Addressing Key Mechanisms of Tumor Drug Resistance

July 2018

Kinase switch control inhibitors for tumor-targeted and immune-targeted cancer therapies
Our Proprietary Kinase Switch Control Platform

Kinase Switched “Off”
- Switch pocket
- Activation switch “Off”

Kinase Switched “On”
- Activation switch “On”

Deciphera Switch Control
- Switch control inhibitor embeds deeply into switch pocket
- Inhibits switch activation

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

## Tumor-Targeted Programs and Indications

<table>
<thead>
<tr>
<th>Program</th>
<th>Pre-Clinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Global Rights</th>
</tr>
</thead>
<tbody>
<tr>
<td>DCC-2618</td>
<td>KIT &amp; PDGFRα</td>
<td>GIST¹</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>PDGFRα</td>
<td>GBM &amp; Glioma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>KIT (D816V)</td>
<td>Advanced Systemic Mastocytosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>KIT &amp; PDGFRα</td>
<td>Other Cancers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Undisclosed</td>
<td>Cancer Metabolism</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Immunokinase Programs and Indications

<table>
<thead>
<tr>
<th>Program</th>
<th>Pre-Clinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Global Rights</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rebatinib</td>
<td>TIE2 Breast Cancer + Chemotherapy²</td>
<td></td>
<td></td>
<td></td>
<td>deciphera</td>
</tr>
<tr>
<td>TIE2 Checkpoint Inhibitor Combination</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>deciphera</td>
</tr>
<tr>
<td>DCC-3014</td>
<td>CSF1R Solid Tumors &amp; Hematological Malignancies</td>
<td></td>
<td></td>
<td></td>
<td>deciphera</td>
</tr>
<tr>
<td>CSF1R Checkpoint Inhibitor Combination</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>deciphera</td>
</tr>
<tr>
<td>Undisclosed Immunokinase</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>deciphera</td>
</tr>
</tbody>
</table>

### Notes:
- (1) Phase 3 Pivotal Study in 4th line & 4th line+ patients.
- (2) Investigator initiated and sponsored research.
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

4th Line GIST

>4th Line GIST

2nd – 3rd Line GIST

Systemic Mastocytosis

Malignant Gliomas

Other Solid Tumors
### ASCO 2018: Phase 1 Demographics and Baseline Characteristics

**GIST Patients at ≥100 mg/d**

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

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

- 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 4th Line GIST Phase 3 Trial

### GIST PATIENTS @ 150 mg QD

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

Note: Data presented at AACR Annual Meeting on April 16, 2018 based on cutoff as of March 18, 2018.
### Best Response, DCR & ORR By Line of Treatment at ≥100 mg/d

<table>
<thead>
<tr>
<th>Line of Therapy</th>
<th>Total Patients(1)</th>
<th>Active(1)</th>
<th>DCR @ 3 Months(2)</th>
<th>ORR(2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2nd Line</td>
<td>25</td>
<td>68%</td>
<td>79%</td>
<td>24%</td>
</tr>
<tr>
<td>3rd Line</td>
<td>29</td>
<td>76%</td>
<td>82%</td>
<td>24%</td>
</tr>
<tr>
<td>≥4th Line</td>
<td>96</td>
<td>53%</td>
<td>64%(3)</td>
<td>9%(3)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>150</strong></td>
<td><strong>60%</strong></td>
<td><strong>70%(3)</strong></td>
<td><strong>15%(3)</strong></td>
</tr>
</tbody>
</table>

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 ≥ 4th Line GIST Patients

77% Best Response in ≥ 4th Line for DCC-2618

64% DCR @ 3 Months in ≥ 4th Line for DCC-2618

**Best Response per RECIST**

KIT & PDGFRα ≥ 100 mg/d (n=82)

**Tumor Control per RECIST**

KIT & PDGFRα ≥ 100 mg/d (n=89)

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

Cumulative Reductions in Circulating MAF of KIT Exons 9, 11, 13, 14, 17 and 18 by Lines of Therapy (n=73)\(^{(1)}\)
(Note log scale: -1 = 10-fold reduction, -2 = 100-fold reduction)

- 78% achieved more than 50% KIT MAF reduction
- 48% were KIT negative on treatment

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\(^{nd}\) to ≥ 4\(^{th}\) line GIST

Note: (1) Based on data from 73 patients with detectable KIT mutations at baseline.
Global Pivotal Phase 3 GIST Program
Invictus Study Design

3 prior lines of therapy

2:1 Randomization
Double Blind
n=120

DCC-2618
150 mg QD
n=80

Placebo
N/A
n=40

Primary Endpoint for Approval = PFS
Following progression: (a) placebo patients can crossover to DCC-2618 and (b) DCC-2618 patients can continue on treatment or escalate to 150 mg BID

(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%
- 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
  • https://clinicaltrials.gov/ct2/show/study/NCT03353753

• http://www.invictusclinicalstudy.com

• Deciphera’s contact information:
  • Clinical Team INVICTUS +1 781.209.6400
  • clinicaltrials@deciphera.com
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.

Prior imatinib therapy\(^{(2)}\)

1:1 Randomization
Open Label
n=350

DCC-2618
150 mg QD
n=175

Sunitinib
50 mg QD
n=175

Primary Endpoint for Approval = PFS

No cross-over option