



DEFEATING  
CANCER:  
The Challenge.  
Our Mission.

May 2020

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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.



Ripretinib: **Positive results** from INVICTUS Phase 3 study in  $\geq 4$ th line GIST



Ripretinib: **NDA accepted** and preparing for potential U.S. launch

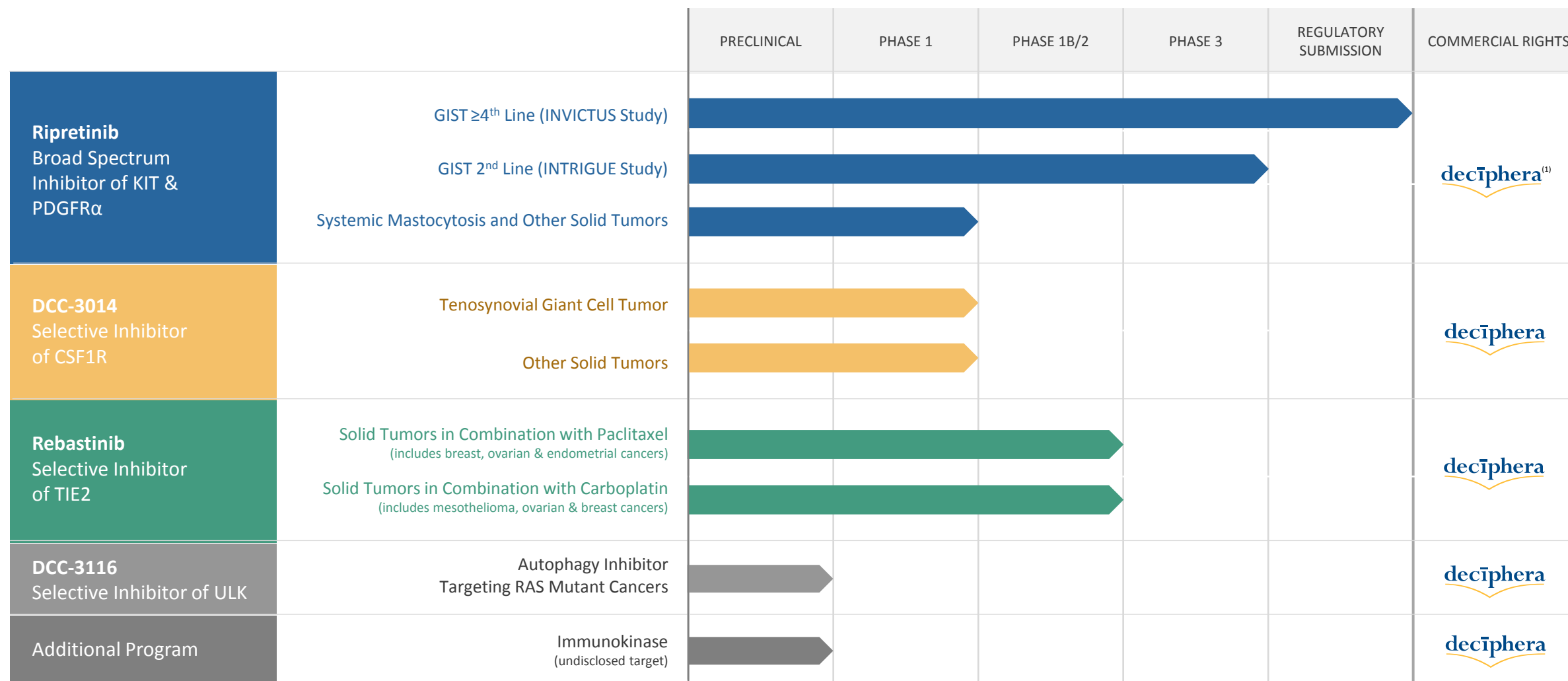


**Rapidly advancing wholly-owned** clinical-stage portfolio<sup>(1)</sup>



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

### Ripretinib

- ✓ FDA grants Priority Review and sets PDUFA data of August 13, 2020 in advanced GIST
- Potential commercial launch in advanced 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

### DCC-3116

- Submit IND application to FDA

# Ripretinib: Potential to Change Practice in Advanced GIST

Novel TKI designed to inhibit broad range of mutations in KIT and PDGFR $\alpha$



Strong efficacy and safety data from randomized Phase 3 INVICTUS study



NDA accepted by the FDA for advanced GIST



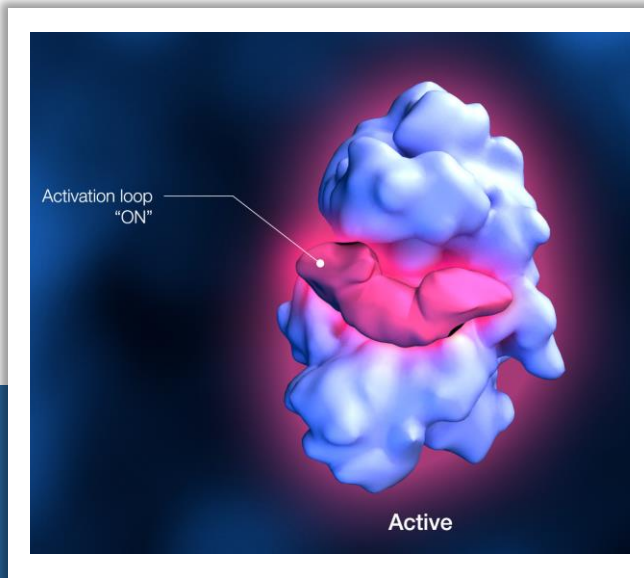
- Priority Review granted; PDUFA date of August 13, 2020
- Breakthrough Therapy Designation
- NDA being reviewed under FDA Real-Time Oncology Review (pilot program)



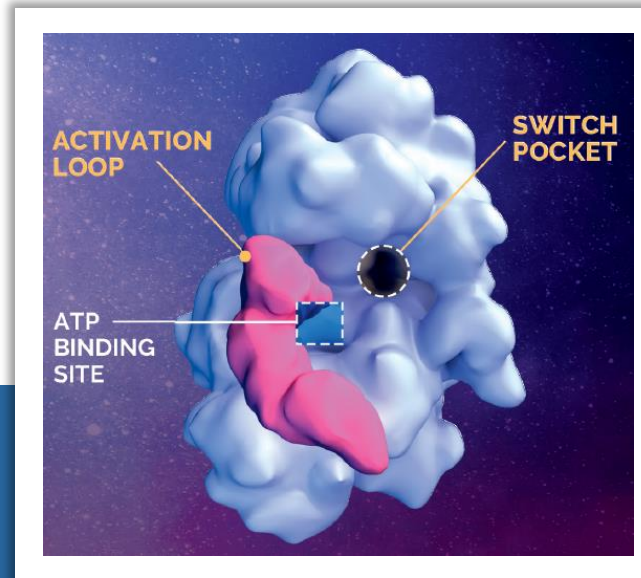
Marketing applications submitted to Health Canada and Australian Therapeutic Goods Administration for advanced GIST and are being reviewed under FDA Project Orbis (initiative)

# Ripretinib: A Novel Kinase Switch Control Inhibitor

**Switched on:** Kinase active



**Switched off:** Kinase inactive



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

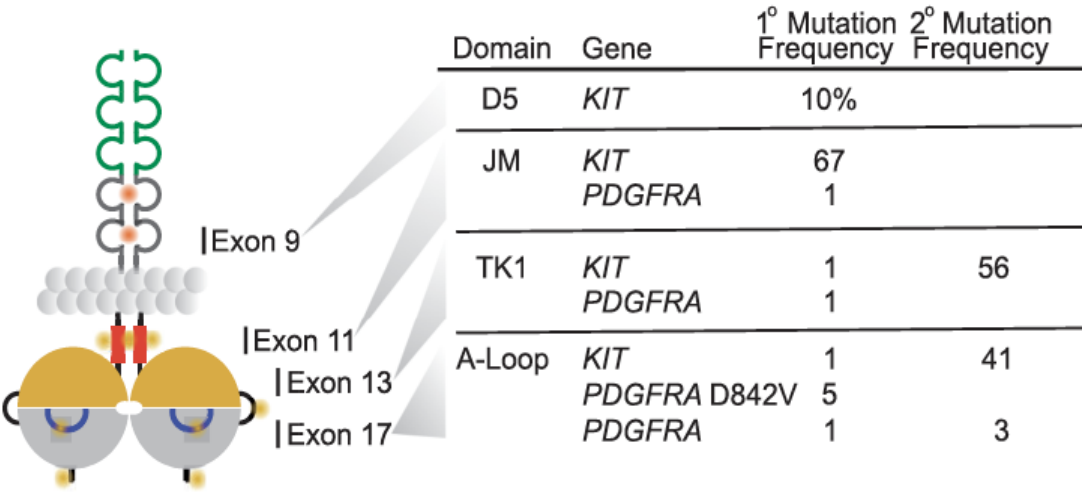
**A unique dual mechanism of action that regulates the kinase switch pocket and activation loop**

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



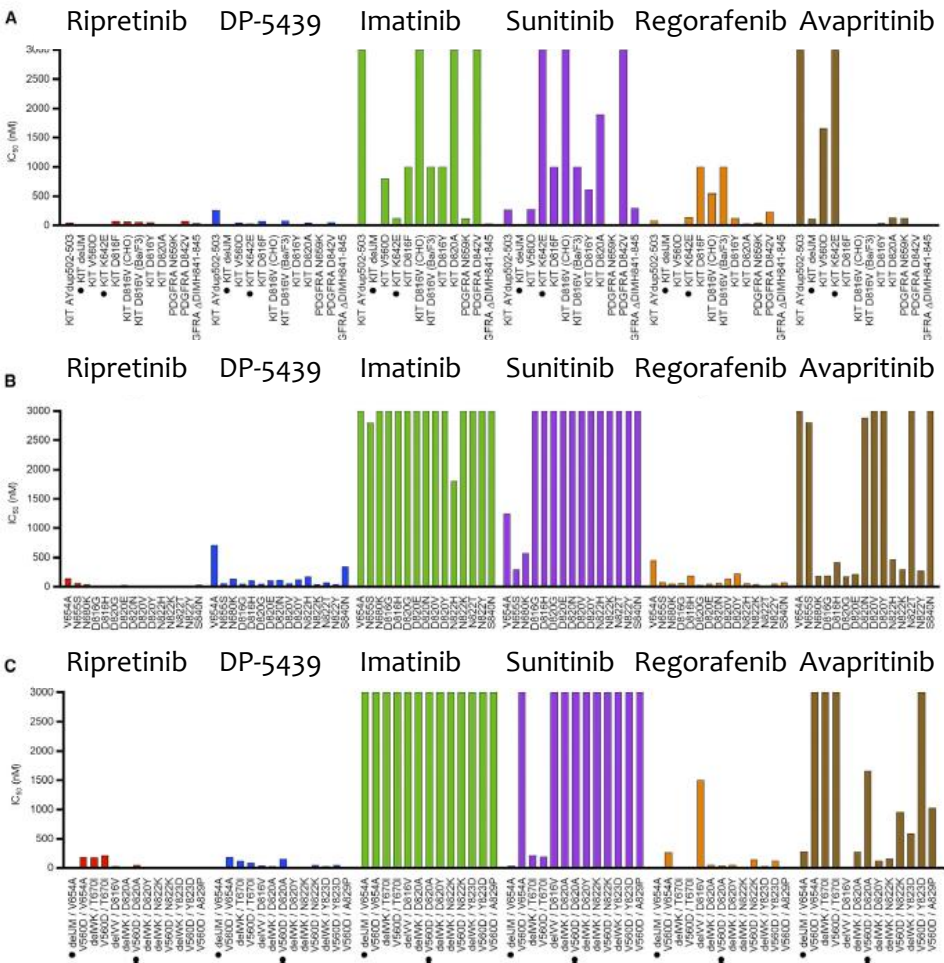
# Ripretinib: Designed to Address a Broad Range of Mutations in GIST

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.



# Significant Unmet Medical Need Post-Imatinib

Estimated Incidence of GIST: U.S. 4,000-6,000<sup>(1)</sup>

## 1<sup>st</sup> Line Treatment: **Imatinib\***

- mPFS: 18.9 months<sup>(2)</sup>
- mOS: 46.8 months<sup>(3)</sup>

1L

## 2<sup>nd</sup> Line Treatment: **Sunitinib\***

- mPFS: 5.6 months<sup>(4)</sup>
- mOS: 17.0 months<sup>(4)</sup>

2L

~2,000 U.S. incident  
patients eligible for  
treatment<sup>(6)</sup>

## 3<sup>rd</sup> Line Treatment: **Regorafenib\***

- mPFS: 4.8 months<sup>(5)</sup>
- mOS: 17.4 months<sup>(5)</sup>

3L

~70-80% eligible  
patients from  
prior line<sup>(7)</sup>

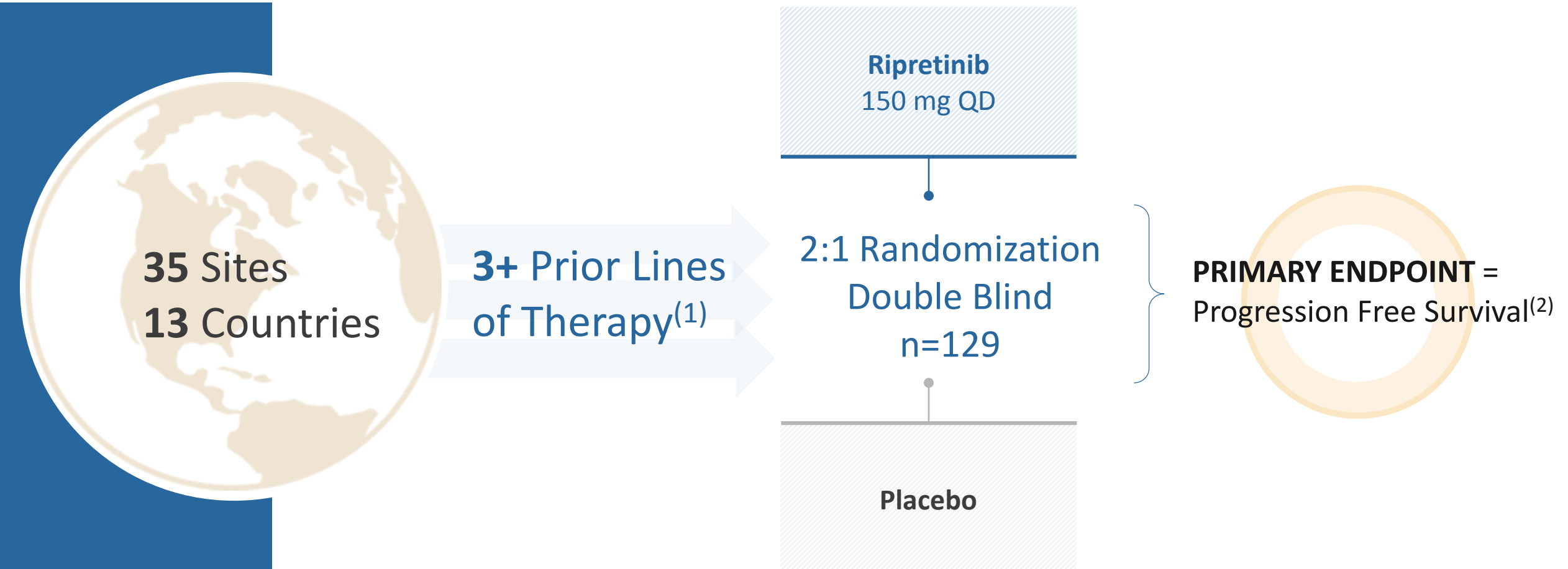
## 4<sup>th</sup> Line Treatment: **No Approved Treatment\***

4L

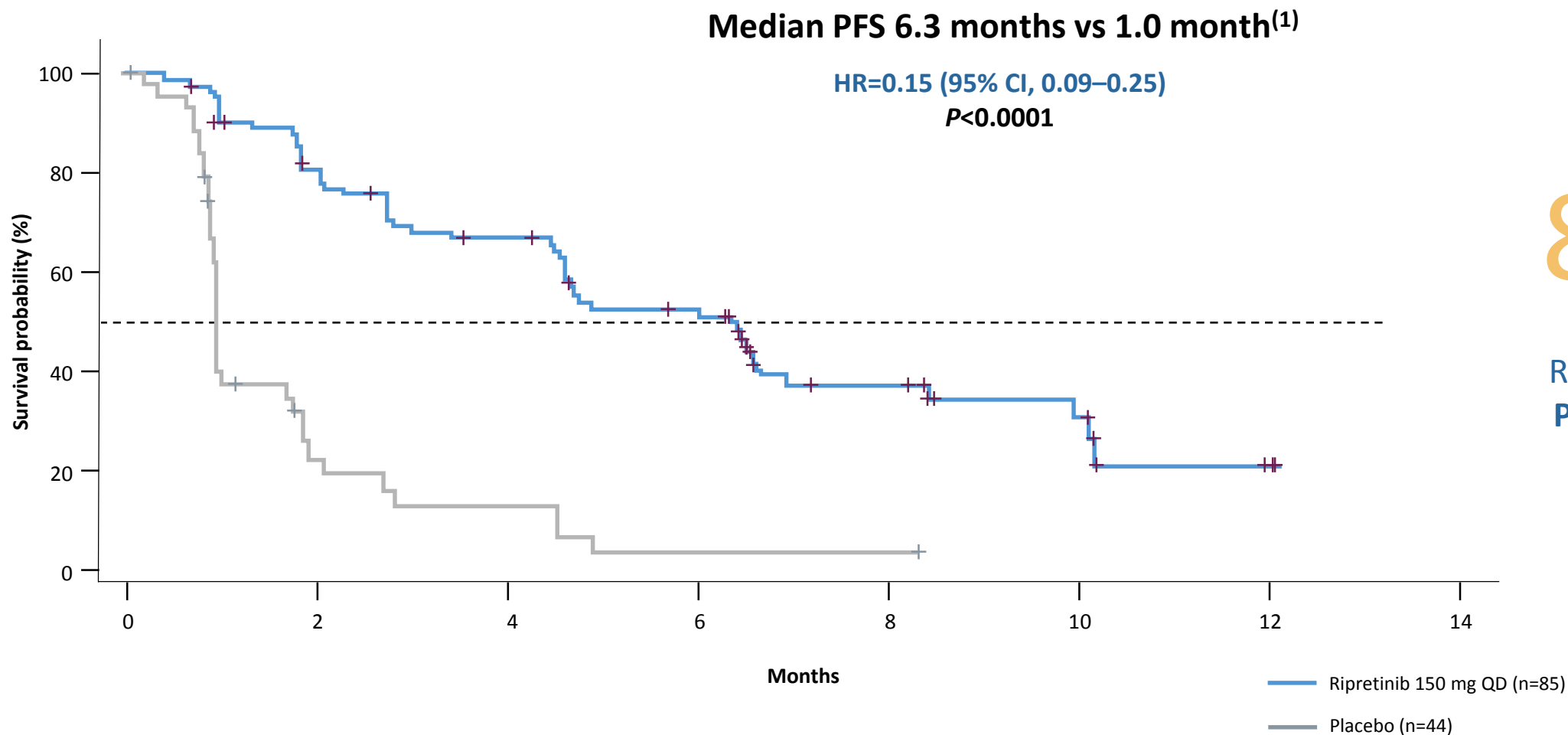
~70-80% eligible  
patients from  
prior line<sup>(7)</sup>


*\*Avapritinib is approved in the U.S. for GIST patients with PDGFRA exon 18 mutations only, which mutations are harbored by an estimated ~6% of patients with newly diagnosed GIST.*

# invictus > Global Pivotal Phase 3 Study in $\geq 4^{\text{th}}$ Line GIST



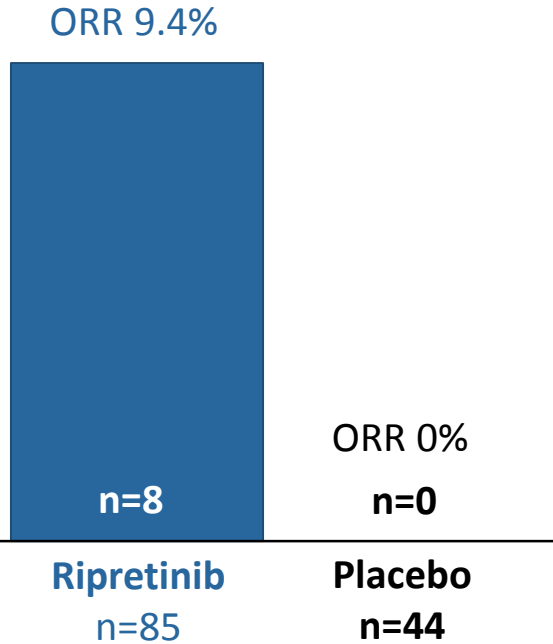
# invictus > Progression-Free Survival (PFS) Benefit



  
**85%**  
Reduction in  
Risk of **Disease  
Progression or  
Death** Versus  
Placebo

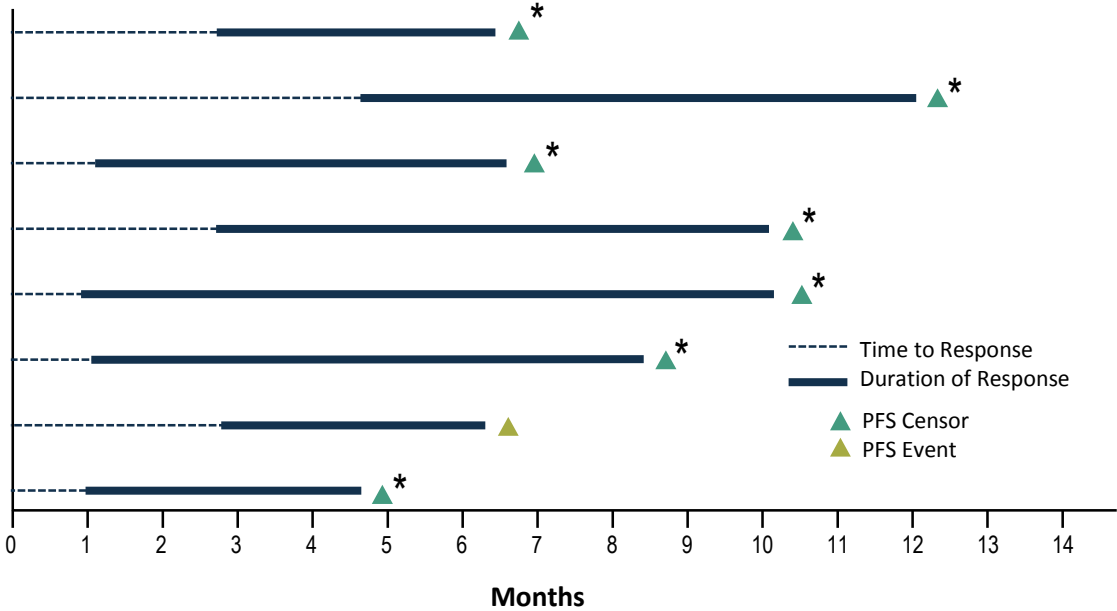
# invictus > Durable Response with Ripretinib

## Confirmed ORR



*P*=0.0504

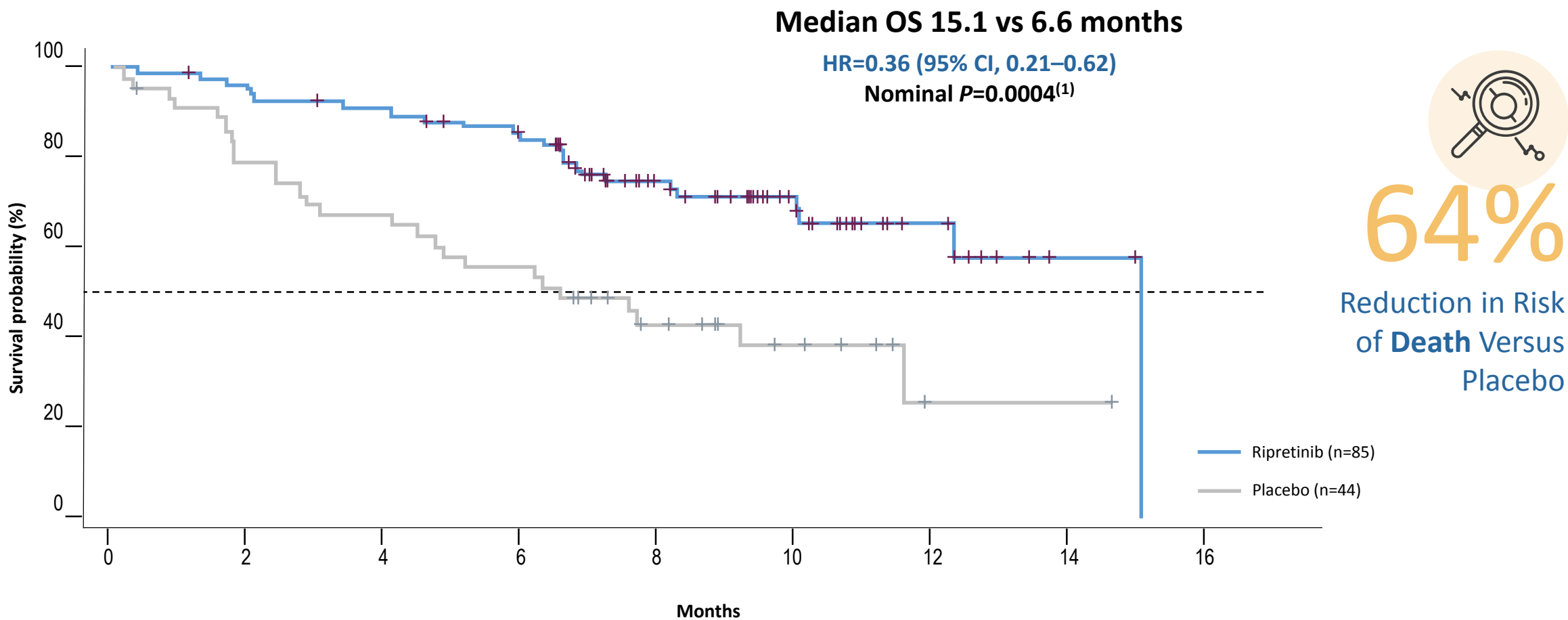
## Patients Who Responded (n=8)



- Median duration of response has not been reached yet
- \*7 of 8 ripretinib responders are still responding as of data cutoff
- All responders had partial responses



# invictus > Overall Survival (OS) Benefit



Notes: Data presented at ESMO Congress 2019; Data includes all time periods, including dose escalations. Placebo arm includes patients taking placebo who, following progression, were crossed-over to ripretinib treatment; (1) Due to hierarchical testing procedures of the end points, the OS end point could not be formally tested because the ORR was not statistically significant.

# invictus > Ripretinib Was Generally Well Tolerated

| TEAEs in >20%<br>of patients<br><br>Preferred Term | RIPRETINIB          |                                    | PLACEBO                            |  |
|--|---------------------|------------------------------------|------------------------------------|--|
|  | Any Grade<br>(n=85) | Grade 3/4<br>(n=85) <sup>(1)</sup> | Any Grade<br>(n=43) <sup>(2)</sup> | Grade 3/4<br>(n=43) <sup>(1),(2)</sup> |
| Any TEAE or grade 3/4 TEAE <sup>(3)</sup>          | 84 (99%)            | 42 (49%)                           | 42 (98%)                           | 19 (44%)                               |
| Alopecia   | 44 (52%)            | 0                                  | 2 (5%)                             | 0                                      |
| Fatigue  | 36 (42%)            | 3 (4%)                             | 10 (23%)                           | 1 (2%)                                 |
| Nausea   | 33 (39%)            | 3 (4%)                             | 5 (12%)                            | 0                                      |
| Abdominal pain                                     | 31 (37%)            | 6 (7%)                             | 13 (30%)                           | 2 (5%)                                 |
| Constipation                                       | 29 (34%)            | 1 (1%)                             | 8 (19%)                            | 0                                      |
| Myalgia  | 27 (32%)            | 1 (1%)                             | 5 (12%)                            | 0                                      |
| Diarrhea   | 24 (28%)            | 1 (1%)                             | 6 (14%)                            | 1 (2%)                                 |
| Decreased appetite                                 | 23 (27%)            | 1 (1%)                             | 9 (21%)                            | 1 (2%)                                 |
| PPE syndrome                                       | 18 (21%)            | 0                                  | 0                                  | 0                                      |
| Vomiting   | 18 (21%)            | 3 (4%)                             | 3 (7%)                             | 0                                      |

| Any TEAE<br>leading to... | RIPRETINIB<br>(n=85) | PLACEBO<br>(n=43) <sup>(2)</sup> |
|---------------------------|----------------------|----------------------------------|
| Dose reduction            | 6 (7%)               | 1 (2%)                           |
| Dose interruption         | 20 (24%)             | 9 (21%)                          |
| Treatment discontinuation | 7 (8%)               | 5 (12%)                          |
| Death <sup>(4)</sup>      | 5 (6%)               | 10 (23%)                         |

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

Ripretinib 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),  $P<0.0001$ )

Ripretinib showed a clinically meaningful improvement in **overall survival** vs. placebo, reducing the risk of death by **64%**

(median OS of 15.1 months vs. 6.6 months; HR=0.36, 95% CI (0.21-0.62), Nominal  $P=0.0004$ )



Ripretinib was associated with a favorable safety profile

## Ripretinib:

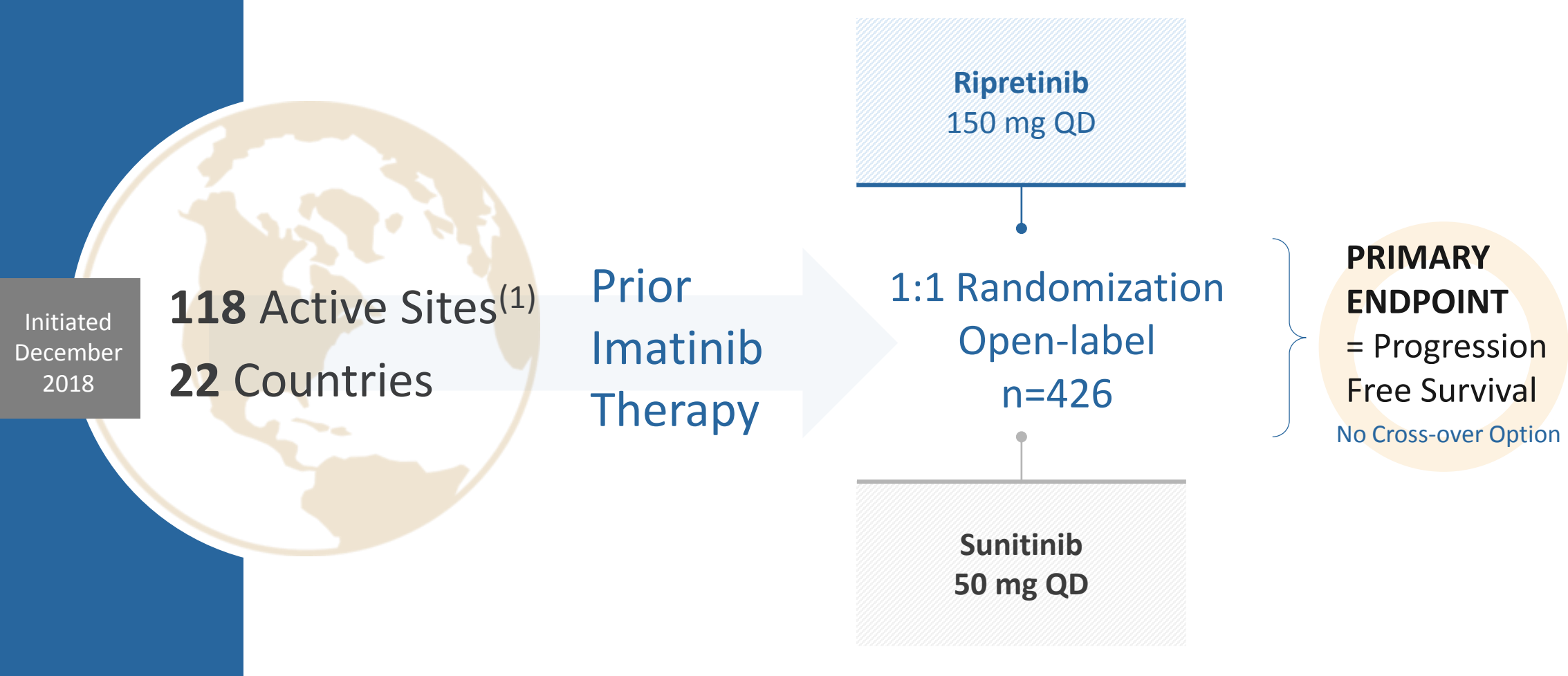
## Phase 1 GIST Cohorts Positive Updated Results Across All Lines of Treatment

| Line of Therapy <sup>(1)</sup>                        | 2 <sup>nd</sup> Line<br>(n=31) | 3 <sup>rd</sup> Line<br>(n=28) | ≥4 <sup>th</sup> Line<br>(n=83) |
|---|--------------------------------|--------------------------------|---------------------------------|
| Median Progression Free Survival                      | 46 weeks                       | 36 weeks                       | 24 weeks                        |
| Objective Response Rate<br>(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)**

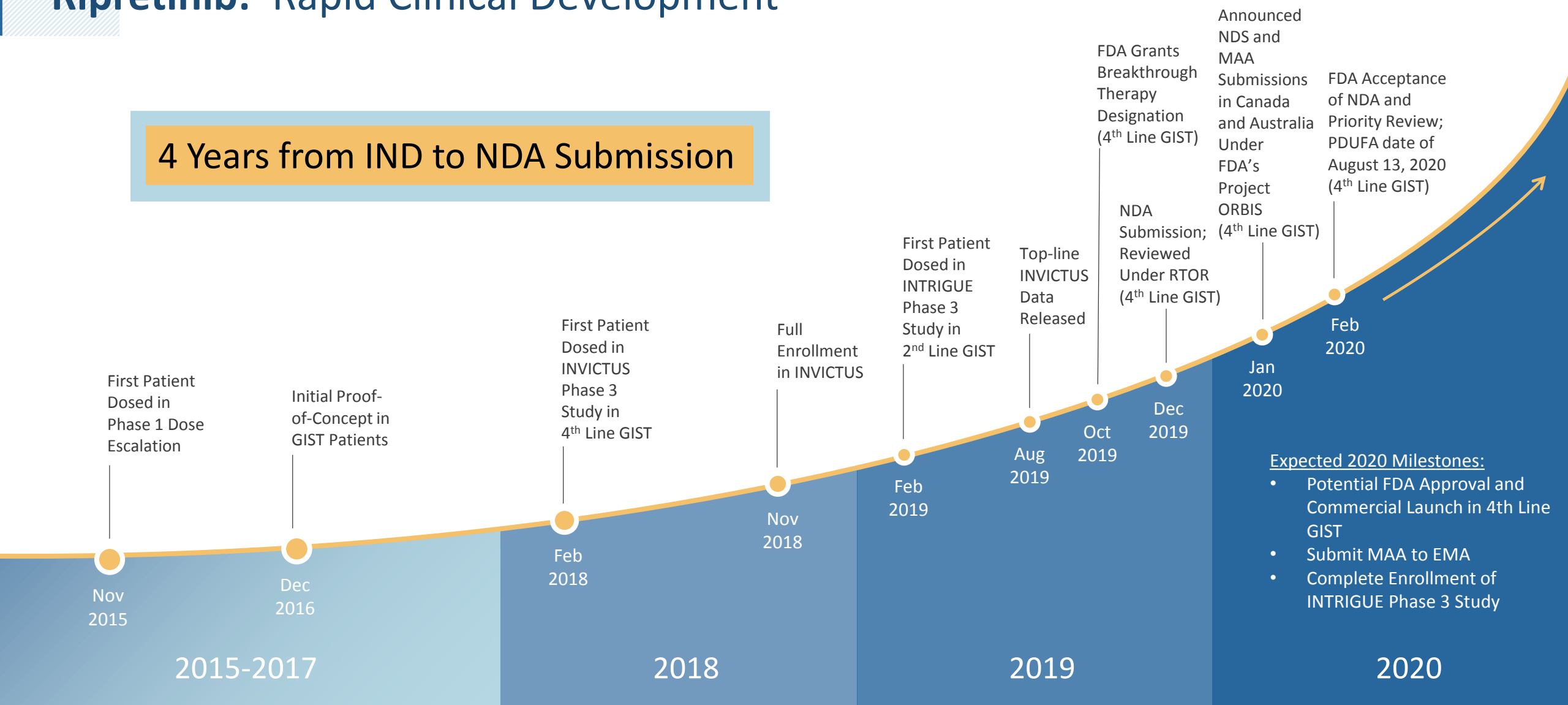


**intrigue** > Ongoing Global Pivotal Phase 3 Study in 2<sup>nd</sup> Line GIST



# Ripretinib: Rapid Clinical Development

4 Years from IND to NDA Submission



# Commercial Preparations are on Track for Potential 2020 Launch



## MEDICAL AFFAIRS

- ✓ MSL team built and engaging with KOLs
- ✓ Publication plan implemented
- ✓ Medical information build on track



## MARKETING

- ✓ Marketing teams in place (HCP and patient)
- ✓ Go-to-market strategies defined
- ✓ Active and appropriate KOL engagement ongoing
- ✓ Disease education program launched



## MARKET ACCESS

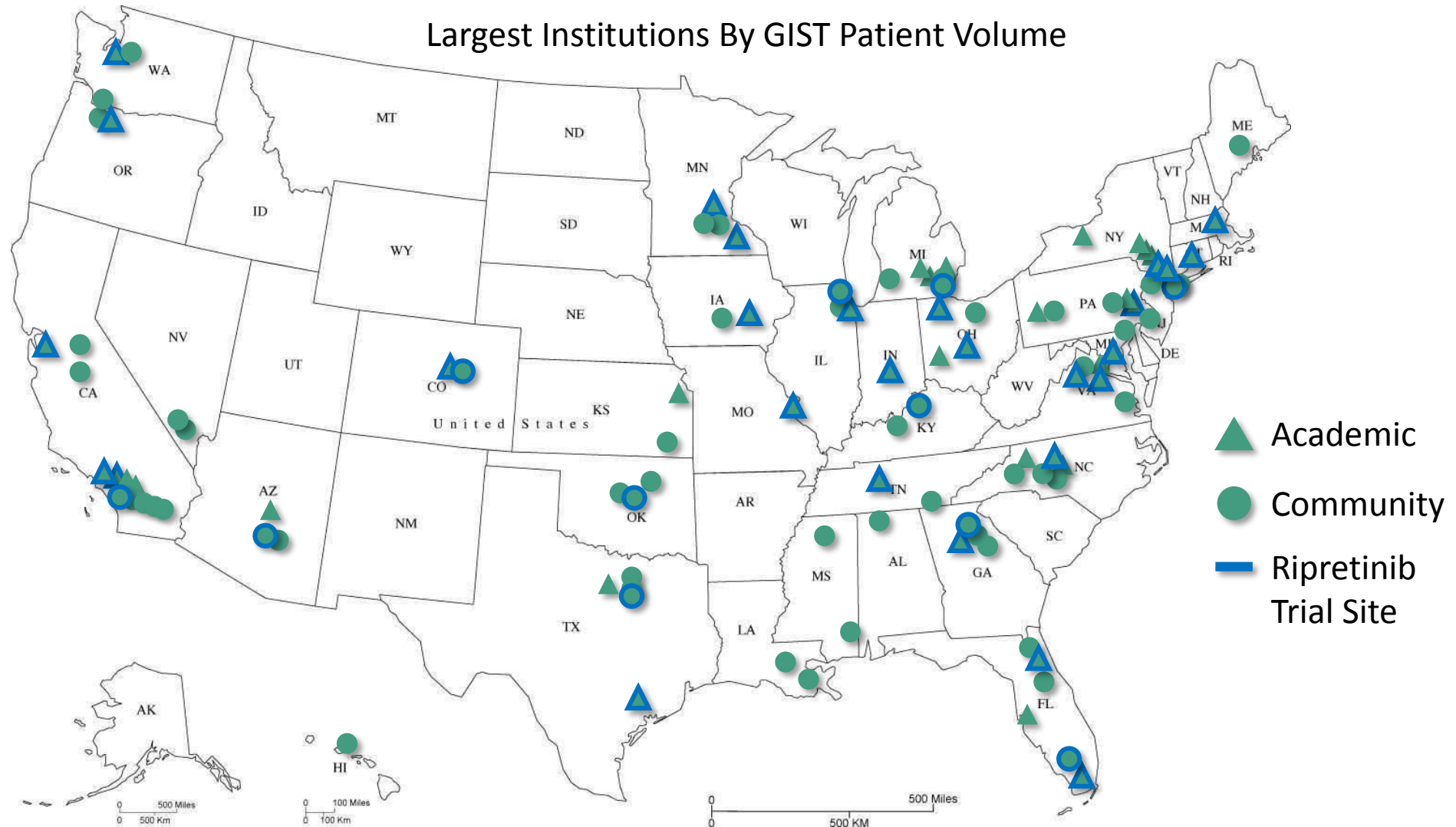
- ✓ Market access leadership in place
- ✓ Market access field team recruiting on track
- ✓ Distribution and patient support/assistance strategies defined and build on track



## SALES

- ✓ Sales leadership team in place
- ✓ Customer segmentation & targeting complete
- ✓ Selling model defined
- ✓ Sales force recruiting complete

# GIST Treatment Occurs in Both Academic (~30%) and Community (~70%) Institutions; Many Leading Institutions Have Participated in Ripretinib Trials





# In Deciphera Market Research, Oncologists Highlight Key Areas of Unmet Need

## Market Research Verbatims



*“We have a **very effective front-line treatment** available... which is very rewarding.”*



*“The toxicity [of post-imatinib therapies] is higher, so the cost in terms of **quality of life is worse** than when we are using imatinib.”*



*“...the transition to [post-imatinib therapy] is **difficult** emotionally as well as clinically.”*

## Commonly Cited Unmet Needs



Need for more effective and tolerable **treatment options** after front-line imatinib



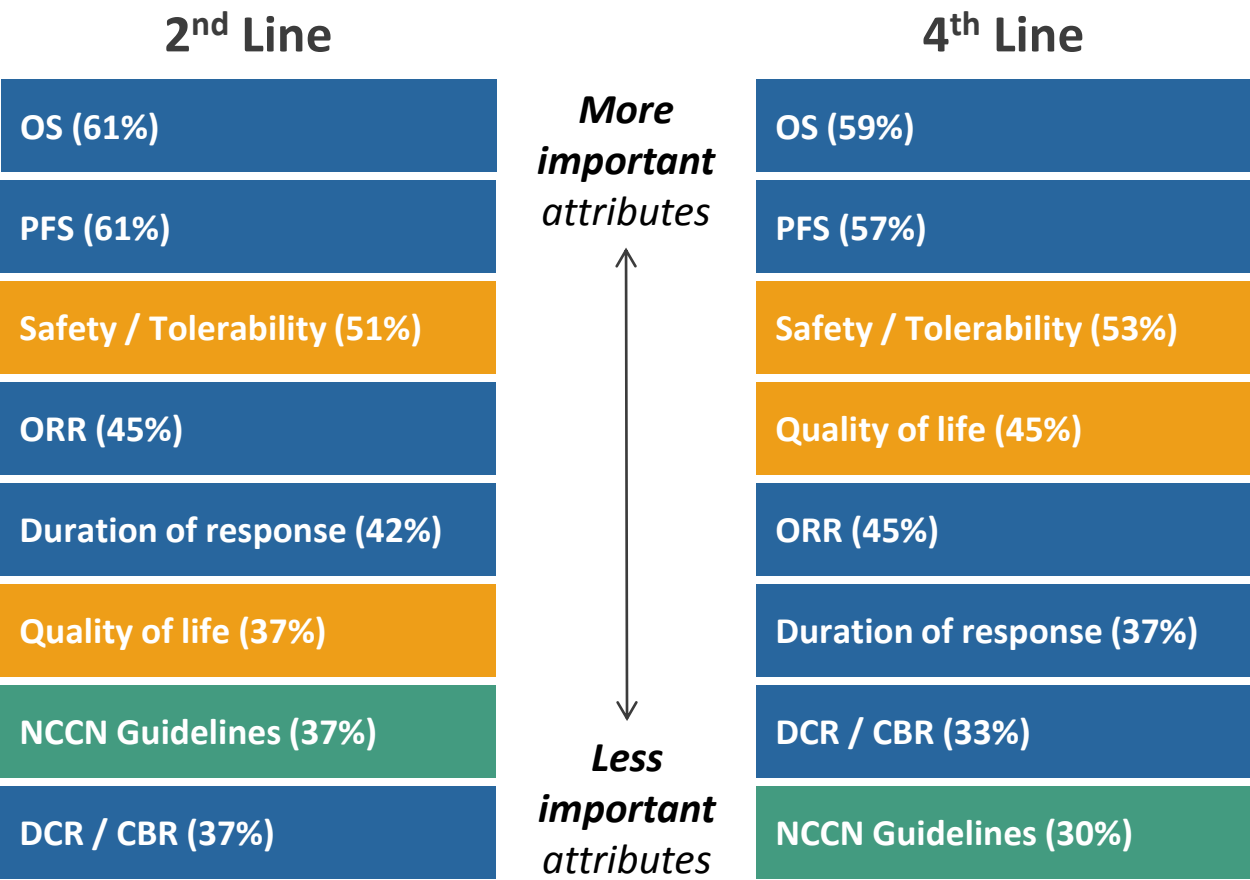
Need for therapies that address **mutational heterogeneity** across and within GIST patients



Need for **novel mechanism of action** to overcome resistance

# Deciphera Market Research Shows the Importance of OS, PFS, and Tolerability in GIST and High Interest in Ripretinib Product Profile

## Ranking of endpoints by level of importance<sup>(1, 2)</sup>



LEGEND: Efficacy Safety Other

97% of oncologists surveyed would consider using a product like ripretinib in advanced GIST<sup>(2)</sup>

Frequently cited reasons:

- ✓ Overall survival benefit
- ✓ Progression free survival benefit
- ✓ Duration of response
- ✓ Safety / tolerability profile
- ✓ Objective response rate

# Deciphera's Vision for Ripretinib in GIST is to be the Standard of Care Across All Approved Indications

Leverage ripretinib's differentiated mechanism of action and currently known clinical profile to address unmet medical needs



**Fast-to-market strategy** designed to fulfill urgent unmet need in 4<sup>th</sup> line GIST



**Expansion strategy**  
in 2<sup>nd</sup> line GIST designed to address need for more effective and tolerable options post-imatinib

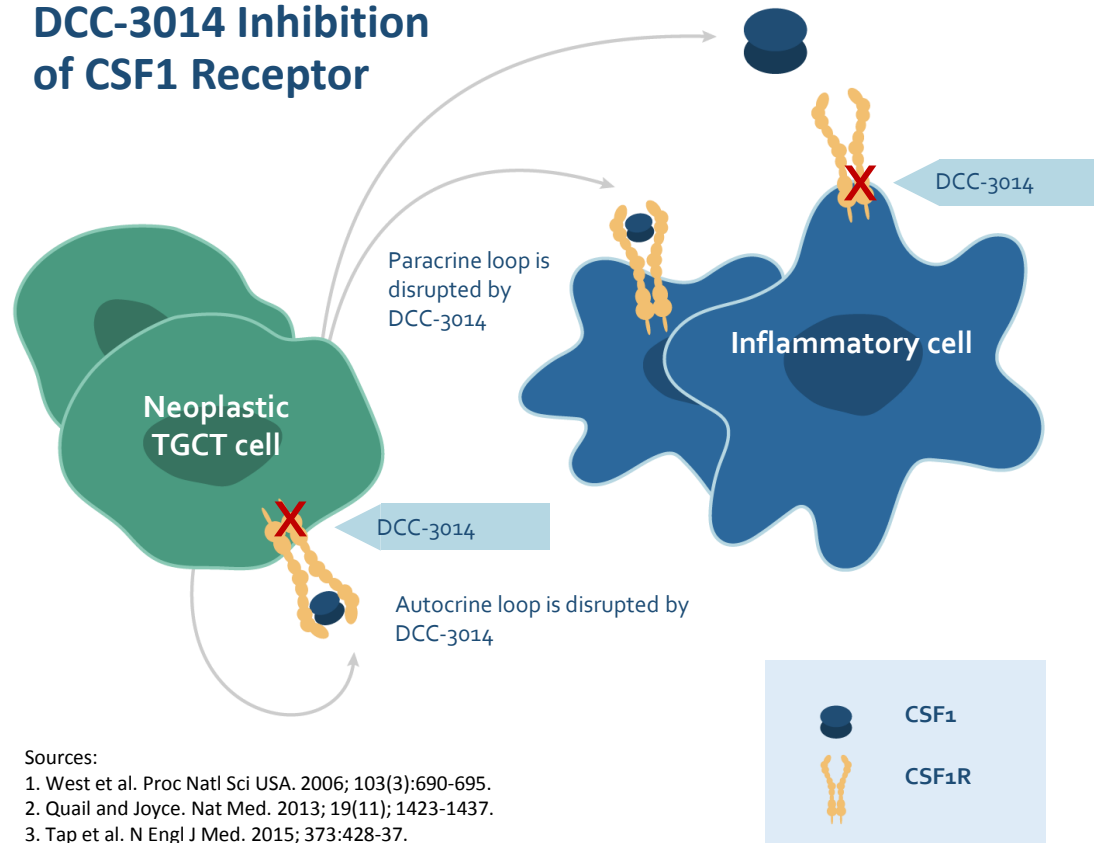


**LCM strategies**  
to explore additional uses and indications

- Front-line opportunities
- Potential combination strategies

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

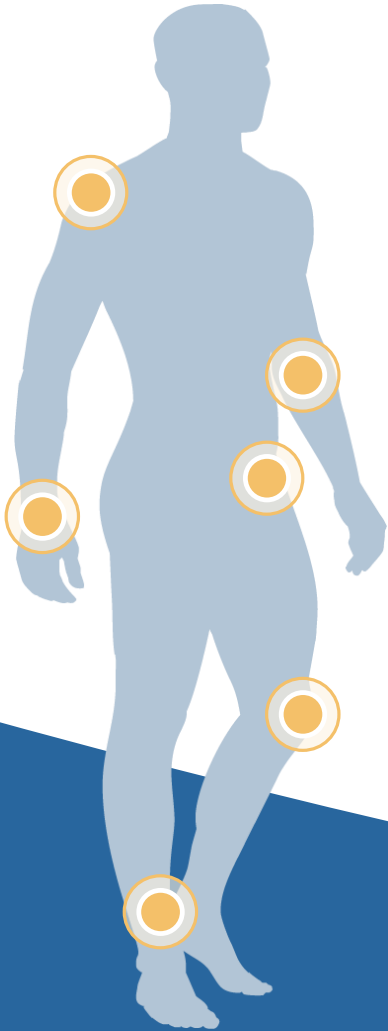
## DCC-3014 Inhibition of CSF1 Receptor



- Phase 1 dose escalation study ongoing
- Generally well tolerated at doses of up to 50 mg in patients 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

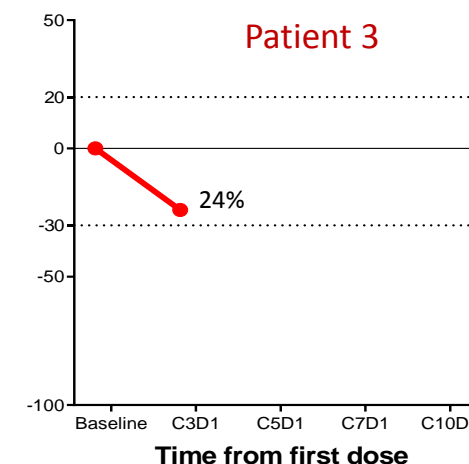
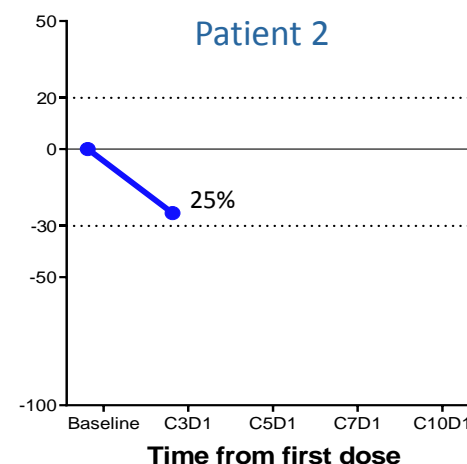
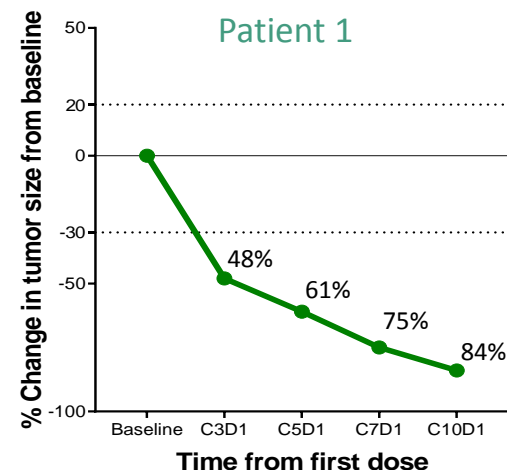
- Most commonly affects the knee, as well as hip, ankle, elbow and shoulder
- Annual incidence of new cases in the U.S.: ~1,300<sup>(1)</sup>

## 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  $\geq 3$  TEAEs observed

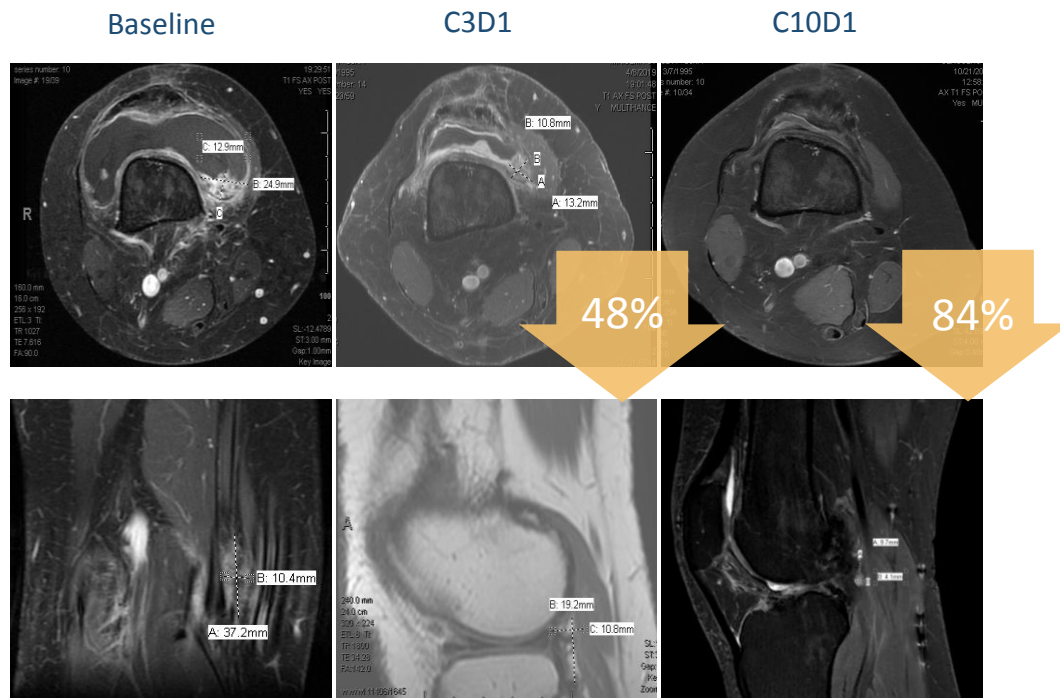
**Preliminary anti-tumor activity and symptomatic improvement**

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**

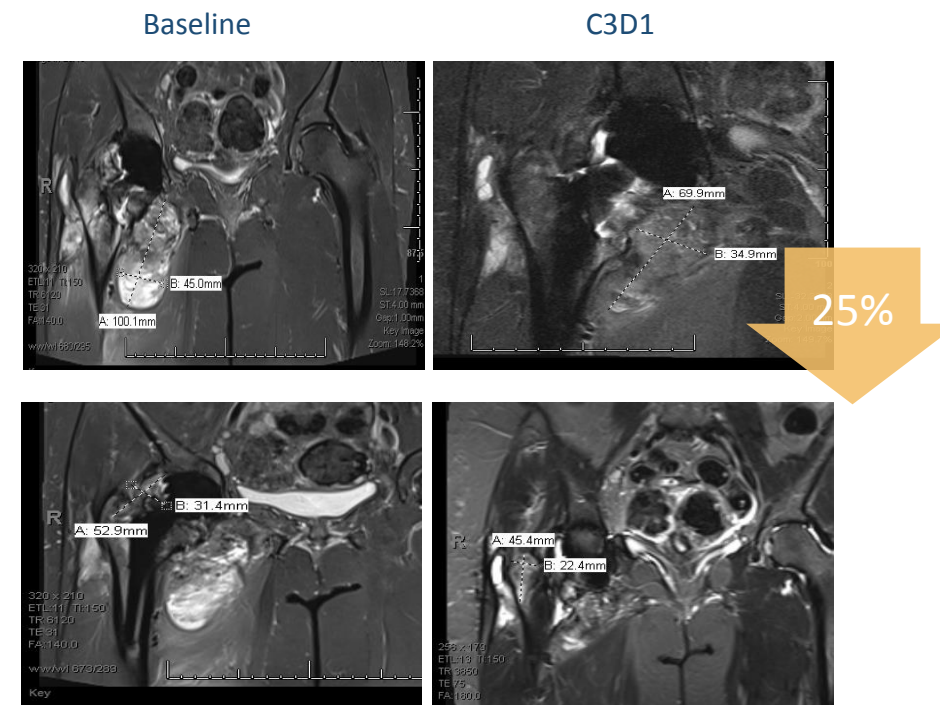
# DCC-3014: TGCT Case Studies from the Phase 1

Patient 1



- 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

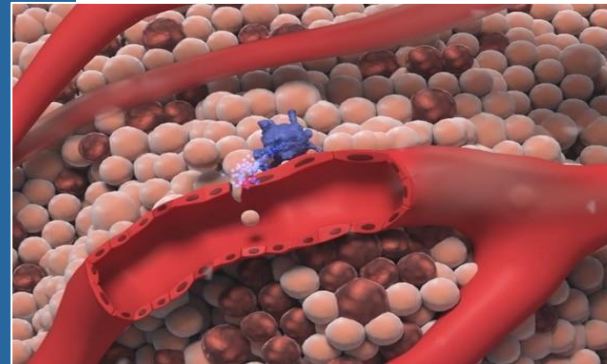


- 57-year-old female patient diagnosed with diffuse-type TGCT (right hip) in 2014, six prior surgeries, and recurrent disease on MRI by February 2019
- Active in Cycle 5 as of data cut-off

# 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
- M2 macrophages serve as pumps for tumor cell intravasation and metastasis
- Rebastinib is designed to inhibit chemotherapy-induced recruitment of M2 macrophages to tumors
- 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

## Part 1

**Rebastinib**  
50 mg BID +  
Paclitaxel<sup>(1)</sup>

n = 24

**Rebastinib**  
100 mg BID +  
Paclitaxel<sup>(1)</sup>

n = 19

**Rebastinib**  
50 mg BID +  
Paclitaxel  
Phase 2 Dose

## Part 2

Simon Two-Stage Design

**Stage 1**  $n \leq 18$  per cohort

**Stage 2**  $n = \text{up to } 33$  per cohort

**Cohort 1**  
Triple Negative Breast Cancer

**Cohort 2**  
Inflammatory Breast Cancer

**Cohort 3**  
Ovarian Cancer

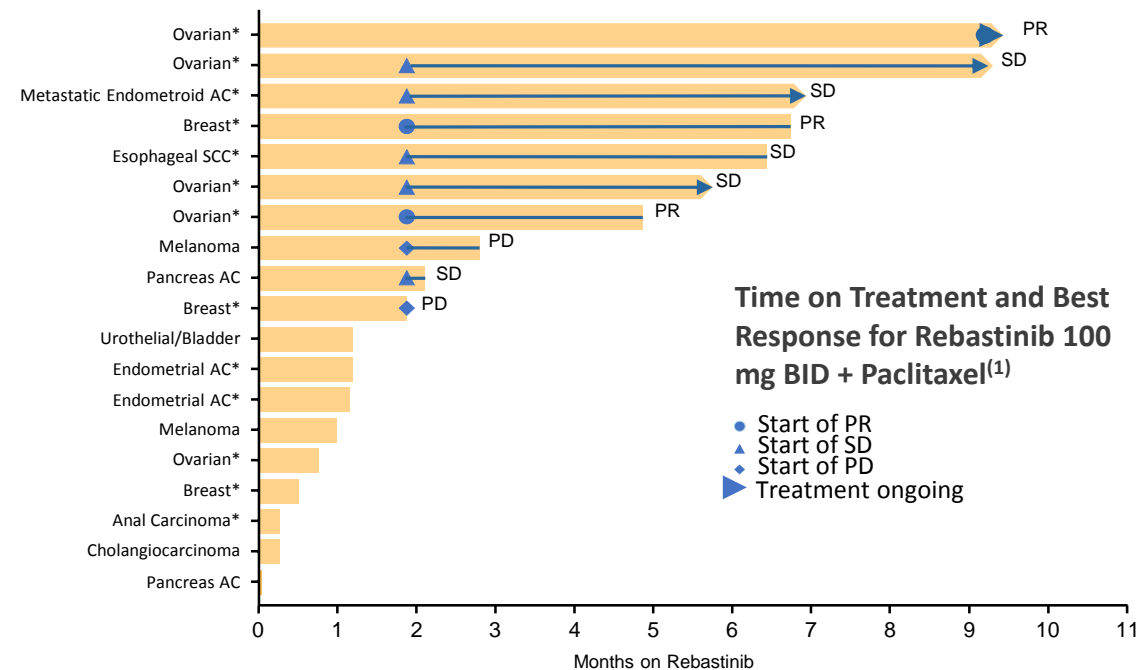
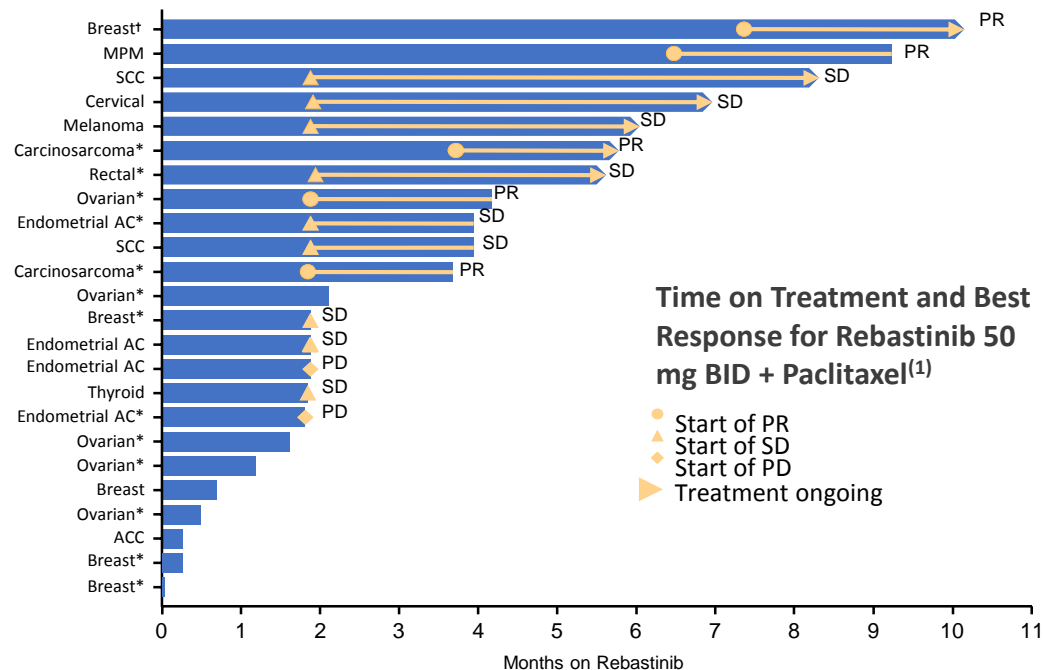
**Cohort 4**  
Endometrial Cancer

**Cohort 5**  
Carcinosarcoma

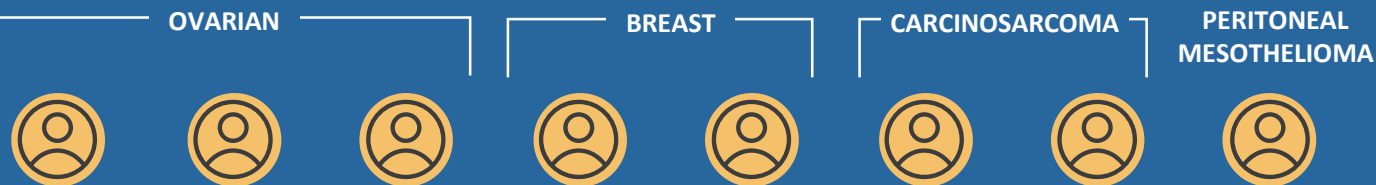
If  $>4$  responses in Stage 1, enroll additional patients in Stage 2 (up to 33 per cohort)

If  $\leq 4$  responses, discontinue the cohort

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



Objective responses





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

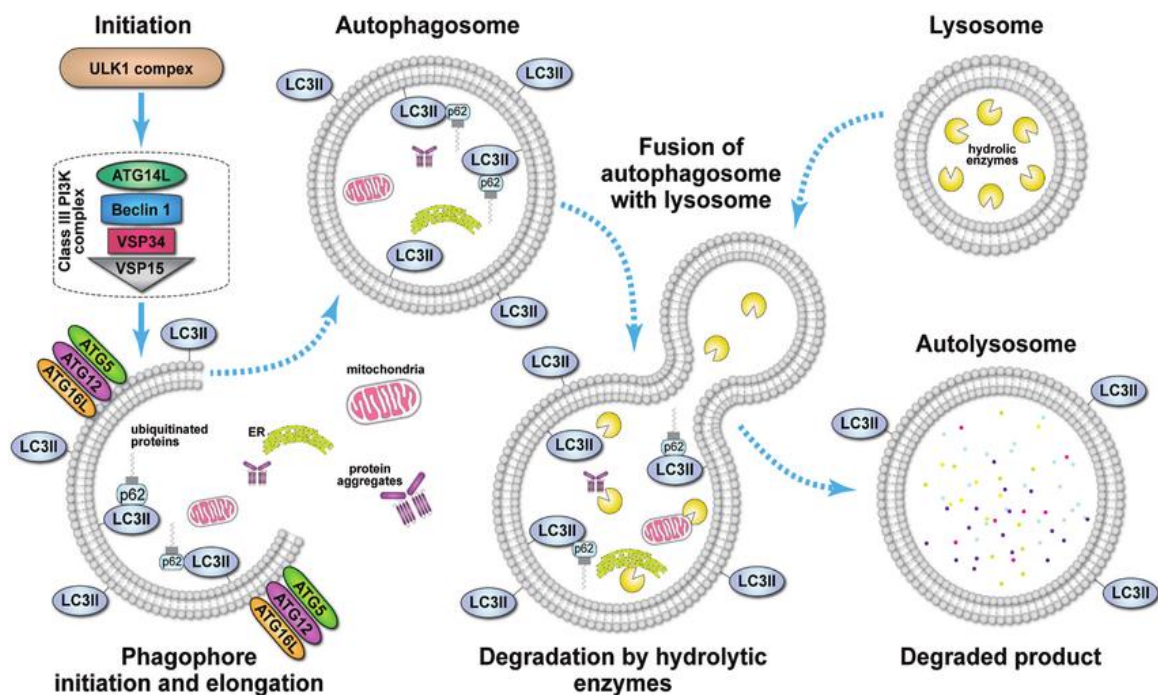
TEAEs ≥ 10% regardless of relatedness

| Preferred Term                | 50 mg BID<br>(n=24) |           | 100 mg BID<br>(n= 19) |           | Total<br>(n=43) |           |
|-------------------------------|---------------------|-----------|-----------------------|-----------|-----------------|-----------|
|                               | 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

As of March 31, 2020

Shares  
Outstanding

55.7 MM (basic)  
63.4 MM (fully-diluted)

Cash Expected to Fund Operating  
Expenses and CapEx into the Second  
Half of 2022

Cash, Cash  
Equivalents  
& Marketable  
Securities

\$692 MM

# Significant Expected 2020 Milestones Across the Pipeline

## Ripretinib

- ✓ FDA grants Priority Review and sets PDUFA data of August 13, 2020 in advanced GIST (1Q20)
- Potential commercial launch in 4<sup>th</sup> line GIST (2H20)
- Submit EU Marketing Authorization Application to EMA (2H20)
- Complete enrollment in the INTRIGUE Phase 3 study in 2<sup>nd</sup> line GIST (2H20)
- Present Phase 1 study expansion data (2H20)

## DCC-3014

- Select Phase 2 dose for TGCT and initiate the expansion portion of study (2H20)
- Update Phase 1 data in TGCT patients (2H20)

## Rebastinib

- ✓ Select Phase 2 dose and activate Part 2 of Phase 1b/2 study in combination with carboplatin (1Q20)
- ✓ Present Phase 1b/2 data in combination with paclitaxel (2Q20)
- Present Phase 1b/2 data in combination with carboplatin (2H20)

## DCC-3116

- Submit IND application to FDA (2H20)





THANK  
YOU