Corporate Presentation
February 2021

NASDAQ: SRRA
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On a Quest to Deliver Targeted Therapies for Rare Cancers

Our team takes an evidence-based approach to understand the limitations of current treatments and explore new ways to change the cancer treatment paradigm.

Transforming Promise into Patient Impact
Sierra Oncology Highlights

Momelotinib
a potential cornerstone MF therapy

Differentiated asset
designed to address a well-defined unmet need

Pivotal Phase 3 MOMENTUM clinical trial in progress: topline results expected 1H 2022

Robust data set: existing data on >800 myelofibrosis patients, some of which have been treated for 10+ years

Global commercial opportunity: ~40k patients worldwide; approved JAK inhibitors generate > $2 Billion annually

Experienced management team across Development, Regulatory & Commercial

Well-funded with $109M in cash/equivalents*; Runway extends beyond pivotal data readout

Focused on commercializing in North America

*As of 9/30/2020
Myelofibrosis Overview

Myelofibrosis (MF): a bone marrow cancer
- Caused by constitutive activation of JAK-STAT signaling; can progress through polycythemia vera
  - Inflammation and fibrosis impair red blood cell production

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

Current treatments: Allogeneic stem-cell transplantation, hydroxyurea and JAK inhibitors (JAKi)
- Intermediate and high-risk patients primarily receive JAKi
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

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

Approved JAK inhibitors address spleen and symptoms, but not anemia
- JAKi treatment leads to myelosuppression
- Dose reductions are common
- Some patients never receive JAKi due to hemoglobin and platelet count
Four Factors Figure into Treatment Decisions

- **Anemia**: 70 – 90% of patients at diagnosis. May be managed with frequent RBC transfusions, but no curative treatments are available.

- **Splenomegaly**: 50 – 70% of patients at diagnosis. Patients experience early satiety leading to weight loss and severe left upper quadrant pain.

- **Const. Symptoms\(^1\)**: 40 – 60% of patients at diagnosis. Common symptoms include: fatigue, bone pain, pruritus, night sweats, and fever.

- **Thrombocytopenia**: 10 – 30% of patients at diagnosis. May cause significant bleeding, bruising, headaches, and pain in the joints or muscles.

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

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

Anemia

70 – 90% of patients at diagnosis

Normal (~10–30% of patients)
Hemoglobin (Hb) ≥13 g/dL

Anemic (~50–60% of patients)
Hemoglobin (Hb) 8-12 g/dL

Severe Anemia (~20–30% of pts)
Hemoglobin (Hb) <8 g/dL
Transfusion Dependence

Most Patients Will Experience Anemia Progression Over Time

Transfusion Dependence and Low Hb Have a Significant Impact on Quality of Life (QoL)

Sources: Sierra Market Research, Simplify 1 and 2 studies, https://doi.org/10.1182/blood.V114.22.2500.2500
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

Hepcidin 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

P < 0.0001

Nicolosi M et al, Leukemia 2018

Pardanani et al, American Journal of Hematology 2013
Momelotinib
A JAK1, JAK2 and ACVR1 inhibitor
Mechanism of Action: Momelotinib Inhibits Drivers of All Three Disease Hallmarks

**Constitutional Symptoms**
- Inflammation and aberrant cytokine signaling producing debilitating constitutional symptoms

**Splenomegaly**
- Clonal proliferation leading to extra medullary hematopoiesis and burdensome splenomegaly

**Anemia**
- Aberrant activation of hepcidin transcription via hyperactivated ACVR1 signaling resulting in profound functional iron deficiency anemia

Cell Wall

Cytoplasm

Nucleus

JAK1

JAK2

ACVR1

MOMELOTINIB

MOMELOTINIB

MOMELOTINIB

STAT

STAT

STAT

P

P

P
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>
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<tbody>
<tr>
<td>COMPLETED</td>
<td>COMPLETED</td>
<td>Ongoing Data Expected H1 2022</td>
<td>Ongoing &gt;10 Years</td>
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<tr>
<td><strong>SIMPLIFY-1</strong></td>
<td><strong>SIMPLIFY-2</strong></td>
<td><strong>MOMENTUM</strong></td>
<td><strong>XAP</strong></td>
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**Patient Population**
- JAKi-naïve patients (n=432)
- Prior ruxolitinib-treated patients (n=156)
- Ongoing pivotal study for patients previously-treated with JAKi (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 on Trial Design**
- No washout period
- 21-day taper & washout period

More Than 1,000 Myelofibrosis Patients Will Have Received Momelotinib When the Registration-enabling MOMENTUM Study is Complete
Prior Clinical Results:
Efficacy from the SIMPLIFY Phase 3 Trials

<table>
<thead>
<tr>
<th>Primary Endpoint</th>
<th>SIMPLIFY-1</th>
<th>SIMPLIFY-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Splenic reduction ≥35% @w24</td>
<td>MMB 7% RUX 6%</td>
<td>Non-Inferior?</td>
</tr>
<tr>
<td>Symptom score reduction &gt;50% @w24</td>
<td>27% 29%</td>
<td>Superior?</td>
</tr>
<tr>
<td>Transfusion independence for &gt;12weeks*</td>
<td>49% 29%</td>
<td>Superior?</td>
</tr>
</tbody>
</table>

(✓) = nominal significance

* Measured in patients who were transfusion-dependent at baseline

- Study design elements played a role in outcome
- Data set provided a roadmap for registration-enabling MOMENTUM study
The Pivotal Phase 3 ‘MOMENTUM’ Trial is Underway

Global Study, currently enrolling patients
Topline Data Expected H1 2022

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

Subjects
N=180

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.
Background: Completed Phase 3 Studies SIMPLIFY-1 and 2

SIMPLIFY-1

1\textsuperscript{st}-Line Population
JAK inhibitor naïve

<table>
<thead>
<tr>
<th>JAKi-naïve Double-blind, N=432</th>
</tr>
</thead>
</table>

- 1:1 randomization
- Double-blind treatment
- Open label
- LTFU

Primary Endpoint

Day 1 Week 24 Year 7

JAKi-naïve

Momelotinib 200 mg QD

Ruxolitinib 20 mg BID

Goal: Non-Inferiority

MMB N=215

RUX N=217

Primary Endpoint: Splenic Response Rate

Secondary Endpoints

- Total Symptom Score
- Transfusion Independence Rate

SIMPLIFY-2

2\textsuperscript{nd}-Line Population
Prior ruxolitinib complicated by hematologic toxicity

<table>
<thead>
<tr>
<th>RUX-exposed Open label, N=156</th>
</tr>
</thead>
</table>

- 2:1 randomization
- Randomized treatment
- Extension
- LTFU

Primary Endpoint

Day 1 Week 24 Year 7

RUX-exposed

Momelotinib 200 mg QD

Best available therapy

Goal: Superiority

MMB N=104

BAT N=52

Primary Endpoint: Splenic Response Rate

Secondary Endpoints

- Total Symptom Score
- Transfusion Independence Rate

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

The Lancet Haematology, 2018 5(2): 7
Momelotinib Data:
Hemoglobin and Platelet Levels Over Time

**SIMPLIFY-1**

Momelotinib increased hemoglobin levels and maintained platelet counts

Momelotinib Data: SRR & TSS Compared by Baseline PLT Strata

- 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.

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
Momelotinib Data: Anemia Response & Transfusion Dependency

**SIMPLIFY-1**

### W24 TI (Anemia) Response

<table>
<thead>
<tr>
<th>PLTs (×10^9/L)</th>
<th># in stratum</th>
<th>% Response</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>n=47</td>
<td>62%</td>
<td>50%</td>
<td></td>
<td>42%</td>
<td></td>
</tr>
<tr>
<td>&gt;150-300</td>
<td>n=89</td>
<td>72%</td>
<td>70%</td>
<td></td>
<td>54%</td>
<td></td>
</tr>
<tr>
<td>&gt;300</td>
<td>n=79</td>
<td>63%</td>
<td>60%</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.

OS Benefit Seen in Both JAKi-naïve and JAKi-exposed Patients

SIMPLIFY-1

JAKi-naïve Patients

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

Week 24 Crossover to open-label MMB

Treatment

- MMB
- RUX→MMB

HR = 0.99
p = 0.97

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

SIMPLIFY-2

JAKi-exposed Patients

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

Week 24 Crossover to open-label MMB

Treatment

- MMB
- BAT/RUX→MMB

HR = 0.95
p = 0.98

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

### SIMPLIFY-1 Trial: Safety Results

#### SIMPLIFY-1

**24-Week RT Period**

<table>
<thead>
<tr>
<th>Select TEAEs, by PT</th>
<th>MMB (N=214)</th>
<th>RUX (N=216)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Grade 3/4 TEAEs:</strong></td>
<td></td>
<td></td>
</tr>
<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>
<tr>
<td><strong>Any Grade TEAEs:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pts with Any Grade TEAE, n (%)</td>
<td>198 (92.5%)</td>
<td>206 (95.4%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>39 (18.2%)</td>
<td>43 (19.9%)</td>
</tr>
<tr>
<td>Anemia</td>
<td>31 (14.5%)</td>
<td>81 (37.5%)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>40 (18.7%)</td>
<td>63 (29.2%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>34 (15.9%)</td>
<td>8 (3.7%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>31 (14.5%)</td>
<td>26 (12.0%)</td>
</tr>
<tr>
<td>Headache</td>
<td>38 (17.8%)</td>
<td>43 (19.9%)</td>
</tr>
</tbody>
</table>

- 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

1 RT = Randomized Treatment
Preparing for Commercialization
Executive Leadership:
Purpose-Built Team for the Next Phase

Stephen G. Dilly, MBBS, PhD
President & Chief Executive Officer
Former CEO and Board Member of Aimmune Therapeutics

Sukhi Jagpal, CPA, CA, CBV, MBA
Chief Financial Officer
Former CFO of QLT Inc

Barbara Klencke, MD
Chief Development Officer
Former SVP of Onyx Pharmaceuticals
Former Group Medical Director Genentech

Mark Kowalski, MD, PhD
Chief Medical Officer
Former CMO and SVP of Arbutus Biopharma, Former CMO of YM BioSciences Inc

Kevin Norrett, MS, MBA
Chief Business Officer
Former Chief Commercial Officer of Angion Biomedica

Christina Thomson, MS, JD
General Counsel and Corporate Secretary
Former General Counsel of Athira Pharma, APT Pharmaceuticals and Avigen

William Turner
Chief Regulatory & Technical Operations Officer
Former SVP of Technical Operations and Regulatory Science at Aimmune Therapeutics


Recent and Upcoming Milestones

Dec 2020: ASH Presented Abstracts

Abstract #54: Long-term outcome data, including updated OS results with MMB

Abstract #3086: Further data analyses from SIMPLIFY-1 and SIMPLIFY-2 highlighting efficacy of MMB vs RUX based on platelet counts

Mid-2021: MOMENTUM Enrollment Completion

June 2021: EHA (Virtual)

H1 2022: Topline Data

H2 2022: File New Drug Application with FDA

2023: Expected Approval & Commercialization

Abstract #3086: Further data analyses from SIMPLIFY-1 and SIMPLIFY-2 highlighting efficacy of MMB vs RUX based on platelet counts

Abstract #54: Long-term outcome data, including updated OS results with MMB
The Long-term Vision of Sierra

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**