Building Momentum for Patients with Myelofibrosis

Q1 2020

NASDAQ: SRRA
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MOMELOTINIB

Positioned to potentially provide benefits on all three myelofibrosis hallmarks: symptoms, anemia and spleen

>20 studies
Phase 1, 2 and 3

>1,200 people
dosed with momelotinib

>820 patients
with myelofibrosis treated

>8 years
on treatment for several patients
Myelofibrosis
The Challenge of Anemia

"Anemia is major area of unmet need... a quarter of the patients at the beginning may require transfusions, and after one year of therapy almost half of the patients already require transfusion”

Srdan Verstovsek, MD, PhD
Professor in the Department of Leukemia at The University of Texas MD Anderson Cancer Center, Houston

Unmet Medical Needs In Myelofibrosis; company conference call October 2018

Three Hallmarks of a Progressive Disease

**ANEMIA**
Bone marrow cancer that significantly impairs red blood cell production

- 64%
- Transfusion Dependent
- Many patients need regular blood transfusions to sustain life

**SPLENOMEGALY**
Spleen tries to compensate by making blood cells, leading to pain and discomfort

- 46%

**CONSTITUTIONAL SYMPTOMS**
Patients also experience debilitating symptoms that dramatically impact their lives

- 34%

Myelofibrosis Biology: JAK1, JAK2 & ACVR1 Drive Myelofibrosis Disease Hallmarks

- Aberrant activation of hepcidin transcription via hyperactivated ACVR1 signaling resulting in profound functional iron deficiency anemia
- Inflammation and aberrant cytokine signaling producing debilitating constitutional symptoms
- Clonal proliferation leading to extramedullary hematopoiesis and burdensome splenomegaly

Interleukins
Interferons
Cytokine Receptors

JAK1
JAK2

Ligand
EPOR / MPL

BMP2, BMP6
ACVR1

SMAD1,5
Myelofibrosis Biology: Momelotinib Uniquely Inhibits All Three Disease Drivers

• Decreased inflammation and aberrant cytokine signaling improves constitutional symptoms

• Reduced extramedullary hematopoiesis improves splenomegaly

• Decreased hepcidin transcription restores iron homeostasis and increases hemoglobin leading to array of anemia benefits
Myelofibrosis Anemia: Momelotinib Could Positively Impact Multiple Pathways to Anemia

**FIBROSIS & EXTRAMEDULLARY HEMATOPOIESIS (JAK2)**
- Displacement of marrow erythropoietic tissue by fibrosis
- Extramedullary hematopoiesis and splenomegaly
- Inadequate extramedullary hematopoiesis and red blood cell sequestration

**INFLAMMATION (JAK1)**
- Alterations in bone marrow cytokine expression
- Pro-inflammatory cytokine profile
- Impaired erythroid differentiation

**HEPCIDIN (ACVR1)**
- Activated ACVR1
- Elevated hepcidin
- Impairment of iron metabolism

**OTHER JAKi THERAPIES**
- Other JAK inhibitors induce myelosuppression

**ANEMIA**
Myelofibrosis Anemia: High Hepcidin & Severe Anemia Predict Poor Survival

Hepcidin predicts poor survival in myelofibrosis

Anemia predicts poor survival in myelofibrosis

P<0.0001

No anemia
Median survival 7.9 years

Mild anemia
Median survival 4.9 years

Moderate anemia
Median survival 3.4 years

Severe anemia
Median survival 2.1 years

0 5 10 15 20 25 30 35
Years

0 2 4 6 8 10
Cumulative Survival

0 2 4 6 8 10
Survival

0

Pardanani et al; American Journal of Hematology 2013

Nicolosi M et al; Leukemia. 2018
Myelofibrosis Anemia: Reducing Hepcidin Restores Red Blood Cell Production

Momelotinib-mediated plasma iron elevation leads to stimulation of erythropoiesis and red blood cell production
Momelotinib: SIMPLIFY Data Strongly Support Benefits in Three Hallmarks of Myelofibrosis

INHIBITS ACVR1

ANEMIA
Increased hemoglobin: lower rates of red blood cell transfusion, fewer transfusion dependent patients, higher odds of being transfusion free

INHIBITS JAK1

CONSTITUTIONAL SYMPTOMS
Pronounced TSS benefit: clinically consistent symptom improvement across all domains in 1st-line & 2nd-line

INHIBITS JAK2

Splenomegaly
Only JAKi to show equivalent splenic response to ruxolitinib in 1st-line

Momelotinib
MOMELOTINIB
JAK1 JAK2 ACVR1
Building Momentum for Patients with Myelofibrosis

LAUNCHED Q4 2019!
A Randomized, Double-Blind, Phase 3 Study to Evaluate the Activity of Momelotinib (MMB) versus Danazol (DAN) in Symptomatic, Anemic Subjects with Primary Myelofibrosis (PMF), Post-Polycythemia Vera (PV) Myelofibrosis, or Post Essential Thrombocythemia (ET) Myelofibrosis who were Previously Treated with JAK Inhibitor Therapy

2:1 randomization

Double-Blind Treatment

Primary Endpoint

Week 24

Open Label/Crossover

Long Term Follow-up

Day 1

Momelotinib 200 mg daily + Placebo

Momelotinib 200 mg daily

Danazol* 600 mg daily + Placebo

*Spleen progression (Momelotinib 200mg)

*Spleen progression (Momelotinib 200mg)

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

Subjects
N=180

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

2:1 randomization JAKi taper/washout ≥ 21 day

Momelotinib has been selected as an appropriate treatment comparator given its use to ameliorate anemia in myelofibrosis patients, as recommended by NCCN and ESMO guidelines.

MOMENTUM MYELOFIBROSIS CLINICAL TRIAL

Momentum P3 Trial: Phase 3 Registration Trial Schema
Momentum P3 Trial: Study Objectives

Primary Endpoint:
• Total symptom score (TSS) response rate of momelotinib vs. danazol at Week 24 in symptomatic and anemic patients with PMF, post-PV myelofibrosis, or post-ET myelofibrosis who were previously treated with an approved JAK inhibitor therapy

Secondary & Exploratory Endpoints:
• Transfusion independence (TI) rate at Week 24
• Splenic response rate (SRR) at Week 24
• Duration of TSS response for subjects treated with momelotinib
• Other measures of anemia benefit, including TD-TI rate and measures of cumulative transfusion burden
• Additional Patient Reported Outcomes, including assessments of fatigue and physical function
**Momentum P3 Trial: Key Design Elements**

**Chief Investigator:**
Dr. Srdan Verstovsek, MD Anderson Cancer Center, Houston, Texas, USA

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Order &amp; Powering</th>
<th>Supporting Data/Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom (TSS) response rate</td>
<td>Primary (W24)</td>
<td>99% powered; p&lt;0.05, FDA preferred measure of clinical benefit in myelofibrosis Consistent and meaningful TSS responses in SIMPLIFY-1 and SIMPLIFY-2</td>
</tr>
<tr>
<td>Transfusion Independence rate</td>
<td>Secondary (W24)</td>
<td>&gt;90% powered; p&lt;0.05, Favorable and statistically significant TI rates in SIMPLIFY-1 and SIMPLIFY-2</td>
</tr>
<tr>
<td>Spleen (SRR) response rate</td>
<td>Secondary (W24)</td>
<td>&gt;90% powered; p&lt;0.05, Defined washout allows for splenic rebound and SRR benefit Non-inferior SRR benefit head-to-head vs ruxolitinib in SIMPLIFY-1</td>
</tr>
<tr>
<td>Durability of TSS response</td>
<td>Secondary (W48)</td>
<td>Durability of symptomatic benefit to W48 established in SIMPLIFY-1 and SIMPLIFY-2</td>
</tr>
<tr>
<td>Other anemia measures</td>
<td>Secondary &amp; Exploratory</td>
<td>Consistent suite of benefits: TD-TI rates, improved hemoglobin, reduced transfusion frequency, etc.</td>
</tr>
</tbody>
</table>

*Stratified for baseline TSS, RBC transfusions & spleen*
Pronounced Symptom Benefit

**SIMPLIFY-2**

Statistically Significant Symptom Response

Momelotinib compared to best available therapy (~90% ruxolitinib) in 2nd-line patients

26.2% Total Symptom Score (TSS)

vs 5.9% best available therapy (BAT)

(p < 0.001)

Baseline TSS was a stratification factor in SIMPLIFY-2

TSS response is defined as the proportion of subjects who achieve a ≥ 50% reduction in TSS over the 28 days immediately prior to the end of Week 24 compared to baseline.
Maintenance of Transfusion Independence

SIMPLIFY-1

66% ✓

vs 49% ruxolitinib

Statistically significant transfusion independence rate (p < 0.001)

SIMPLIFY-2

43% ✓

vs 21% BAT (~90% ruxolitinib)

Statistically significant transfusion independence rate (p = 0.001)

Secondary Endpoint

>90% Powered

Transfusion Independence response defined as the proportion of subjects who were transfusion independent at Week 24, where transfusion independence was defined as the absence of red blood cell (RBC) transfusion and no hemoglobin level below 8 g/dL in the prior 12 weeks.
Eliminating Need for Frequent Transfusions

**Transfusion Dependent Subset Analysis**

**SIMPLIFY-1**

49.1%

vs 28.8% ruxolitinib

\( p = 0.0299 \)

**SIMPLIFY-2**

46.6%

vs 18.6% BAT

\( p = 0.0048 \)

\( \geq 12 \) Week Transfusion Dependence Response Rate*

Transfusion Dependence response defined as the proportion of transfusion dependent subjects who became transfusion independent for any 12 week or greater period on study, where transfusion independence was defined as the absence of RBC transfusion and no hemoglobin level below 8 g/dL.

*Data from Sierra’s post-hoc analyses of SIMPLIFY-1 & SIMPLIFY-2 studies.
Dramatic Reduction in Odds of Being Transfused

"Overall, these highly persuasive statistical analyses further confirm that momelotinib treatment elicits a substantive mechanistically-driven anemia benefit."

Dr. Ruben Mesa
Director of the Mays Cancer Center
Home to UT Health San Antonio MD Anderson Cancer Center
Dec 2019

\[
\text{SIMPLIFY-1}
\]

Remarkable Reduction in Need for Transfusions

9.3x ✓

Odds of \textbf{not being transfused} on momelotinib compared to ruxolitinib

\( (p < 0.0001) \)

*Data from Sierra’s post-hoc analyses of SIMPLIFY-1 & SIMPLIFY-2 studies*
Equivalent Clinical Benefit on Splenomegaly

SIMPLIFY-1

27% Splenic Response

vs 29% ruxolitinib

(p=0.011)

Momelotinib clinically equivalent to ruxolitinib on spleen

Only JAKi to show comparable spleen response to ruxolitinib

Splenic Response Rate (SRR) defined as ≥ 35% reduction in spleen volume at W24 versus baseline
Momelotinib Safety: Favourable Toxicity Profile

<table>
<thead>
<tr>
<th>Common Adverse Event</th>
<th>Momelotinib</th>
<th>Ruxolitinib</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombocytopenia*</td>
<td>19%</td>
<td>29%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>18%</td>
<td>20%</td>
</tr>
<tr>
<td>Headache</td>
<td>17%</td>
<td>20%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>16%</td>
<td>12%</td>
</tr>
<tr>
<td>Nausea</td>
<td>16%</td>
<td>4%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>15%</td>
<td>12%</td>
</tr>
<tr>
<td>Anemia**</td>
<td>14%</td>
<td>38%</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>10%</td>
<td>11%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Grade 3 or 4 Adverse Event</th>
<th>Momelotinib</th>
<th>Ruxolitinib</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombocytopenia*</td>
<td>7%</td>
<td>5%</td>
</tr>
<tr>
<td>Anemia**</td>
<td>6%</td>
<td>23%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3%</td>
<td>4%</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>3%</td>
<td>5%</td>
</tr>
</tbody>
</table>

*denote reduction/interruption for thrombocytopenia: 
Momelotinib = 5.6%  Ruxolitinib = 24.5%

**denote reduction/interruption for anemia: 
Momelotinib = 1.4%  Ruxolitinib = 6.0%

<table>
<thead>
<tr>
<th>Safety outcomes</th>
<th>Momelotinib (n=214)</th>
<th>Ruxolitinib (n=216)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AEs</td>
<td>92%</td>
<td>95%</td>
</tr>
<tr>
<td>Grade 3 or 4 AE</td>
<td>34%</td>
<td>44%</td>
</tr>
<tr>
<td>≥Grade 3 AE Related to Study Drug</td>
<td>21%</td>
<td>29%</td>
</tr>
<tr>
<td>Serious AE</td>
<td>23%</td>
<td>18%</td>
</tr>
<tr>
<td>Serious AE Related to Study Drug</td>
<td>7%</td>
<td>6%</td>
</tr>
</tbody>
</table>

Momelotinib Safety:
- No Adverse Event concerns flagged in our Regulatory interactions
- No evidence of cumulative toxicity/safety issues in long-term dosing and follow-up
Momentum Phase 3 Trial: Key Trial Assumptions

**Study Launch**
Q4 2019

**Estimated Time to Enroll**
~18 months*

**Topline Data**
~Q4 2021* (~6 months to primary endpoint after enrollment)*

**Filing Date**
~Q2 2022*

**Potential Regulatory Approval**
~Q4 2022**

Patients: 180 (2:1 randomization)

Territory: Global study (North America, EU, APAC, etc.)

*Company estimates
**Assuming priority regulatory review; Fast Track granted June 2019
Momelotinib: Totality of Data to Support Potential Registration

**PHASE 3 CLINICAL TRIAL**

**Pivotal study data**
~180 subjects
- Primary endpoint: TSS response rate (99% powered; p < 0.05)
- Secondary endpoints:
  - Transfusion Independence rate
  - Spleen (SRR) response rate
  - Durability of TSS response
  - Other anemia measures

**SIMPLIFY-1**
**SIMPLIFY-2**

**Patient data from completed P3 studies**
>550 subjects
- Statistically non-inferior spleen response vs ruxolitinib (S-1; p = 0.011)
- Statistically significant TSS response vs BAT/ruxolitinib (S-2; p < 0.001)
- Statistically significant transfusion independent rates (S-1; p < 0.001) (S-2; p = 0.001)
- Crossover data: momelotinib efficacy and safety data in patients who switch from ruxolitinib (S-1) or BAT/ruxolitinib (S-2) after Week 24

**XAP EXTENDED ACCESS PROGRAM**

**Long term treatment data**
- Durable response data (some patients treated >8 years)
- Long term safety and tolerability data
Momelotinib Market Opportunity*

**Diagnosis**
- ~50K patients living with myelofibrosis
- ~75% are intermediate/high risk

**1st-Line**
- ~70% receive 1st-line treatment
- >70% of Int/High risk myelofibrosis patients have anemia
- >50% of patients are transfusion dependent

**2nd-Line**
>75% will need 2nd-line treatment
- >75% will need 2nd-line treatment
- >70% of Int/High risk myelofibrosis patients have anemia
- >50% of patients are transfusion dependent

**Favorable patent exclusivity**
- potential extensions to 2040**
- provide a compelling commercial opportunity

*Company estimates
**assumes anticipated 5 years PTE and SPC extensions
Clinician Enthusiasm For Momelotinib Supports 1L & 2L Market Opportunity

“The dual mechanism and clinical data… point to a strong anemia benefit, so I would definitely look to prescribe this in my front-line patients who have severe anemia”

US High Volume Prescriber*
February 2020

“The majority of patients in second-line would potentially be candidates for momelotinib.”

Dr. Srdan Verstovsek
June 2019

“Transfusions can be a major problem for patients and this product shows a clear benefit for transfusion independence in all studies, so I would use it in the majority of my front-line patients with severe anemia”

EU KOL*
February 2020

Momelotinib Market Opportunity:

- 1L - patients with severe anemia or transfusion dependency
- 2L – broad utility across all patients; particularly anemic/cytopenic

*Sierra market research conducted by 3rd party
Improved agreement and commitment from Gilead meaningfully enhances the potential long-term value of momelotinib for Sierra and its stockholders:

- Gilead has become a stockholder in Sierra (~7%)
- Blended annual royalty rates payable to Gilead substantially reduced
- Net royalties range from very low double digits (sub-$B revenue) to teens (>$/B revenue)
- Milestone payment eliminated that would have been due to Gilead upon initiation of MOMENTUM, further extending our financial resources

“Gilead continues to believe in the potential of momelotinib, and we are pleased that Sierra will continue development of the compound in hopes that it will benefit patients in the future.”

Andrew Dickinson, Chief Financial Officer of Gilead
• Momelotinib – differentiated JAKi potentially addressing all three hallmarks of myelofibrosis
  • MOMENTUM Phase 3 in 2nd-line myelofibrosis launched in Q4 2019
• Highly experienced management team with proven track record in drug development
• Strong financial standing:
  • $147.5M in cash and cash equivalents (as of December 31, 2019)
  • Key investors include Vivo Capital, Longitude Capital, OrbiMed and Abingworth
• Topline data warrant: Expires 75 days post-announcement; Potential ~$34M in additional funding