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Momelotinib is the potential treatment of choice for MF patients with anemia

<6 months from pivotal data
- Low-risk study
- FDA approval and launch expected <18 months

~$4B market opportunity
- ~20K MF patients with anemia WW
- Current JAKi’s priced at an average > $200K / year

Current market cap of ~$420M
- ~20M FD shares outstanding\(^{(1)}\)
- ~$90.7M cash as of 6/30/21\(^{(2)}\)

(1) Assuming treasury stock method to account for outstanding options and warrants and $21 stock price
(2) ~$34M gross proceeds raised in Q3 as of 8/9/21
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
Importance of Treating Anemia in Myelofibrosis
Anemia and Hepcidin Predict Poor Survival in Myelofibrosis

Anemia of inflammation driven by elevated hepcidin

Elevated hepcidin inhibits iron transport and iron homeostasis

Anemia and elevated hepcidin are negative prognostic indicators

New therapies should provide anemia benefits in addition to symptom, spleen benefits

Anemia Predicts Poor Survival in Myelofibrosis*

- No anemia (Hb ≥12 g/dL) Median survival 7.9 years
- Mild anemia (Hb 10–12 g/dL) Median survival 4.9 years
- Moderate anemia (Hb 8–10 g/dL) Median survival 3.4 years
- Severe anemia (Hb <8 g/dL) Median survival 2.1 years

Hepcidin Predicts Poor Survival in Myelofibrosis**

- Low hepcidin
- High hepcidin

Momelotinib
A JAK1, JAK2 and ACVR1 (ALK2) Inhibitor
Momelotinib Inhibits JAK1, JAK2 and ACVR1/ALK2

Hyperactive JAK-STAT signaling is driving the disease in myelofibrosis

Preclinical and clinical studies suggest that the clinical anemia benefits of momelotinib result from suppression of ACVR1/ALK2-mediated hepcidin production

Momelotinib Inhibits all Three Disease Drivers, Potentially Improving Splenomegaly and Symptoms of Myelofibrosis While Maintaining or Improving Hemoglobin

Completed Phase 3 Studies SIMPLIFY-1 and -2

**SIMPLIFY-1**

**1st-Line Population**
JAK inhibitor naïve

- **Primary Endpoint**
  - Double-blind treatment
  - Open label
  - LTFU

- **Randomization**
  - 1:1

- **Treatments**
  - **JAKI-naive**
    - Double-blind, N=432
    - Momelotinib 200 mg QD
    - Ruxolitinib 20 mg BID
  - **RUX-exposed**
    - Open label, N=156
    - Best available therapy

- **Results**
  - 88.5% = RUX/RUX+

---

**SIMPLIFY-2**

**2nd-Line Population**
Prior ruxolitinib complicated by hematologic toxicity

- **Primary Endpoint**
  - Randomized treatment
  - Extension
  - LTFU

- **Randomization**
  - 2:1

- **Treatments**
  - **RUX-exposed**
    - Open label, N=156
    - Momelotinib 200 mg QD
  - **Best available therapy**
  - Momelotinib 200 mg QD

- **Results**
  - 88.5% = RUX/RUX+

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*Wet endpoint
Journal of Clinical Oncology, 2017 35(34):3844

The Lancet Haematology, 2018 5(2): 7
Momelotinib Demonstrated an Increase in Hemoglobin and a Decreased Transfusion Requirement vs. Ruxolitinib
Transfusion Independence is Achieved for Anemic Patients and all Patients, Irrespective of Baseline Platelets or Transfusion Status

**SIMPLIFY-1 Anemic Patients**

**W24 TI-Response by Baseline Hgb**

**SIMPLIFY-1**

**W24 TI-Response by Baseline PLT**

**SIMPLIFY-1**

**W24 TI-Response by Baseline Transfusion Status**

The W24 TI-R Rate in S1 Was Higher in Patients Randomized to MMB vs RUX, Irrespective of the Degree of Baseline Anemia, or the Baseline PLT Count or Transfusion Status

Week 24 Transfusion Independence Response (TI-R): no RBC transfusion within ≥ 12 weeks immediately prior to Week 24, with Hgb ≥ 8 g/dL

Transfusion Dependent (TD): ≥4 units of RBCs or Hgb level, ≤ 8 g/dL in the 8 weeks prior to randomization

Transfusion Independent (TI): absence of RBC transfusions and no Hgb < 8 g/dL in the 12 weeks prior to randomization

Transfusion Requiring (TR): neither TD nor TI

Hgb = hemoglobin, MMB = momelotinib, Plts = platelets, RUX = ruxolitinib, TD = transfusion dependent, TI = transfusion independent, TR = transfusion requiring

Transfusion Independence (TI) with Momelotinib is Associated with Improved Overall Survival

SIMPLIFY-1

Week 24 TI response = no RBC transfusion for ≥ 12 weeks immediately prior to Week 24, Hgb level ≥ 8 g/dL.

Mesa, R. et.al. European Hematology Association, June 2021, oral presentation S202; Virtual.

Achieving or Maintaining TI Predicted Better Survival in Patients Treated with Momelotinib – The Goal of Achieving TI Should Become an Important Driver of Treatment Decisions

Week 24 TI response = no RBC transfusion for ≥ 12 weeks immediately prior to Week 24, Hgb level ≥ 8 g/dL.

Mesa, R. et.al. European Hematology Association, June 2021, oral presentation S202; Virtual.
Comparative Efficacy MMB vs RUX/BAT in Anemic Patients

MMB’s anemia benefits are accompanied by similar splenic and symptomatic response rates in SIMPLIFY-1 and significantly better symptom control relative to BAT in SIMPLIFY-2.

Week 24 Response Rates

SIMPLIFY-1: Patients with Hgb < 12 g/dL at Baseline

- Anemia (TI) Response: MMB 62%, RUX 37%
- Splenic Response: MMB 29%, RUX 29%
- Symptom (TSS) Response: MMB 30%, RUX 39%

SIMPLIFY-2: Patients with Hgb < 12 g/dL at Baseline

- Anemia (TI) Response: MMB 41%, RUX/BAT 15%
- Splenic Response: MMB 8%, RUX/BAT 4%
- Symptom (TSS) Response: MMB 28%, RUX/BAT 4%
**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

**Mixed-Effect Model Repeated Measure (MMRM) Based TSS Change from Baseline (70-point scale)**

<table>
<thead>
<tr>
<th>ITT Population</th>
<th>Symptomatic Population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MMB</td>
</tr>
<tr>
<td>Baseline TSS, LS mean</td>
<td>19.0</td>
</tr>
<tr>
<td>Week 24 Change from Baseline, LS Mean</td>
<td>-6.4</td>
</tr>
<tr>
<td>Difference from RUX in W24 Change from Baseline, LS Mean</td>
<td>1.5</td>
</tr>
</tbody>
</table>
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
Comparative Efficacy MMB vs RUX in Patients with Low Platelet Counts

MMB does not require dose adjustment based on platelet count. By retaining full dose intensity, efficacy is maintained with MMB in contrast to RUX in patients with low platelet counts.

Week 24 Response Rates

SIMPLIFY-1: Patients with 50 - 150 x10⁹ platelets/L at Baseline

- Anemia (TI) Response: MMB 62%, RUX 42%
- Splenic Response: MMB 23%, RUX 4%
- Symptom (TSS) Response: MMB 28%, RUX 33%

SIMPLIFY-2: Patients with ≤150 x10⁹ platelets/L at Baseline*

- Anemia (TI) Response: MMB 45%, RUX/BAT 22%
- Splenic Response: MMB 6%, RUX/BAT 5%
- Symptom (TSS) Response: MMB 24%, RUX/BAT 3%

*Including patients with <50 x 10⁹ platelets / L
Safety and Tolerability from the SIMPLIFY Phase 3 Trials

• Safety generally similar for momelotinib, ruxolitinib in the 24-week double-blind period
  - Anemia and thrombocytopenia were more common in the ruxolitinib arm
  - Nausea was more common with momelotinib, as was the early withdrawal rate in S-1

• Tolerability persists with extended treatment
  - No evidence of long-term cumulative toxicity observed

• Safety profile enables long duration of dosing
  - Several patients from early trials have now received >10 years of continuous momelotinib therapy
  - Many patients from SIMPLIFY-1 and -2 continue to receive momelotinib

<table>
<thead>
<tr>
<th>SIMPLIFY-1</th>
<th>Randomized Treatment Period</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MMB (N=214)</td>
</tr>
<tr>
<td>Pts with any TEAE, n (%)</td>
<td>198 (92.5%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>39 (18.2%)</td>
</tr>
<tr>
<td>Anemia</td>
<td>31 (14.5%)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>40 (18.7%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>34 (15.9%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>31 (14.5%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>S-1 Extended</th>
<th>Extended duration MMB Final Safety Analysis (N=411)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pts with any TEAE, n (%)</td>
<td>397 (96.6%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>99 (24.1%)</td>
</tr>
<tr>
<td>Anemia</td>
<td>93 (22.6%)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>94 (22.9%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>85 (20.7%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>84 (20.4%)</td>
</tr>
</tbody>
</table>

1 TEAEs occurring in >20% pts in the “Overall exposed to MMB” population including the 214 subjects receiving blinded momelotinib and 197 additional subjects who received momelotinib after cross-over from ruxolitinib
Danazol was selected as an appropriate comparator given its use to ameliorate anemia in MF patients, as recommended by NCCN, ESMO guidelines.

**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
MMB Could Become the Cornerstone of Future Combinations for MF Patients

Myelofibrosis landscape is evolving with multiple combination studies ongoing

• BET inhibition has shown initial proof-of-concept with disease-modifying potential
• Unlike other BET inhibitors, SRA515 has a novel bivalent binding bode
  • A stronger connection on the cellular level leads to improved potency
• SRA515 has favorable PK, PD and safety profile when dosed as monotherapy and in combination

Clinical validation of MMB + BET combination

• SRA515 has synergistic preclinical efficacy in combination with diverse agents
  • Best-in-class potential
• As a non-myelosuppressive inhibitor of JAK1, JAK2, and ACVR1, MMB is an ideal combination partner for novel agents
• SRA515+MMB has the potential to improve outcomes in patients with MF

Momelotinib + SRA515 may provide the opportunity for longer and more durable responses for myelofibrosis patients
Sierra Oncology Pipeline

**Phase 1**
- **Compound**: SRA515
  - **Therapeutic Area**: Myelofibrosis
  - **Details**: In combination with momelotinib; trial to start 1H 2022

**Phase 2**
- **Compound**: Momelotinib
  - **Therapeutic Area**: Myelofibrosis
  - **Details**: Topline data anticipated by February 2022

**Phase 3**
- **Compound**: Momelotinib
  - **Therapeutic Area**: Myelofibrosis

*Momelotinib has been granted Fast Track Designation by the US Food & Drug Administration.*
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