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

- Profile has demonstrated anemia improvement, symptom and spleen control, without platelet decreases

Less than 1 month from pivotal Phase 3 MOMENTUM data

- High probability of success trial; FDA approval and launch expected <18 months

~$3B addressable market* in anemic MF patients in the US

- ~15K prevalent patients with anemia in the US

Could become the cornerstone of future combinations in myelofibrosis

- Momelotinib + SRA515 combination will provide proof-of-concept
- Targeting patient subsets where the unmet medical need remains

Current market cap of ~$506M

- ~22M FD shares outstanding(1)
- ~$97.1M cash as of 9/30/21(2)

Source: Sierra Market Research

*Sierra estimates ~15k U.S. prevalent patients at $200k/patient/year

(1) Assuming treasury stock method to account for outstanding options and Series A warrants and $23 stock price
Additional $12.6M raised off ATM subsequent to the close of the third quarter.
Myelofibrosis: Disease Overview

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
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**

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**Anemia Predicts Poor Survival in MF**

Nicolosi et al. Leukemia. 2018

**Transfusion Dependency Predicts Poor Survival in MF**

Elena et al. Haematologica. 2011

**Elevated Hepcidin Predicts Poor Survival in MF**

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

- **Goal:** Non-Inferiority
- **Endpoints at Week 24:**
  - SRR ≥35% (primary)*
    - MMB: 27%
    - RUX: 29%
  - Symptom score reduction ≥50%
    - MMB: 28%
    - RUX: 42%
  - TI for ≥12weeks
    - MMB: 67%
    - RUX: 49%

SIMPLIFY-2

2nd-Line Population
Prior ruxolitinib complicated by hematologic toxicity

- **Goal:** Superiority
- **Endpoints at Week 24:**
  - SRR ≥35% (primary)
    - MMB: 7%
    - RUX/BAT: 6%
  - Symptom score reduction ≥50%
    - MMB: 26%
    - RUX/BAT: 6%
  - TI for ≥12weeks
    - MMB: 43%
    - RUX/BAT: 21%

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

The Lancet Haematology, 2018 5(2): 7
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 Highlighted MMB’s Unique Impact on Hemoglobin and Transfusions

Hemoglobin Level

Transfusion Requirement

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 ≤ 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, PLT = platelets, RUX = ruxolitinib, TD = transfusion dependent, TI = transfusion independent, TR = transfusion requiring

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

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.

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

### SIMPLIFY-1

**Frequent TEAEs¹ by PT**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Pts with any TEAE, n (%)</th>
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</thead>
<tbody>
<tr>
<td>MMB (N=214)</td>
<td>198 (92.5%)</td>
</tr>
<tr>
<td>RUX (N=216)</td>
<td>206 (95.4%)</td>
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<tr>
<td>Diarrhea</td>
<td>39 (18.2%)</td>
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<tr>
<td>Anemia</td>
<td>31 (14.5%)</td>
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<tr>
<td>Thrombocytopenia</td>
<td>40 (18.7%)</td>
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<tr>
<td>Nausea</td>
<td>34 (15.9%)</td>
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<tr>
<td>Fatigue</td>
<td>31 (14.5%)</td>
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</table>

### S-1 Extended

**Most Frequent TEAEs¹ by PT**

<table>
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<tr>
<th>Treatment</th>
<th>Pts with any TEAE, n (%)</th>
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<tbody>
<tr>
<td>Final Safety Analysis (N=411)</td>
<td>397 (96.6%)</td>
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<tr>
<td>Diarrhea</td>
<td>99 (24.1%)</td>
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<tr>
<td>Anemia</td>
<td>93 (22.6%)</td>
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<tr>
<td>Thrombocytopenia</td>
<td>94 (22.9%)</td>
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<td>Nausea</td>
<td>85 (20.7%)</td>
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<tr>
<td>Fatigue</td>
<td>84 (20.4%)</td>
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</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
Anemia Could Become the Primary Driver of JAKi Choice

- Momelotinib could become the JAKi of choice for anemic myelofibrosis patients
  - In S-1 at baseline, ~75% of anemic with 30% requiring transfusions
  - In Rux-experienced patients, 90% are anemic with more than two thirds require transfusions
- A differentiated JAKi could allow hem/oncs to transition patients early in their treatment journey
- Upside potential with a broad label that allows for use in JAKi-naïve patients

**JAKi Naïve Patients (S-1) – at Baseline**

- Hgb ≥12g/dL: 25%
- Mild anemia Hgb 10-<12g/dL: 31%
- Moderate Anemia Hgb 8-<10g/dL: 32%
- Severe anemia Hgb <8 g/dL: 12%

**RUX Experienced Patients (S-2) – at Baseline**

- Hgb ≥12g/dL: 11%
- Mild anemia Hgb 10-<12g/dL: 22%
- Moderate Anemia Hgb 8-<10g/dL: 46%
- Severe anemia Hgb <8 g/dL: 21%

~30% Require Transfusions

Source: SIMPLIFY-1, -2 analysis
Danazol was selected as an appropriate comparator given its use to ameliorate anemia in MF patients, as recommended by NCCN, ESMO guidelines.

2:1 randomization

JAKi taper/washout ≥ 21 day

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

Subjects
N=180

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

Day 1

Week 24

Momelotinib 200 mg daily + Placebo

Danazol* 600 mg daily + Placebo

Momelotinib 200 mg daily

Early crossover to open label in the event of confirmed symptomatic splenic progression

Open Label/Crossover

Long Term Follow-up

24/720.0x405.0

Enrollment complete with 195 patients

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Momelotinib + SRA515 Combinations Could Expand the Myelofibrosis Opportunity

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
MMB + SRA515 May be the “Winning” Combination

- **SRA515** potentially the most potent BETi with selective target inhibition
  - Novel bivalent binding mode; Allows for maintained dosing durability

- **MMB** may be the best combination agent as only JAKi with anemia benefit in MF
  - Novel JAK1, JAK2 and ACVR1/ALK2 MOA does not add to myelosuppression of BETi

- **Sierra wholly owns both compounds**, allowing for data-driven development approach

- **Distinct advantage of extensive MMB clinical experience with almost 1,000 MF patients dosed**

- **Can create intelligent development plan due to both internally- and externally-derived data sources**
### Sierra Oncology Clinical Program

Sierra’s pipeline affords numerous combination opportunities, with SOC and with other investigational agents.

<table>
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<tr>
<th>Program</th>
<th>Indication</th>
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<th>Phase 2</th>
<th>Phase 3</th>
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<tr>
<td>SRA737 + IO/gemcitabine</td>
<td>Solid tumors</td>
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</table>

*Formerly AZD5153

**Opportunities currently under consideration include co-operative trials