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Sierra Oncology Highlights

Momelotinib (MMB) a potential cornerstone myelofibrosis therapy

- Pivotal Phase 3 data expected Q1 2022
- Robust data set on >820 myelofibrosis patients, some of whom have been treated for >10 years
- Global commercial opportunity; JAK inhibitors approved for MF generate > $2 Billion annually
- Experienced management team across Development, Regulatory & Commercial
- $108 million in cash/equivalents as of 3/31/21
- Focused on commercializing in North America
Myelofibrosis (MF): a bone marrow cancer
- Caused by constitutive activation of JAK-STAT signaling
- Inflammation and fibrosis impair red blood cell production

Common manifestations of disease include constitutional symptoms, enlarged spleen and progressive anemia

Current treatments: JAK inhibitors are the mainstay option for intermediate and high-risk patients
Myelofibrosis: Global Market Overview

Rare oncology condition with ~40k diagnosed patients worldwide
- Median Age at Diagnosis: 60–67 years
- Median Survival for Intermediate / High-risk Patients: 2–7 years

Hematologist-oncologists (Hem-Oncs) are the primary disease manager
- 60–70% of patients treated by community physicians
- Referrals to academic centers driven by availability of SCT and clinical trials
- Hem-Oncs are reachable with a small sales force

FDA approved JAK inhibitors for myelofibrosis—ruxolitinib and fedratinib—with ruxolitinib reaching >$2.0 Billion in annual revenues globally

Approved JAK inhibitors address spleen and symptoms, but can worsen anemia
- JAKi treatment leads to myelosuppression
- Dose reductions are common, leading to loss of activity
- Some patients never receive JAKi due to hemoglobin and platelet count
Four Factors Figure into Treatment Decisions

<table>
<thead>
<tr>
<th>Anemia</th>
<th>Splenomegaly</th>
<th>Const. Symptoms</th>
<th>Thrombocytopenia</th>
</tr>
</thead>
<tbody>
<tr>
<td>70 – 90% of patients at diagnosis</td>
<td>50 – 70% of patients at diagnosis</td>
<td>40 – 60% of patients at diagnosis</td>
<td>10 – 30% of patients at diagnosis</td>
</tr>
</tbody>
</table>

May be managed with frequent RBC transfusions, but no curative treatments are available. Patients experience early satiety leading to weight loss and severe left upper quadrant pain. Common symptoms include fatigue, bone pain, pruritus, night sweats, and fever. May cause significant bleeding, bruising, headaches, and pain in the joints or muscles.

While Factors Can Overlap, the Most Burdensome Factor in Terms of Clinical Severity and Quality of Life (QoL) Impact Guides the Treatment Choice.

1. Constitutional or non-specific symptoms. Source: Sierra Qualitative Market Research.
Momelotinib

A JAK1, JAK2 and ACVR1 inhibitor
### Momelotinib: SIMPLIFY Phase 3 Trials Informed MOMENTUM Trial Design

<table>
<thead>
<tr>
<th>Phase 3 Clinical Trial</th>
<th>Phase 3 Clinical Trial</th>
<th>Phase 3 Clinical Trial</th>
<th>Extended Access Program</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SIMPLIFY-1</strong></td>
<td><strong>SIMPLIFY-2</strong></td>
<td><strong>MOMENTUM</strong></td>
<td><strong>XAP</strong></td>
</tr>
</tbody>
</table>

#### Patient Population
- JAKi-naïve patients (n=432)
- Prior ruxolitinib-treated patients (n=156)
- Ongoing pivotal study for JAK-exposed patients (n=180)
- Ongoing with some patients receiving momelotinib for >10 years

#### Comparator
- Ruxolitinib
- Best available therapy (88.5% RUX/RUX+)
- Danazol

#### Primary Endpoint
- Splenic reduction >35% @ Week 24
- Splenic reduction >35% @ Week 24
- Difference in TSS response rate @ Week 24

#### Key Notes
- Met primary endpoint
- No washout period
- Ongoing; 21-day taper & washout period
- First patients reached 10+ years

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More Than 1,000 Myelofibrosis Patients Will Have Received Momelotinib When the Registration-enabling MOMENTUM Study is Complete
SIMPLIFY-1 and SIMPLIFY-2 Clinical Results from Key Endpoints

<table>
<thead>
<tr>
<th></th>
<th>SIMPLIFY-1</th>
<th></th>
<th></th>
<th>SIMPLIFY-2</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MMB</td>
<td>RUX</td>
<td>MMB</td>
<td>BAT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary Endpoint</td>
<td>Splenic reduction ≥35% @w24</td>
<td>27%</td>
<td>29%</td>
<td>7%*</td>
<td>6%*</td>
<td></td>
</tr>
<tr>
<td>Secondary Endpoint</td>
<td>Symptom score reduction ≥50% @w24</td>
<td>28%</td>
<td>42%</td>
<td>26%</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td>Secondary Endpoint</td>
<td>Transfusion independence for &gt;12weeks @w24</td>
<td>67%</td>
<td>49%</td>
<td>43%</td>
<td>21%</td>
<td></td>
</tr>
</tbody>
</table>

* Mean change in both arms was zero

- Study design elements played a role in outcome
- Data set provided a roadmap for registration-enabling MOMENTUM study
Prior Clinical Results
SIMPLIFY-1: JAK Inhibitor-naïve Patients

Potential for MMB to improve outcomes in JAK-naïve patients:

- Splenic control with MMB equivalent to that achieved with RUX (27% vs. 29%)
- Symptom benefit clinically comparable when measured longitudinally and as individual scores
- Higher rates of transfusion independence for MMB-treated patients
- Long overall survival: Medians of 53 months and not reached

Comparable Symptom Benefit for all 7 items within the TSS

<table>
<thead>
<tr>
<th>Item</th>
<th>Baseline TSS, mean</th>
<th>Change in Mean TSS at W24, vs Baseline</th>
<th>Delta on a 70-point scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal Discomfort</td>
<td>19.4</td>
<td>- 6.2</td>
<td>1.1</td>
</tr>
<tr>
<td>Pain Under Left Ribs</td>
<td>17.9</td>
<td>- 7.3</td>
<td>1.1</td>
</tr>
<tr>
<td>Early Satiety</td>
<td>25.3</td>
<td>- 8.9</td>
<td></td>
</tr>
<tr>
<td>Night Sweats</td>
<td>23.3</td>
<td>- 10.0</td>
<td></td>
</tr>
<tr>
<td>Itching</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone Pain</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tiredness</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Absolute Change in Mean TSS at Week 24, From Baseline

<table>
<thead>
<tr>
<th></th>
<th>ITT Population</th>
<th>Symptomatic Population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MMB</td>
<td>RUX</td>
</tr>
<tr>
<td>Baseline TSS, mean</td>
<td>19.4</td>
<td>17.9</td>
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<tr>
<td>Change in Mean TSS at W24, vs Baseline</td>
<td>- 6.2</td>
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</tr>
<tr>
<td>Delta on a 70-point scale</td>
<td>1.1</td>
<td>1.1</td>
</tr>
</tbody>
</table>
Momelotinib Data: Hemoglobin and Platelet Levels Over Time

**SIMPLIFY-1**

**Hemoglobin Level**
- Mean Hemoglobin (g/dL)
- Weeks: 0, 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 28, 32, 36
- Crossover: Ruxolitinib to Momelotinib

**Platelets**
- Mean Platelets (x10³/uL)
- Weeks: 0, 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 28, 32, 36
- Crossover: Ruxolitinib to Momelotinib

Momelotinib increased hemoglobin levels and maintained platelet counts

Momelotinib Data: SRR & TSS Compared by Baseline PLT Strata

**W24 Splenic Response (SRR)**

- In S1, SRR was maintained with MMB across the continuum of baseline platelet counts. MMB achieves good SRR in patients whose baseline count was less than 150 and less than 300 x 10⁹.
- In contrast, a marked reduction in SRR was observed with RUX as the baseline platelet count declined.

**W24 Symptom (TSS) Response**

- In S1, the TSS response rate was maintained with MMB across the continuum of baseline platelet counts, including in patients whose platelet count was less than 150 and less than 300 x 10⁹ at baseline.
- In comparison, in the RUX arm of S1, TSS response rates declined as patient’s baseline platelet counts declined.

Source: Kiladjian, J. et al. ASH 2020. PLT = platelets

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**SIMPLIFY-1**

![Graphs showing W24 splenic and symptom response rates for SRR and TSS](chart.png)
Momelotinib Data:
Anemia Response & Transfusion Dependency

**SIMPLIFY-1**

### W24 TI (Anemia) Response

<table>
<thead>
<tr>
<th>PLTs (×10^5/L)</th>
<th>MMB</th>
<th>MMB Overall (87%)</th>
<th>RUX</th>
<th>RUX Overall (49%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-150</td>
<td>62%</td>
<td></td>
<td>42%</td>
<td></td>
</tr>
<tr>
<td>&gt;150-300</td>
<td>72%</td>
<td></td>
<td>54%</td>
<td></td>
</tr>
<tr>
<td>&gt;300</td>
<td>63%</td>
<td></td>
<td>51%</td>
<td></td>
</tr>
</tbody>
</table>

- MMB treatment elicited a TI response rate greater than 60% in each baseline PLT stratum, higher in each stratum in comparison to rates of 42%-54% for RUX

### Transfusion Requirement

- In SI, the transfusion burden for MMB treatment was approximately one half that of RUX patients

SIMPLIFY-1 Trial: Safety Results

Safety Generally Similar for Momelotinib, Ruxolitinib in the 24-week Double-blind Period

- Grade 3 or 4 hematological AEs were very low for momelotinib
- Anemia and thrombocytopenia were more common in the ruxolitinib arm
- Nausea was more common with momelotinib
- No evidence of long-term toxicity observed during extended momelotinib dosing up to 10 years

SIMPLIFY-1

Select TEAEs, by PT

<table>
<thead>
<tr>
<th>Grade 3/4 TEAEs:</th>
<th>MMB (N=214)</th>
<th>RUX (N=216)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pts with any Gr3/4 TEAE, n (%)</td>
<td>74 (34.6%)</td>
<td>94 (43.5%)</td>
</tr>
<tr>
<td>Gr3/4 Thrombocytopenia</td>
<td>15 (7.0%)</td>
<td>10 (4.6%)</td>
</tr>
<tr>
<td>Gr3/4 Anemia</td>
<td>13 (6.1%)</td>
<td>49 (22.7%)</td>
</tr>
<tr>
<td>Gr3/4 Pneumonia</td>
<td>5 (2.3%)</td>
<td>3 (1.4%)</td>
</tr>
</tbody>
</table>

Any Grade TEAEs:

| Pts with Any Grade TEAE, n (%) | 198 (92.5%) | 206 (95.4%) |
| Diarrhea | 39 (18.2%) | 43 (19.9%) |
| Anemia | 31 (14.5%) | 81 (37.5%) |
| Thrombocytopenia | 40 (18.7%) | 63 (29.2%) |
| Nausea | 34 (15.9%) | 8 (3.7%) |
| Fatigue | 31 (14.5%) | 26 (12.0%) |
| Headache | 38 (17.8%) | 43 (19.9%) |

1 RT = Randomized Treatment
Prior Clinical Results
SIMPLIFY-2: JAK Inhibitor-exposed Patients

In patients previously treated with a JAK inhibitor:

- MMB maintains **splenic control**
  - MMB provides some measure of **splenic shrinkage** in 35% of MMB treated patients at Week 24
  - The mean percent change in spleen volume at Week 24 was 0.2% in the MMB group
- **Higher rates of symptom response and transfusion independence** achieved for MMB-treated patients
- **Long overall survival observed** in this JAK inhibitor-exposed setting
  - Median of 37.5 and 34.3 months

**SIMPLIFY Findings Contribute to the Totality of Evidence Supporting a Momelotinib New Drug Application**
OS Benefit Seen in Both JAKi-naïve and JAKi-exposed Patients

SIMPLIFY-1

JAKi-naïve Patients

Week 24 Crossover to open-label MMB

Median OS 53.1 months in RUX→MMB patients
Median not reached in originally MMB-randomized patients

Treatment

- MMB
- RUX→MMB

HR = 0.99
p = 0.97

SIMPLIFY-2

JAKi-exposed Patients

Week 24 Crossover to open-label MMB

Median OS 37.5 months for BAT/RUX→MMB patients
Median OS 34.3 months for originally MMB-randomized patients

Treatment

- MMB
- BAT/RUX→MMB

HR = 0.95
p = 0.96

Durable survival reflects momelotinib benefit on extended treatment or crossover to momelotinib, regardless of starting therapy.

The OS results are amongst the best survival reported in patients who have been previously treated with ruxolitinib.

The Pivotal Phase 3 ‘MOMENTUM’ Trial is Underway

Global Study, currently enrolling patients
Topline Data Expected Q1 2022

Subjects
N=180

Previously Treated with JAK inhibitor
Symptomatic (TSS ≥ 10) and Anemic (Hgb < 10 g/dL)

2:1 randomization
JAKi taper/washout ≥ 21 day

Primary Endpoint
- Total symptom score (TSS) response rate at Week 24

Secondary Endpoints
- Transfusion independence (TI) rate at Week 24
- Splenic response rate (SRR) at Week 24

*Danazol was selected as an appropriate comparator given its use to ameliorate anemia in MF patients, as recommended by NCCN, ESMO guidelines.
The Long-term Vision of Sierra Oncology

Sierra Oncology has the Vision, the Leadership and the Execution Ability to Deliver Extraordinary Therapeutic Outcomes for Patients with Rare Oncology Diseases

Successful Completion of MOMENTUM Clinical Trial

Regulatory and Commercial Execution for Momelotinib

Expand with Combination Studies and Pipeline Additions
Upcoming Milestones

June 2021: ASCO & EHA Presentations (virtual)

Q1 2022: Topline Data

Dec 2021: ASH (Virtual & Atlanta)

2022

H2 2022: File New Drug Application with FDA

2023

2021

June 2021: MOMENTUM Enrollment Completion

2023: Expected US Approval & Commercialization
Thank You