH deficient	1 (1%)	
Line of Therapy	n (%)	
2 <sup>nd</sup> Line	25 (17%)	
3 <sup>rd</sup> Line	29 (19%)	
≥4 <sup>th</sup> Line <sup>(2)</sup>	96 (64%)	
DCC-2618 Dose	n (%)	
150 mg QD	114 (76%)	
Other (100 mg/d – 400 mg/d)	36 (24%)	

Notes: (1) Includes pts with C1D1 on or before February 26, 2018; (2) Mean number of prior regimens for ≥4th line pts was 3.5.



### **Favorable Tolerability Profile**

Treatment-emergent Adverse Events in ≥ (10%) GIST Patients (n=100) @ 150 mg QD

#### Phase 1 Dose Escalation (n=68)

- Well tolerated up to 400 mg per day
- MTD not reached
- 3 DLTs:
  - Reversible plasma enzyme elevations: lipase (2) and CPK (1)
  - Deemed not clinically significant
- 150 mg QD dose for Phase 1
   Expansion and 4<sup>th</sup> Line GIST Phase 3
   Trial

GIST	PATIENTS @ 150 mg C	D	
ADVERSE EVENT	GRADE 1/2	GRADE 3/4	TOTAL (n= <b>100)</b>
Alopecia	39	0	39 (39%)
Fatigue	39	0	39 (39%)
Myalgia	35	0	35 (35%)
Constipation	29	0	29 (29%)
Hand-Foot-Skin reaction	26	1	27 (27%)
Rash	21	0	21 (21%)
Lipase increased	10	10	20 (20%)
Nausea	19	0	19 (19%)
Decreased appetite	18	0	18 (18%)
Diarrhea	16	2	18 (18%)
Hypertension	15	2	17 (17%)
Abdominal pain	14	2	16 (16%)
Arthralgia	15	0	15 (15%)
Weight decreased	13	0	13 (13%)
Headache	12	0	12 (12%)
Vomiting	12	0	12 (12%)
Anemia	8	3	11 (11%)
Dyspnea	10	1	11 (11%)
Hypomagnesaemia	11	0	11 (11%)
Pain in extremity	11	0	11 (11%)
Dry skin	10	0	10 (10%)
Muscle spasms	10	0	10 (10%)





## Best Response, DCR & ORR By Line of Treatment at ≥100 mg/d

Li	ne of Therapy	Total Patients <sup>(1)</sup>	Active <sup>(1)</sup>	DCR @ 3 Months <sup>(2)</sup>	ORR <sup>(2)</sup>
	2 <sup>nd</sup> Line	25	68%	79%	24%
	3 <sup>rd</sup> Line	29	76%	82%	24%
	≥4 <sup>th</sup> Line	96	53%	64%(3)	9% <sup>(3)</sup>
	Total	150	60%	<b>70</b> % <sup>(3)</sup>	15% <sup>(3)</sup>

Notes: (1) Includes pts with C1D1 on or before February 26, 2018; (2) Pts with C1D1 on or before February 2, 2018, or enrolled later with an available tumor assessment, based on April 18, 2018 cutoff date; (3) Excludes 5 patients with C1D1 after February 2, 2018 and no assessment.

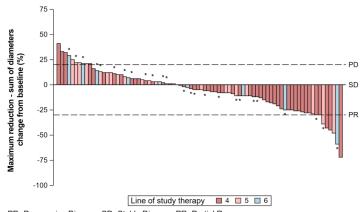


### **Initial Phase 1 Data Demonstrates Robust Clinical Activity in ≥ 4<sup>th</sup> Line GIST Patients**

#### 77% Best Response in ≥ 4<sup>th</sup> Line for DCC-2618

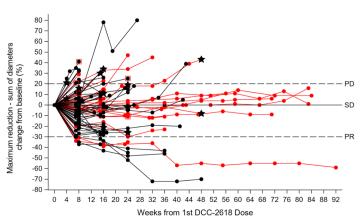
#### 64% DCR @ 3 Months in ≥ 4<sup>th</sup> Line for DCC-2618

# Best Response per RECIST<sup>(1)(2)</sup> KIT & PDGFRα ≥ 100 mg/d (n=82)



PD=Progressive Disease. SD=Stable Disease. PR=Partial Response. \*indicates patients not dosed at 150mg QD Plot include patients with C1D1 on or prior to 31Jan2018.

Tumor Control per RECIST<sup>(1)(2)</sup>
KIT & PDGFRα @ ≥ 100 mg/d (n=89)



Note: Closed circles denote that patient was on DCC-2618 at the time of scan, Squares denote that patient was off DCC-2618 at the time of scar Stars indicate final visit. Red used for patients not dosed at 150mg QD.

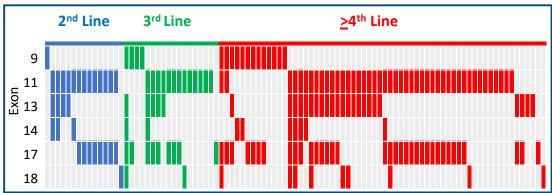
Plot Include admins with C110 no or prior to 31/an2/018.

Notes: (1) RECIST data per investigator assessment; (2) Includes only KIT and PDGFRα GIST patients.



#### Clinical Validation of The Broad Spectrum Mutant KIT Profile in Liquid Biopsies

## KIT Mutations in ctDNA (n=95) in 131 GIST patients by Line of Therapy

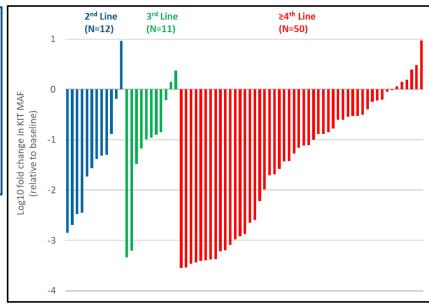


Each column represents an individual GIST patient and each filled entry on rows indicates detection of one or more mutations in Exon 9, 11, 13, 14, 17 and 18.

# Secondary KIT mutations in exons 13, 14 17 and 18 in patients with 2<sup>nd</sup> to ≥ 4<sup>th</sup> line GIST • 78% achieved more than 50% KIT MAF reduction • 48% were KIT negative on treatment

Cumulative Reductions in Circulating MAF of KIT Exons 9, 11, 13, 14, 17 and 18 by Lines of Therapy (n=73)<sup>(1)</sup>

(Note log scale: -1 = 10-fold reduction, -2 = 100-fold reduction)



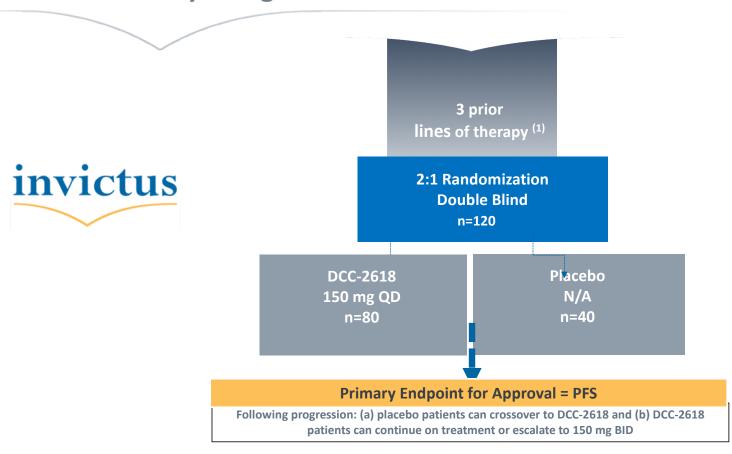
Note: (1) Based on data from 73 patients with detectable KIT mutations at baseline.  $\,$ 



# decīphera



## **Invictus Study Design**



(1) Phase 3 Pivotal Study in ≥4th line patients who previously received at least imatinib, sunitinib, and regorafenib



## **Invictus: Major Inclusion Criteria**

#### **Inclusion Criteria include:**

- GIST
- 18 years and older
- Progressed on or intolerant to imatinib, sunitinib and regorafenib
- ECOG Performance Status: 0-2
- Able to provide an archival tumor tissue sample if no anticancer therapy was administered since the sample was collected; otherwise, a fresh tumor tissue sample is required

#### **Exclusion Criteria include:**

- Arterial thrombotic or embolic events within 6 months
- Venous thrombotic events within 3 months
- Left ventricular ejection fraction <50%</li>
- Major surgeries within 4 weeks
- Use of proton-pump inhibitors within 4 days prior to the first dose of study drug



#### Recruiting Now US, Canada, Europe, Australia and Singapore

#### Current US sites:

- Honor Health, AZ
- USC, CA
- UCLA, CA
- · Stanford, CA
- Mayo Clinic, FL
- Georgia Cancer Specialists, GA
- · U. of Chicago, IL
- Dana Farber, MA
- U of Minnesota, MN
- · Mayo Clinic, MN
- Columbia, NY
- · Memorial Sloan Kettering, NY
- Oregon Health and Science University, OR
- Fox Chase, PA
- MD Anderson, TX

- Canada: Princess Margaret, Toronto and Cross Cancer Centre, Alberta
- Australia: Alfred University, Melbourne
- EU:
  - Belgium
  - France
  - Poland
  - Spain
  - UK
- Singapore: National Cancer Center

MORE SITES STILL TO OPEN IN US, GERMANY, NETHERLANDS, FINLAND AND ITALY

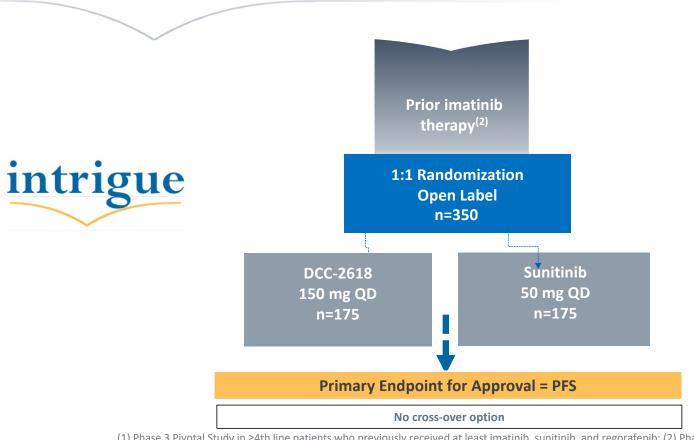


### **Invictus Online Resources and Deciphera's Contact Information**

- ClinicalTrials.gov identifier: NCT03353753
  - <a href="https://clinicaltrials.gov/ct2/show/study/NCT03353753">https://clinicaltrials.gov/ct2/show/study/NCT03353753</a>
- <a href="http://www.invictusclinicalstudy.com">http://www.invictusclinicalstudy.com</a>
- Deciphera's contact information:
  - Clinical Team INVICTUS +1 781.209.6400
  - <u>clinicaltrials@deciphera.com</u>



#### Second Global Pivotal Phase 3 GIST Planned for 2H:18



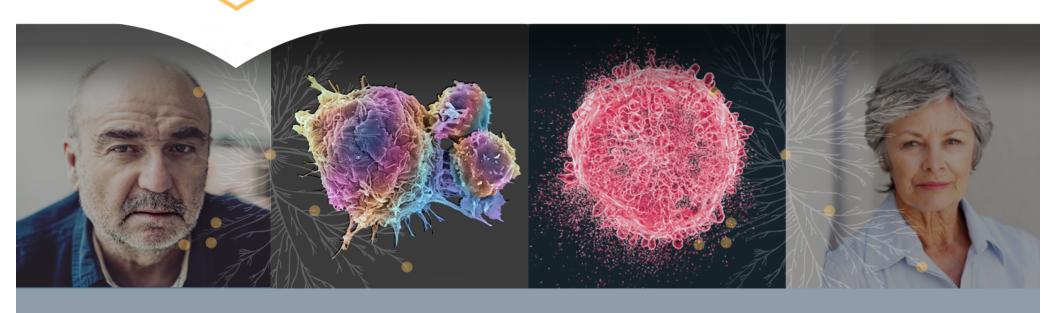
(1) Phase 3 Pivotal Study in ≥4th line patients who previously received at least imatinib, sunitinib, and regorafenib; (2) Phase 3 Pivotal Study in 2nd line patients who previously received imatinib.





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Thank You