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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

<6 months 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 ~$460M

- ~21M FD shares outstanding
- ~$90.7M cash as of 6/30/21

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 $22 stock price. See slide 23 for details.

(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**

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Anemia Predicts Poor Survival in Myelofibrosis*


Hepcidin Predicts Poor Survival in Myelofibrosis**

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

![Diagram of SIMPLIFY-1 study design](image1)

**Primary Endpoint**

- **Day 1**:
  - JAKI-naïve
  - Double-blind, N=432

- **Week 24**:
  - Momelotinib 200 mg QD
  - Ruxolitinib 20 mg BID

- **Year 7**:
  - Double-blind treatment
  - Open label
  - LTFU

**Randomization**

- 1:1 randomization

**Best available therapy**
- 2:1 randomization
- RUX-exposed, N=156

**Primary Endpoint**

- 88.5% = RUX/RUX+

*Met endpoint*

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

**SIMPLIFY-2**

*2nd-Line Population*

Prior ruxolitinib complicated by hematologic toxicity

![Diagram of SIMPLIFY-2 study design](image2)

**Primary Endpoint**

- **Day 1**:
  - RUX-exposed
  - Open label, N=156

- **Week 24**:
  - Momelotinib 200 mg QD

- **Year 7**:
  - Randomized treatment
  - Extension
  - LTFU

**Randomization**

- 2:1 randomization

**Best available therapy**

- 88.5% = RUX/RUX+

*The Lancet Haematology, 2018 5(2): 7*
S-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 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.


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

**SIMPLIFY-2**

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

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.

**Comparative Efficacy MMB vs RUX/BAT in Anemic Patients**

**Week 24 Response Rates**

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

- 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**

- 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

**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><strong>MMB</strong></td>
<td><strong>RUX</strong></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>

**Comparable Symptom Benefit** for all 7 items within the TSS

- **Abdominal Discomfort**
- **Pain Under Left Ribs**
- **Early Satiety**
- **Night Sweats**
- **Itching**
- **Bone Pain**
- **Tiredness**

Transfusion Requirement was ~half for MMB vs. RUX
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
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

SIMPLIFY-1
Frequent TEAEs¹ by PT

<table>
<thead>
<tr>
<th></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>

S-1 Extended
Most Frequent TEAEs¹ by PT

<table>
<thead>
<tr>
<th></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
Pivotal Phase 3 ‘MOMENTUM’ Study: Topline Results Expected February 2022

Enrollment complete with 195 patients

Double-Blind Treatment

Momelotinib 200 mg daily + Placebo

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

Danazol* 600 mg daily + Placebo

Primary Endpoint

Day 1

Week 24

Open Label/Crossover

Momelotinib 200 mg daily

Long Term Follow-up

Preceding text:

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

*Danazol was selected as an appropriate comparator given its use to ameliorate anemia in MF patients, as recommended by NCCN, ESMO guidelines.
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 Will Lead MF Market Expansion with SRA515 and Momelotinib

✓ 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 Pipeline

<table>
<thead>
<tr>
<th>Compound</th>
<th>Therapeutic Area</th>
<th>PHASE 1</th>
<th>PHASE 2</th>
<th>PHASE 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Momelotinib</td>
<td>Myelofibrosis</td>
<td></td>
<td></td>
<td>Topline data anticipated by February 2022</td>
</tr>
<tr>
<td>JAK1/JAK2/ACVR1(ALK2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SRA515</td>
<td>Myelofibrosis</td>
<td></td>
<td></td>
<td>In combination with momelotinib; trial to start 1H 2022</td>
</tr>
<tr>
<td>BRD4 BET</td>
<td></td>
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*Momelotinib has been granted Fast Track Designation by the US Food & Drug Administration.
SRRA Ownership and Capitalization

SRRA ownership is highly concentrated with quality long-term shareholders – the top 10 own ~80% of common shares outstanding (1)

- Vivo Capital
- Longitude Capital
- Orbimed Advisors
- Rock Springs Capital
- Abingworth Management
- Adage Capital
- Frazier Healthcare Partners
- Gilead Sciences
- Ikarian Capital
- Caxton Associates

With conversion of warrants and options, fully diluted shares outstanding are ~21M resulting in a market cap of ~ $460M at a $22 stock price

Common shares outstanding (2) 14,355,150
Series A warrants for common stock (treasury stock method) 3,120,896
Series B warrants for common stock 2,524,732
Gilead warrants for common stock (treasury stock method) 290,113
Employee stock options (3) 628,768
Total FD Shares Outstanding 20,919,660

Fully Diluted Market Cap $460,232,511

(1) Source: public filings as of 9/22/21
(2) Source: Nasdaq.net as of 9/22/21. Note that common shares outstanding will change as the ATM is used and this number should not be relied upon for investment decisions.
(3) Based on 4.8M options outstanding with a weighted average exercise price of $19.11per 10-Q for the period ending 6/30/21. Calculation uses treasury stock method.
Sierra Oncology Overview

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Source: Sierra Market Research
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