**SIMPLIFY-1 and SIMPLIFY-2:** Completed Phase 3 Studies of Momelotinib

### Study Designs

**SIMPLIFY-1**

Phase 3, randomized 1:1, double-blind, head-to-head, non-inferiority comparison of momelotinib (MMB) to ruxolitinib (RUX) in JAK inhibitor naïve myelofibrosis patients, N=432

**SIMPLIFY-2**

Phase 3, 2:1 randomized study comparing MMB to Best Available Therapy (BAT; ~90% RUX) in anemic or thrombocytopenic myelofibrosis patients previously treated with RUX, N=156

### Overview of Results

**Primary endpoint:** Splenic Response Rate (SRR)

- **SIMPLIFY-1**
  - Non-inferiority demonstrated
- **SIMPLIFY-2**
  - Superiority was not demonstrated

**Secondary endpoints:** Total Symptom Score (TSS), Transfusion Independence Rate, Transfusion Dependence Rate, Red Blood Cell (RBC) Transfusion Rate

**MMB is the only JAK inhibitor to show equivalent splenic response to RUX in 1st-line**

- **SIMPLIFY-1**
  - Non-inferiority demonstrated: 26.5% (MMB) vs. 29% (RUX), p=0.011
- **SIMPLIFY-2**
  - Superiority not demonstrated but washout from prior RUX was prohibited, 6.7% vs. 5.8%

**Symptom Improvement**

- **SIMPLIFY-1**
  - Pre-specified TSS analysis: 28.4% (MMB) vs. 42.2% (RUX)
  - Single item analysis demonstrates clinically comparable head-to-head symptom benefit

- **SIMPLIFY-2**
  - Pre-specified TSS analysis demonstrated robust symptom benefit with MMB with a 4-fold higher TSS Response Rate at Week 24 compared to BAT (~90% RUX): 26.2% vs. 5.9% (p<0.001)

**Anemia Benefits**

- **SIMPLIFY-1**
  - Transfusion Independence, Week 24: 66% vs. 49% (p<0.001)

- **SIMPLIFY-2**
  - Transfusion Independence in Transfusion Dependent subset: 49% vs. 29% (p=0.030)

- **Reduced transfusion burden vs. RUX**
- **Long-term, maintained hemoglobin (Hgb) increase**

**Single item analysis**

**SIMPLIFY-1**

- **Similifications**
  - Abdominal Discomfort
  - Pain under left rib
  - Early satiety
  - Night sweats
  - Itching
  - Bone pain
  - Tiredness

**SIMPLIFY-2**

- **Similifications**
  - Abdominal Discomfort
  - Pain under left rib
  - Early satiety
  - Night sweats
  - Itching
  - Bone pain
  - Tiredness

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High MMB dose-intensity is maintained throughout treatment course, including in patients who switch from RUX to MMB, in contrast to a substantial loss of RUX dose intensity.

A similar pattern was seen in SIMPLIFY-2, with high MMB dose intensity maintained throughout treatment course.

Safety

• 550 patients received MMB at any time (as randomized or following cross-over) in the SIMPLIFY-1 and -2 studies.
• In contrast to RUX, MMB therapy produced low rates of hematological adverse events consistent with MMB’s differentiated pharmacological and clinical profile as an inhibitor of JAK1, JAK2 and ACVR1.
• No new safety signals or cumulative toxicity were observed during extended MMB dosing.
• Peripheral neuropathy was uncommon, of low grade, and not progressive.

Grade 3/4 Adverse Events Randomized and Extended Treatment Phase (Overall Exposure)

<table>
<thead>
<tr>
<th>SIMPLIFY-1</th>
<th>MMB (N=214)</th>
<th>RT Period</th>
<th>RUX (N=216)</th>
<th>Overall MMB exposure in RT and ET (N=411)</th>
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</thead>
<tbody>
<tr>
<td>Number of patients with any Gr3/4 TEAE, n (%)</td>
<td>74 (34.6%)</td>
<td>94 (43.5%)</td>
<td>251 (61.1%)</td>
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<tr>
<td>Thrombocytopenia</td>
<td>15 (7.0%)</td>
<td>10 (4.6%)</td>
<td>55 (13.4%)</td>
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<tr>
<td>Anemia</td>
<td>13 (6.1%)</td>
<td>49 (22.7%)</td>
<td>48 (11.7%)</td>
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<tr>
<td>Pneumonia</td>
<td>5 (2.3%)</td>
<td>3 (1.4%)</td>
<td>30 (7.3%)</td>
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</table>

<table>
<thead>
<tr>
<th>SIMPLIFY-2</th>
<th>MMB (N=104)</th>
<th>RT Period</th>
<th>BAT (N=52)</th>
<th>Overall MMB exposure in RT and ET (N=144)</th>
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</thead>
<tbody>
<tr>
<td>Number of patients with any Gr3/4 TEAE, n (%)</td>
<td>57 (54.8%)</td>
<td>22 (42.3%)</td>
<td>104 (72.2%)</td>
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<tr>
<td>Anemia</td>
<td>14 (13.5%)</td>
<td>9 (17.3%)</td>
<td>33 (22.9%)</td>
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<tr>
<td>Thrombocytopenia</td>
<td>11 (10.6%)</td>
<td>3 (5.8%)</td>
<td>22 (15.3%)</td>
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<tr>
<td>Asthenia</td>
<td>5 (4.8%)</td>
<td>1 (1.9%)</td>
<td>11 (7.6%)</td>
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<tr>
<td>Neutropenia</td>
<td>5 (4.8%)</td>
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<tr>
<td>Pneumonia</td>
<td>2 (1.9%)</td>
<td>1 (1.9%)</td>
<td>9 (6.3%)</td>
<td></td>
</tr>
</tbody>
</table>

*Most Frequent Grade 3 or 4 Adverse Events by Preferred Term1 Treatment Emergent Adverse Events occurring in >5% patients in the "Overall exposed to MMB".

Momelotinib Survival Data

Noteworthy survival post-RUX in context of historical control data.

• At Week 24, the stratified hazard ratio for overall survival favored MMB: HR 0.62 (p = 0.24).
• Median Overall Survival (mOS) with extended follow up: 28 months.
• Historical control mOS in post-RUX treated patients: 7-14 months.

Conclusion

The totality of data reinforce MMB’s tolerability profile and clinical activity evidenced by beneficial spleen, symptom and anemia-related outcomes in myelofibrosis.

References: