Targeting the genetic and immunological drivers of cancer

Corporate Presentation
February 2021
Safe Harbor Statement

This presentation contains certain forward-looking statements regarding the business of Mirati Therapeutics, Inc. (“Mirati”). Any statement describing Mirati’s goals, expectations, financial or other projections, intentions or beliefs, development plans and the commercial potential of Mirati’s drug development pipeline, including without limitation adagrasib (MRTX849), sitravatinib and MRTX1133, is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to risks and uncertainties, particularly those challenges inherent in the process of discovering, developing and commercialization of new drug products that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such drugs.

Mirati’s forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause its results to differ materially from those expressed or implied by such forward-looking statements. Although Mirati’s forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Mirati. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Mirati’s programs are described in additional detail in Mirati’s quarterly reports on Form 10-Q and annual reports on Form 10-K, which are on file with the U.S. Securities and Exchange Commission (the “SEC”) available at the SEC’s Internet site (www.sec.gov). Mirati assumes no obligation to update the forward-looking statements, or to update the reasons why actual results could differ from those projected in the forward-looking statements, except as required by law.
A Bold Approach to Develop Novel Oncology Therapies, Including Two Registration-Enabling Programs in Large NSCLC Patient Populations

**IO Resistance**

Sitravatinib
Inhibitor of TAM and VEGFR2

- NSCLC
- Bladder
- Others

Compelling preliminary Phase 2 data in combination with a PD-1 support and inform SAPPHIRE Phase 3 approach in NSCLC

**KRAS Selective Inhibition**

Adagrasib (MRTX849)
G12C selective inhibitor

- NSCLC
- CRC
- Others

Compelling early efficacy and favorable tolerability with broad development in both monotherapy and combinations

MRTX1133
G12D selective inhibitor

- Pancreatic
- CRC
- Others

Potential first-in-class G12D inhibitor advancing through IND-enabling studies

Meaningful operational and commercial synergies across portfolio, particularly in NSCLC

Continued progress and advancement across our targeted oncology research platform

$1.4 billion in cash, cash equivalents and short-term investments as of 12/31/20

NSCLC: non-small cell lung cancer; CRC: colorectal cancer; IO: immuno-oncology; IND: investigational new drug
BeiGene is currently running a subset of combination studies of sitravatinib + tislelizumab (their anti-PD-1) in Asia for multiple solid tumor indications including NSCLC, HCC, RCC, ovarian and gastric cancers.

BeiGene has Asian commercialization rights (ex-Japan) for sitravatinib as part of our development and commercialization agreement (Jan. 2018) and is responsible for additional data disclosures. Additional data is expected in 2021.

### Robust Pipeline Spans Multiple Targets & Tumor Types with Near-Term Catalysts

<table>
<thead>
<tr>
<th>Compound</th>
<th>Development Approach</th>
<th>Indication</th>
<th>Lead Optimization</th>
<th>IND-enabling</th>
<th>Phase 1/1b</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Planned Near-Term Catalysts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adagrasib (MRTX849)</td>
<td>Monotherapy</td>
<td>2L+ NSCLC, CRC, Pancreatic, Other</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2L+ NSCLC data update and NDA filing in 2H:2021</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1L NSCLC: STK11 Co-Mutation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>P2 initiated in Q1:2021</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2L NSCLC</td>
<td>Randomized to Docetaxel</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>P3 initiated in Q1:2021</td>
</tr>
<tr>
<td>Pembrolizumab (PD-1)</td>
<td>Monotherapy</td>
<td>1L NSCLC</td>
<td>2 Arms: &lt;1% TPS and ≥1% TPS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>P2 initiated Q4:2020; POC data in 2H:2021</td>
</tr>
<tr>
<td>Cetuximab (EGFR)</td>
<td>Monotherapy</td>
<td>2L CRC</td>
<td>Randomized to FOLFIRI or FOLFOX</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>P3 initiation by Q2:2021; POC data in 2H:2021</td>
</tr>
<tr>
<td>POC Combinations: SHP2, Pan-EGFR, CDK4/6, SOS1</td>
<td></td>
<td>2L+ NSCLC &amp; CRC</td>
<td>Proof of Concept (POC)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Initial SHP2 data in Q2/Q3:2021; CDK4/6 &amp; SOS1 initiations in 2021</td>
</tr>
<tr>
<td>MRTX1133</td>
<td>Monotherapy</td>
<td>Pancreatic, CRC, NSCLC, Other</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>IND in 1H:2021</td>
</tr>
<tr>
<td>KRAS G12D Inhibitor</td>
<td>PD-1</td>
<td>2/3L NSCLC</td>
<td>SAPPHIRE (Checkpoint Refractory) – in combination with nivolumab</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>P3 interim OS analysis in 2H:2022</td>
</tr>
<tr>
<td>Sitravatinib</td>
<td>PD-1</td>
<td>NSCLC, Bladder &amp; Other</td>
<td>Mirati-Sponsored Studies / ISTs / BeiGene (1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Additional data in 2022</td>
</tr>
<tr>
<td>Multi Kinase Inhibitor</td>
<td>Synthetic Lethal PRMT5 Inhibitor</td>
<td>MTAP-Deleted Cancers</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>IND in 1H:2022</td>
</tr>
<tr>
<td>Discovery Programs</td>
<td>RAS Signaling Modifier</td>
<td>Solid Tumors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mutant KRAS Inhibitor</td>
<td>Solid Tumors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NSCLC: non-small cell lung cancer; CRC: colorectal cancer; HCC: hepatocellular carcinoma; RCC: renal cell carcinoma

1. BeiGene is currently running a subset of combination studies of sitravatinib + tislelizumab (their anti-PD-1) in Asia for multiple solid tumor indications including NSCLC, HCC, RCC, ovarian and gastric cancers. BeiGene has Asian commercialization rights (ex-Japan) for sitravatinib as part of our development and commercialization agreement (Jan. 2018) and is responsible for additional data disclosures. Additional data is expected in 2021.
Adagrasib (MRTX849): KRAS G12C Selective Inhibitor
KRAS is the Most Frequently Mutated Gene in Human Cancer

**KRAS Signaling**
A key regulator of cell growth and survival

**Abnormal KRAS Signaling**
Mutated KRAS activity is uncontrolled
KRAS G12C Mutations Occur Frequently in Multiple Tumor Types

Prevalent in Tumors with High Unmet Need

**KRAS G12C Mutational Frequencies**

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Frequency</th>
<th>Total US/Europe Pts</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSCLC</td>
<td>14%</td>
<td>~ 44,000</td>
</tr>
<tr>
<td>Colorectal</td>
<td>3-4%</td>
<td>~ 20,000</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>2%</td>
<td>~ 4,000</td>
</tr>
</tbody>
</table>

**Large Patient Population**

US and Europe Patients

- KRAS G12C: ~ 70,000
- ALK: ~ 25,000
- RET: ~ 13,000
- TRK: ~ 2,000


2. Mirati estimates based on epidemiology data reported in Globocan 2022 (accessed 2019) and frequencies by mutation; Europe includes EU, Russia and 10 additional European countries; RET estimate does not include thyroid cancer. Rounded to the nearest 1,000.
Adagrasib (MRTX849):
KRAS G12C Selective Inhibitor-Clinical Results NSCLC
Adagrasib: Designed to Fully Inhibit Mutant KRAS G12C for Entire Dose Interval

Long Half Life

- New synthesis of the mutant KRAS protein (half-life ~ 24h) can reactivate signaling in the absence of drug\(^2\)
- Long half-life ensures the pathway is maximally inhibited throughout the entire dosing interval

Extensive Tissue Distribution

- Maximize systemic exposure for duration of dosing
- Extensive volume of tissue distribution ensures optimal target coverage throughout dosing interval

Initial Clinical Activity\(^4\)

Depth of response

- 70% of NSCLC responders had shown a >40% reduction in tumor change from baseline
- 86% of NSCLC patients showed tumor shrinkage

Brain penetrance

- Encouraging and clinically meaningful measure of CSF / CNS penetration observed preclinically: \(K_{p,uu}\) of 0.4 (1hr)
- Clinical POC: heavily pre-treated NSCLC patient experienced 63% reduction of primary lung tumor and disappearance of active brain metastases

---

Incidence of Treatment-Related Adverse Events

<table>
<thead>
<tr>
<th>TRAEs&lt;sup&gt;b,c&lt;/sup&gt;, %</th>
<th>Any grade</th>
<th>Grades 3-4</th>
<th>Grade 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any TRAEs</td>
<td>85%</td>
<td>30%</td>
<td>2%</td>
</tr>
</tbody>
</table>

Most frequent TRAEs<sup>a,d</sup>, %

<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>54%</td>
<td>2%</td>
<td>0%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>51%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>35%</td>
<td>2%</td>
<td>0%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>32%</td>
<td>6%</td>
<td>0%</td>
</tr>
<tr>
<td>Increased ALT</td>
<td>20%</td>
<td>5%</td>
<td>0%</td>
</tr>
<tr>
<td>Increased AST</td>
<td>17%</td>
<td>5%</td>
<td>0%</td>
</tr>
<tr>
<td>Increased blood creatinine</td>
<td>15%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>15%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>QT prolongation</td>
<td>14%</td>
<td>3%</td>
<td>0%</td>
</tr>
<tr>
<td>Anemia</td>
<td>13%</td>
<td>2%</td>
<td>0%</td>
</tr>
</tbody>
</table>

- Grade 5 TRAEs included pneumonitis in a patient with recurrent pneumonitis (n=1) and cardiac failure (n=1)
- 4.5% of Treatment Related AE led to discontinuation of treatment (7.3% of AEs led to discontinuation of treatment)

<sup>a</sup>Includes patients pooled from Phase 1/1b and Phase 2 NSCLC (n=79), and CRC and Phase 2 other tumor cohorts (n=31).
<sup>b</sup>Includes events reported between first dose and 30 August 2020.
<sup>c</sup>The most common treatment-related SAEs reported (2 patients each) reported were diarrhea (grade 1, grade 2) and hyponatremia (both grade 3).
<sup>d</sup>Occurred in ≥10%.

NSCLC: non-small cell lung cancer; BID: twice daily dosing

Data as of 30 August 2020.
## Patient Demographics and Baseline Characteristics: NSCLC

<table>
<thead>
<tr>
<th></th>
<th>Phase 1/1b 600 mg BID (n=18)</th>
<th>Phase 1/1b and 2 600 mg BID (n=79)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median age, y (range)</strong></td>
<td>65 (40-76)</td>
<td>65 (25-85)</td>
</tr>
<tr>
<td><strong>Female, n (%)</strong></td>
<td>11 (61%)</td>
<td>45 (57%)</td>
</tr>
<tr>
<td><strong>Race, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>15 (83%)</td>
<td>67 (85%)</td>
</tr>
<tr>
<td>Black</td>
<td>3 (17%)</td>
<td>5 (6%)</td>
</tr>
<tr>
<td>Asian</td>
<td>0 (0%)</td>
<td>5 (6%)</td>
</tr>
<tr>
<td>Other</td>
<td>0 (0%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td><strong>ECOG PS, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>8 (44%)</td>
<td>17 (22%)</td>
</tr>
<tr>
<td>1</td>
<td>10 (56%)</td>
<td>62 (78%)</td>
</tr>
<tr>
<td><strong>Current/former smokers</strong></td>
<td>16 (89%)</td>
<td>75 (95%)</td>
</tr>
<tr>
<td><strong>Non-squamous histology, n (%)</strong></td>
<td>18 (100%)</td>
<td>76 (96%)</td>
</tr>
<tr>
<td><em><em>Prior lines of anticancer therapy</em>, median (range)</em>*</td>
<td>3 (1-9)</td>
<td>2 (1-9)</td>
</tr>
<tr>
<td><strong>Prior anti-PD-1/L1 inhibitor, n (%)</strong></td>
<td>16 (89%)</td>
<td>73 (92%)</td>
</tr>
</tbody>
</table>

*Phase 2 patients with NSCLC received prior treatment with platinum regimens.
NSCLC: non-small cell lung cancer; BID: twice daily dosing
Data as of 30 August 2020. Pooled includes NSCLC Phase 1/1b and Phase 2 600 mg BID.
## Adagrasib in Patients With NSCLC: Pooled Dataset

<table>
<thead>
<tr>
<th>Efficacy Outcome&lt;sup&gt;a&lt;/sup&gt;, n (%)</th>
<th>Phase 1/1b, NSCLC 600 mg BID (n=14)</th>
<th>Phase 1/1b and 2, NSCLC 600 mg BID (n=51)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Objective Response Rate</strong></td>
<td>6 (43%)</td>
<td>23 (45%)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Best Overall Response</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete Response (CR)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Partial Response (PR)</td>
<td>6 (43%)</td>
<td>23 (45%)</td>
</tr>
<tr>
<td>Stable Disease (SD)</td>
<td>8 (57%)</td>
<td>26 (51%)</td>
</tr>
<tr>
<td>Progressive Disease (PD)</td>
<td>0 (0%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Not Evaluable (NE)</td>
<td>0 (0%)</td>
<td>1 (2%)&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Disease control</strong></td>
<td>14 (100%)</td>
<td>49 (96%)</td>
</tr>
</tbody>
</table>

<sup>a</sup>Based on investigator assessment of the clinically evaluable patients (measurable disease with ≥1 on-study scan); 14/18 patients (Phase 1/1b) and 51/79 patients (Phase 1/1b and 2 pooled) met these criteria. <sup>b</sup>At the time of the 30 August 2020 data cut off, 5 patients had unconfirmed PRs. All 5 were confirmed by scans that were performed after the 30 August 2020 data cut off. <sup>c</sup>One patient had tumor reimaging too early for response assessment.

- Data as of 30 August 2020. Pooled includes NSCLC Phase 1/1b and Phase 2 600 mg BID.
- NSCLC: non-small cell lung cancer; BID: twice daily dosing
Adagrasib 600 mg BID in Patients With NSCLC: Clinically Meaningful Depth of Response

- Clinical benefit (DCR) observed in 96% (49/51) of patients
- Best tumor response in 70% (16/23) of responders was greater than 40% from baseline

Data as of 30 August 2020. Pooled includes NSCLC Phase 1/1b and Phase 2 600 mg BID.

**Note:** Two timepoint assessments of CR were separated by recurrent disease associated with treatment interruption due to hypoxia; this patient remains on treatment and in two consecutive scans (1 after August 30 data cutoff) demonstrated 100% tumor regression in target and non-target lesions after resuming treatment.
Phase 1/1b Adagrasib 600 mg BID in Patients With NSCLC: Treatment Duration and Change in Tumor Burden

Duration of Treatment, n=14

- As of August 30, 2020, the median follow-up was 9.6 months
  - Treatment ongoing >11 months in 4 responders
- As of October 16, 2020, 7 patients remain on treatment
  - 5 of 6 responders remain on treatment; 4 of 6 remain in response

Change in Tumor Burden Over Time, n=14

- # Treatment ongoing

As of August 30, 2020

Median (range) 8.2 (1.4, 13.1+)

Presented at the 32nd EORTC-NCI-AACR Symposium, October 24-25, 2020
Duration of Treatment in Patients With NSCLC Treated With Adagrasib 600 mg BID in Pooled Dataset

- Median follow-up: 3.6 months
- Median time to response: 1.5 months
- 87% (20/23) of responders remain on treatment
- 65% (33/51) of patients remain on treatment

Data as of 30 August 2020. Pooled includes NSCLC Phase 1/1b and Phase 2 600 mg BID

*Graphical output for this patient has been adjusted to reflect actual DoT of 2.8 months as of Aug 30, 2020

NSCLC: non-small cell lung cancer; BID: twice daily dosing; PR: partial response; SD: stable disease; PD: progressive disease; NE: not evaluable

Presented at the 32nd EORTC-NCI-AACR Symposium, October 24-25, 2020
Adagrasib Clinical Activity in NSCLC Patients with Brain Metastases

- Preclinical research has shown adagrasib to have a dose dependent drug penetration into the CSF and the central nervous system
- Heavily pre-treated KRAS G12C mutated NSCLC patient with active brain metastases was evaluated following several cycles of adagrasib therapy
  - Patient experienced 63% reduction in size of primary lung tumor and disappearance of the active brain metastases
- Cohort of patients being enrolled to assess adagrasib in NSCLC patients with a G12C mutations and active brain metastases

Mean Plasma and Brain Concentrations of Adagrasib After a Single 100 mg/kg Oral Dose in Mice

Presented at the 32nd EORTC-NCI-AACR Symposium, October 24-25, 2020
Co-mutations in KRAS and STK11 are Associated with Poor Prognosis and Outcomes on Checkpoint Inhibitor Therapy in NSCLC

Adagrasib Clinical Activity in NSCLC in Patients with KRAS G12C and STK11 Co-Mutations

Co-mutations in KRAS and STK11 in NSCLC Patients

- KRAS and STK11 co-mutations comprise approximately 30% of KRAS G12C mutant NSCLC
- The co-occurrence of KRAS and STK11 mutations may cooperate to create an immune-suppressed tumor microenvironment
- Initial adagrasib clinical activity shows promising response
- Phase 2 monotherapy study in 1st line NSCLC patients with STK11 co-mutation initiated in Q1:2021

Best Tumor Change From Baseline for Patients Harboring KRAS G12C and STK11 Co-mutations Shows 64% (9 of 14 patients) ORR

Evaluable Patients
Adagrasib (MRTX849): 

KRAS G12C Selective Inhibitor-Clinical Results CRC and Other Tumor Types
### Patient Demographics and Baseline Characteristics in CRC and Other Solid Tumors

<table>
<thead>
<tr>
<th></th>
<th>CRC (Pooled), 600 mg BID (n=24)</th>
<th>“Other” Cohort, 600 mg BID (n=7)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median age, y (range)</strong></td>
<td>59 (37-79)</td>
<td>64 (25-80)</td>
</tr>
<tr>
<td><strong>Female, n (%)</strong></td>
<td>12 (50%)</td>
<td>2 (29%)</td>
</tr>
<tr>
<td><strong>Race, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>18 (75%)</td>
<td>5 (71%)</td>
</tr>
<tr>
<td>Black</td>
<td>4 (17%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Asian</td>
<td>2 (8%)</td>
<td>1 (14%)</td>
</tr>
<tr>
<td>Other</td>
<td>0 (0%)</td>
<td>1 (14%)</td>
</tr>
<tr>
<td><strong>ECOG PS, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>9 (38%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>1</td>
<td>15 (63%)</td>
<td>7 (100%)</td>
</tr>
<tr>
<td><strong>Tumor type, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRC</td>
<td>24 (100%)</td>
<td></td>
</tr>
<tr>
<td>Pancreatic ductal adenocarcinoma</td>
<td></td>
<td>2 (29%)</td>
</tr>
<tr>
<td>Cholangiocarcinoma</td>
<td>1 (14%)</td>
<td></td>
</tr>
<tr>
<td>Endometrial cancer</td>
<td>1 (14%)</td>
<td></td>
</tr>
<tr>
<td>Ovarian cancer</td>
<td>1 (14%)</td>
<td></td>
</tr>
<tr>
<td>Appendiceal cancer</td>
<td>2 (29%)</td>
<td></td>
</tr>
<tr>
<td><strong>Prior lines of anticancer therapy, median (range)</strong></td>
<td>4 (1-9)</td>
<td>2 (1-5)</td>
</tr>
</tbody>
</table>

- 87% of CRC patients treated were at least 3rd line

Data as of 30 August 2020. Pooled includes Phase 1/1b (n=2) and Phase 2 (n=22) 600 mg BID. CRC: colorectal cancer; BID: twice daily dosing.
Adagrasib Monotherapy in Patients with CRC: Best Overall Response and Disease Control Rate

- Clinical Benefit (DCR) observed in 94% (17/18) of patients
- Confirmed ORR 17% (3/18) of patients; SD 78% (14/18)
- Time to response in 3 patients with partial responses: 6.0, 12.9 and 19.3 weeks

*All results based on investigator assessments.
Data as of 30 August 2020. Pooled includes Phase 1/1b and Phase 2 600 mg BID.

CRC: colorectal cancer; BID: twice daily dosing; ORR: overall response rate; PR: partial response; SD: stable disease; DCR: Disease Control Rate

Presented at the 32nd EORTC-NCI-AACR Symposium, October 24-25, 2020
Adagrasib Monotherapy in Patients With Advanced CRC: Duration of Treatment

**Monotherapy Duration of Treatment**

- **Evaluable Patients:** 10
- **Duration of Treatment, week:**
  - Phase 1/1b
  - Phase 2
  - First response
  - Progression
  - Treatment ongoing
  - Death

**MONOTHERAPY ADAGRASIB DATA**

1. Data as of 30 August 2020. Pooled includes Phase 1/1b and Phase 2 600 mg BID. Presented at the 32nd EORTC-NCI-AACR Symposium, October 24-25, 2020

2. “Regorafenib monotherapy for previously treated metastatic colorectal cancer (CORRECT): an international, multicentre, randomised, placebo-controlled, phase 3 trial”. Axel Grothey, MD et al. VOLUME 381, ISSUE 9863, P303-312, JANUARY 26, 2013

**HISTORICAL DATA**

- Data points for standard of care (regorafenib and LONSURF®), regardless of KRAS status show:
  - ORR of ~1%
  - PFS of ~2 months
  - OS of 6-7 months

CRC: colorectal cancer; PR: partial response; SD: stable disease; PD: progressive disease; ORR: Objective Response Rate; PFS: Progression Free Survival; OS: Overall Survival
Adagrasib in Patients With Other Advanced Solid Tumors: Best Overall Response

Best Tumor Change From Baseline$^a$

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Maximum % Change From Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucinous appendiceal</td>
<td>SD</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>PR $^b$</td>
</tr>
<tr>
<td>Ovarian</td>
<td>PR $^b$</td>
</tr>
<tr>
<td>Endometrial</td>
<td>PR</td>
</tr>
<tr>
<td>Cholangiocarcinoma</td>
<td>PR $^b$</td>
</tr>
</tbody>
</table>

$^a$All results based on investigator assessments. $^b$At the time of the 30 August 2020 data cut off, the cholangiocarcinoma and ovarian cancer patients had unconfirmed PRs, which were subsequently confirmed by scans that were performed after the 30 August 2020 data cut off.

Data as of 30 August 2020. All patients treated at 600 mg BID.

CRC: colorectal cancer; BID: twice daily dosing; ORR: overall response rate; PR: partial response; SD: stable disease

Presented at the 32nd EORTC-NCI-AACR Symposium, October 24-25, 2020
Adagrasib Clinical Activity Including Depth of Response Shown in Patients with Pancreatic and Other Advanced Solid Tumors

- All patients remain on treatment

Duration of Treatment

<table>
<thead>
<tr>
<th>Evaluable Patients</th>
<th>Duration of Treatment, week</th>
<th>Tumor Type</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>Mucinous appendiceal</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>Pancreatic</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>Ovarian</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>Endometrial</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>Cholangiocarcinoma</td>
</tr>
</tbody>
</table>

Change in Sum of Target Lesion Over Time

- % Change From Baseline
- Tumor Type:
  - Mucinous appendiceal
  - Pancreatic
  - Ovarian
  - Endometrial
  - Cholangiocarcinoma

Data as of 30 August 2020. All patients treated at 600 mg BID.

PR: partial response; SD: stable disease

Presented at the 32nd EORTC-NCI-AACR Symposium, October 24-25, 2020
Adagrasib (MRTX849):
KRAS G12C Selective Inhibitor-Novel Combinations
**Adagrasib Combination Development Approach**

*Combination therapy will support testing of adagrasib in earlier-lines of therapy*

---

**NSCLC**

- **Adagrasib + PD-1 (pembrolizumab)**
  - Dose limiting toxicity evaluation period cleared
  - Phase 2 trial initiated in 1st line

- **Adagrasib + pan-EGFR Inhibitor (afatinib)**
  - Initiated in 2nd/3rd line

- **Adagrasib + CDK 4/6 Inhibitor (palbociclib)**
  - Study planned in 2nd/3rd line

---

**CRC**

- **Adagrasib + EGFR (cetuximab)**
  - Dose limiting toxicity evaluation period cleared
  - Phase 3 will initiate by Q2 2021

---

**NSCLC & CRC**

- **Adagrasib + SHP2 Inhibitor (TNO155 from Novartis)**
  - Initial dose expansion and dose escalation cohorts ongoing
  - Enrollment ongoing

- **Adagrasib + SOS1 (BI 1701963 from Boehringer Ingelheim)**
  - Study planned in 2nd/3rd line

---

**NSCLC**: non-small cell lung cancer; **CRC**: colorectal cancer
Patient Case: Response in Combination with Adagrasib + TNO155 (SHP2 inhibitor)*

Baseline

Post Cycle 3
PR, (-60%)

Adagrasib (600mg BID) + TNO155 (initial dose)
53-year-old male, smoker diagnosed with NSCLC

Treatment History
- Neoadjuvant Carboplatin/Pemetrexed x 4 (2017)
- Carboplatin/Pemetrexed/Bevacizumab > Pemetrexed/Bevacizumab maintenance (2017-2018)
- Atezolizumab x 6 cycles (2018-2019)
- Pemetrexed + Pembrolizumab x 6 cycles (March – October 2019)
- KRAS G12Ci AMG510 x 4 cycles November 2019 – February 2020 (-40% → PD)
- SHP2i RMC4630 + Cobimetinib x 1 cycle (off for AE)
- FCN-437c (CDK4/6 inhibitor) (March – June 2020)

TRAEs: Grade 1 diarrhea

Disease Assessments
- Off O₂ and wheelchair within days, neck mass flattened within 1 week
  - Currently in Cycle 4

Data as of August 24, 2020.

NSCLC: non-small cell lung cancer; BID: twice daily dosing

* Study of combination of adagrasib and TNO155 in collaboration with Novartis. ClinicalTrials.gov. NCT04330664.
MRTX1133: KRAS G12D Selective Inhibitor
Targeting KRAS G12D Mutations: Significant Opportunity with High Unmet Need

- KRAS G12D is a driver mutation
- KRAS G12D is sufficient to induce pancreatic and lung cancers in genetically engineered mouse models
- KRAS G12D and KRAS G12C are similarly potent oncogenes in cell transformation assays and functional genomics studies

KRAS G12D\(^1\) Frequency: Large Patient Population

US and Europe Patients\(^2\)

- ~70,000 Pancreatic 36%
- ~80,000 Colorectal 12%
- ~15,000 Endometrial 6%
- ~13,000 NSCLC adenocarcinoma 4%

**NSCLC**: non-small cell lung cancer; **CRC**: colorectal cancer

2. Mirati estimates based on epidemiology data reported in Globocan 2022 (accessed 2019) and frequencies by mutation; Europe includes EU, Russia and 10 additional European countries; RET estimate does not include thyroid cancer. Rounded to the nearest 1,000.
### MRTX1133: Potential First-in-Class G12D Selective Inhibitor

<table>
<thead>
<tr>
<th>Assay</th>
<th>Criteria</th>
<th>MRTX1133</th>
</tr>
</thead>
<tbody>
<tr>
<td>KRAS G12D cell activity</td>
<td>&lt;10nM</td>
<td>~5 nM</td>
</tr>
<tr>
<td>Selectivity over KRAS&lt;sup&gt;WT&lt;/sup&gt;</td>
<td>&gt;100-fold</td>
<td>&gt;1,000-fold</td>
</tr>
<tr>
<td>Predicted human half-life</td>
<td>&gt;24 hours</td>
<td>~50 hours</td>
</tr>
<tr>
<td>Low risk for hERG/off-target pharmacology</td>
<td>&gt;10µM</td>
<td>✓</td>
</tr>
<tr>
<td>Drug-drug interaction (CYPs)</td>
<td>Low risk</td>
<td>✓</td>
</tr>
</tbody>
</table>

- MRTX1133 is a small molecule that selectively & reversibly binds to & inhibits KRAS G12D in both active & inactive states.
- MRTX1133 demonstrates selective inhibition of cell viability of KRAS G12D mutant, but not KRAS wild-type, tumor cells.
MRTX1133: Anti-Tumor Activity Observed in Pancreatic and CRC *In-Vivo* Models

- MRTX1133 demonstrates dose-dependent inhibition of KRAS-dependent signaling, demonstrating tumor regression in G12D mutant tumor models
MRTX1133: Path to Clinical Development

MRTX1133 has a low predicted target plasma concentration (~25-100 ng/mL) required for near complete sustained target inhibition and maximal anti-tumor activity based on its potency and high unbound fraction.

To ensure sustained therapeutic levels are achieved, we are pursuing both oral and parenteral routes of administration in parallel into Phase 1:

- Estimated fraction absorbed of 15% in preclinical studies
- Long predicted human half-life (~50 hours), low target plasma concentration and high solubility support both routes
- This will allow direct comparison and selection of the most promising path for further development

Both routes are commercially attractive and compatible with development as a monotherapy or in combination with standard of care regimens.
MRTX1133: Initial Development Plan and Next Steps

CLINICAL TRIAL DESIGN PRINCIPLES

- Multi-cohort Phase 1 monotherapy trial comparable to adagrasib
  - Rapid dose escalation strategies to define a tolerated and active dose
- Multiple expansion cohorts for pancreatic, colon, lung and other G12D patients
- Rational combination approaches are similar to G12C and enabled in first-in-human clinical trials

NEXT STEPS

- Planned 1H:2021 IND filing
  - Advancing through GLP toxicology studies
  - GMP manufacturing is on track and not on critical path
- Additional preclinical data to be presented at a scientific conference in 2021

IND: investigational new drug; GLP: good laboratory practice
Sitravatinib + Checkpoint Inhibitors
Sitravatinib Inhibits TAM (TYRO3, AXL and MER), VEGFR2, and KIT Receptors and May Restore Immune Response

Rationale for Targeting TAM & Split RTKs to Enhance Immune Response to Checkpoint Inhibitors

Targeting Split RTKs:
- Targeting VEGFR2 reduces Tregs & MDSCs
- Targeting KIT also depletes MDSCs
- Releases brakes for expansion of CD8+ T cells via PD-1 inhibition

Targeting TAM:
- Targeting MERTK & AXL shifts tumor associated macrophage (TAM) type to M1
- M1 macrophages secrete cytokines that enhance immune response (IL-12, TNF)

Both TAM & Split RTKs cooperate to:
- Increase dendritic cell maturity & antigen presentation capacity
- Increase NK cell response
- Increase T cell expansion & trafficking into tumors

References:
- Garton et al., Anti-KIT Monoclonal Antibody Treatment Enhances the Antitumor Activity of Immune Checkpoint Inhibitors by Reversing Tumor-Induced Immunosuppression. Mol Cancer Ther, 2017. 16(4)
Compelling Phase 2 Results Support and Inform SAPPHIRE Phase 3 Trial in 2nd / 3rd Line Non-Squamous NSCLC

- Encouraging preliminary Overall Survival (OS) data from ongoing Phase 2 clinical trial 1
  - Preliminary median OS of 15.6 months 1 in full Prior Clinical Benefit (PCB) cohort in 2L+ patients
  - Historical data points for standard of care (docetaxel) show median OS to be ~ 8.5 – 9.6 months 2,3

- Phase 3 SAPPHIRE clinical trial inclusion criteria focused on PCB patients who received the combination as either 2nd or 3rd line therapy after progressing on treatment with checkpoint inhibitor.

- Potential to establish sitravatinib + nivolumab as new standard of care after checkpoint inhibitor failure
  - >2nd line NSCLC U.S. & EU Populations (circa 2020): over 100,000 patients with ~70,000 being non-squamous

OS: overall survival; NSCLC: non-small cell lung cancer
1. MRTX-500 Phase 2 trial: full Prior Benefit Cohort (PCB) (n=87), data cut-off 30 Jan-2020. Patients with PCB on a checkpoint inhibitor as part of their last treatment regimen prior to enrollment. PCB is defined as either complete response, partial response or stable disease for ≥12 weeks. Subset of PCB patients (n=73) who received the combination as either 2nd or 3rd line of therapy after progressing on treatment with a checkpoint inhibitor.
2. Data represented are from the CheckMate 057, KEYNOTE 010 and OAK studies and do not reflect results that might have been obtained from head-to-head studies. Results from Mirati’s on-going Phase 3 SAPPHIRE trial comparing sitravatinib + nivolumab to docetaxel may differ materially from prior studies presented.
Financial Update
## Select Company Financials

<table>
<thead>
<tr>
<th>NASDAQ</th>
<th>MRTX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash as of December 31, 2020*</td>
<td>$1.4B</td>
</tr>
<tr>
<td>Shares outstanding as of December 31, 2020**</td>
<td>58.6M</td>
</tr>
<tr>
<td>Q4 2020: Operating Expenses</td>
<td>$108.0M</td>
</tr>
<tr>
<td>Q4 2020: Operating Expenses net of stock-based compensation***</td>
<td>$86.3M</td>
</tr>
</tbody>
</table>

*This amount is comprised of cash, cash equivalents and short-term investments.

**Shares outstanding as of December 31, 2020 includes 50.4 million shares of common stock outstanding and pre-funded warrants to purchase a total of 8.2 million shares of common stock. The pre-funded warrants have a per share exercise price of $0.001.

***Amount disclosed is calculated as Q4 2020 operating expenses ($108.0M) less Q4 2020 stock-based compensation expense ($21.7M).
BeiGene is currently running a subset of combination studies of sitravatinib + tislelizumab (their anti-PD-1) in Asia for multiple solid tumor indications including NSCLC, HCC, RCC, ovarian and gastric cancers.

BeiGene has Asian commercialization rights (ex-Japan) for sitravatinib as part of our development and commercialization agreement (Jan. 2018) and is responsible for additional data disclosures. Additional data is expected in 2021.

### Robust Pipeline Spans Multiple Targets & Tumor Types with Near-Term Catalysts

<table>
<thead>
<tr>
<th>Compound</th>
<th>Development Approach</th>
<th>Indication</th>
<th>Lead Optimization</th>
<th>IND-enabling</th>
<th>Phase 1/1b</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Planned Near-Term Catalysts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adagrasib (MRTX849)</td>
<td>Monotherapy</td>
<td>2L+ NSCLC, CRC, Pancreatic, Other</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2L+ NSCLC data update and NDA filing in 2H:2021</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1L NSCLC: STK11 Co-Mutation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>P2 initiated in Q1:2021</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2L NSCLC</td>
<td></td>
<td></td>
<td>Randomized to Docetaxel</td>
<td></td>
<td></td>
<td>P3 initiated in Q1:2021</td>
</tr>
<tr>
<td>Pembrolizumab (PD-1)</td>
<td>Monotherapy</td>
<td>1L NSCLC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>P2 initiated Q4:2020; POC data in 2H:2021</td>
</tr>
<tr>
<td>Cetuximab (EGFR)</td>
<td>Monotherapy</td>
<td>2L CRC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>P3 initiation by Q2:2021; POC data in 2H:2021</td>
</tr>
<tr>
<td>POC Combinations: SHP2, Pan-EGFR, CDK4/6, SOS1</td>
<td>Monotherapy</td>
<td>2L+ NSCLC &amp; CRC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Initial SHP2 data in Q2/Q3:2021; CDK4/6 &amp; SOS1 initiations in 2021</td>
</tr>
<tr>
<td>MRTX1133</td>
<td>Monotherapy</td>
<td>Pancreatic, CRC, NSCLC, Other</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>IND in 1H:2021</td>
</tr>
<tr>
<td>Sitratavatinib Multi Kinase Inhibitor</td>
<td>PD-1</td>
<td>2/3L NSCLC</td>
<td></td>
<td></td>
<td>SAPPHIRE (Checkpoint Refractory) – in combination with nivolumab</td>
<td></td>
<td></td>
<td>P3 interim OS analysis in 2H:2022</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NSCLC, Bladder &amp; Other</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Additional data in 2022</td>
</tr>
<tr>
<td>Discovery Programs</td>
<td>Discovery Programs</td>
<td>MTAP-Deleted Cancers</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>IND in 1H:2022</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Solid Tumors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Solid Tumors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mutant KRAS Inhibitor</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NSCLC: non-small cell lung cancer; CRC: colorectal cancer; HCC: hepatocellular carcinoma; RCC: renal cell carcinoma

1. BeiGene is currently running a subset of combination studies of sitratavatinib + tislelizumab (their anti-PD-1) in Asia for multiple solid tumor indications including NSCLC, HCC, RCC, ovarian and gastric cancers. BeiGene has Asian commercialization rights (ex-Japan) for sitratavatinib as part of our development and commercialization agreement (Jan. 2018) and is responsible for additional data disclosures. Additional data is expected in 2021.
Targeting the genetic and immunological drivers of cancer

Corporate Presentation
February 2021