Building Momentum for Patients with Myelofibrosis

Q1 2020
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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
The Three Hallmarks of a Progressive Disease

>1 YEAR AFTER DIAGNOSIS

**ANEMIA**
Progressive bone marrow fibrosis due to inflammation; decreased erythropoiesis

45% Transfusion Dependent

**SPLENOMEGALY**
Extramedullary hematopoiesis in the spleen and other organs

46%

**CONSTITUTIONAL SYMPTOMS**
Anemia, chronic inflammation, and splenomegaly lead to constitutional symptoms

34%

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Myelofibrosis
The Challenge of Anemia

“Anemia is major area of unmet need. That’s one of the major problems… 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. Anemia and transfusion dependency are important prognostic factors.”

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

Myelofibrosis Biology: JAK1, JAK2 & ACVR1 Drive MF 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
JAK2
EPOR / MPL
ACVR1
BMP2, BMP6

Ligand
SMAD1,5

P

P

P
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

- High hepcidin
- Low hepcidin

Anemia predicts poor survival in myelofibrosis

- 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

P<0.0001

Nicolosi M et al; Leukemia. 2018

Pardanani et al; American Journal of Hematology 2013
Myelofibrosis Anemia: Reducing Hepcidin Restores Red Blood Cell Production

PLASMA IRON DEFICIENCY

PLASMA IRON NORMALIZATION

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 MF

**ANEMIA**
Increased hemoglobin: lower rates of red blood cell transfusion, fewer transfusion dependent patients, etc. in 1L & 2L

**CONSTITUTIONAL SYMPTOMS**
Pronounced TSS benefit: clinically consistent symptom improvement across all domains in 1L & 2L

**Splenomegaly**
Only JAKi to show equivalent splenic response to ruxolitinib in 1L
Building Momentum for Patients with Myelofibrosis

LAUNCHED Q4 2019!
Momentum P3 Trial: Phase 3 Registration Trial Schema

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

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 200 mg daily + Placebo

Spleen progression (Momelotinib 200mg)

Danazol 600 mg daily + Placebo

Momelotinib 200 mg daily

Primary Endpoint

Long Term Follow-up

Danazol has been selected as an appropriate treatment comparator given its use to ameliorate anemia in myelofibrosis patients, as recommended by NCCN and ESMO guidelines.
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 for subjects treated with momelotinib vs danazol
• Splenic response rate (SRR) at Week 24 for subjects treated with momelotinib vs danazol
• 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>
</table>
| Symptom (TSS) response rate      | **Primary (W24)** 99% powered; p<0.05 | FDA preferred measure of clinical benefit in myelofibrosis  
Consistent and meaningful TSS responses in S-1 and S-2                                                   |
| Transfusion Independence rate    | **Secondary (W24)** >90% powered; p<0.05 | Favorable and statistically significant TI rates in S-1 and S-2                                                                                       |
| Spleen (SRR) response rate       | **Secondary (W24)** >90% powered; p<0.05 | Defined washout allows for splenic rebound and SRR benefit  
Non-inferior SRR benefit head-to-head vs ruxolitinib in S-1                                              |
| Durability of TSS response       | **Secondary (W48)** | Durability of symptomatic benefit to W48 established in S-1 and S-2                                                                                   |
| Other anemia measures            | **Secondary & Exploratory** | Consistent suite of benefits: TD-TI rates, improved hemoglobin, reduced transfusion frequency, etc.                                                        |

*Stratified for baseline TSS, RBC transfusions & spleen
SIMPLIFY-2 Symptom Response: Pronounced TSS Benefit in 2L: Relevance to MOMENTUM

SIMPLIFY-2

Statistically Significant Symptom Response

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

26.2\% TSS ✓

vs 5.9\% best available therapy

\( p < 0.001 \)

Baseline TSS was a stratification factor in SIMPLIFY-2
Maintenance of Transfusion Independence

**SIMPLIFY-1**

- 66% transfusion independence vs 49% ruxolitinib
- Statistically significant transfusion independence rate \( p < 0.001 \)

**SIMPLIFY-2**

- 43% transfusion independence vs 21% best available therapy (~90% ruxolitinib)
- Statistically significant transfusion independence rate \( p = 0.001 \)

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 RBC transfusion and no hemoglobin level below 8 g/dL in the prior 12 weeks.
Conversion from Transfusion Dependence to Transfusion Independence

Transfusion Dependent Subset Analysis

<table>
<thead>
<tr>
<th>Study</th>
<th>≥ 12 Week Transfusion Dependence Response Rate*</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIMPLIFY-1</td>
<td>49.1% vs 28.8% ruxolitinib (p = 0.0299)</td>
</tr>
<tr>
<td>SIMPLIFY-2</td>
<td>46.6% vs 18.6% best available therapy (p = 0.0048)</td>
</tr>
</tbody>
</table>

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.
Momelotinib:
ASH 2019 Poster / Abstract #1663

Dynamic and Time-To-Event Analyses Demonstrate Marked Reduction in Transfusion Requirements for Janus Kinase Inhibitor–Naïve Myelofibrosis Patients Treated with Momelotinib Compared Head to Head with Ruxolitinib

ZINB Model Demonstrates Increased Odds of Zero Transfusions on Momelotinib

Odds of zero transfusion 9.3 times higher on momelotinib

"Overall, these highly persuasive statistical analyses further confirm that momelotinib treatment elicits a substantive mechanistically-driven anemia benefit… …and nearly 10-fold higher odds of receiving no transfusions during the 24-week study period, directly compared to ruxolitinib."

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

- The outcomes of the covariate ZINB model demonstrate that a typical patient in S1 had an 82% chance of receiving no transfusions when receiving momelotinib vs only a 33% chance when receiving ruxolitinib
- The odds of zero red blood cell units transfused were 9.3 times higher on momelotinib than on ruxolitinib (p < 0.0001)
Non-Inferior Head-to-Head Activity on Splenomegaly in 1L

**SIMPLIFY-1**

26.5% SRR vs 29% ruxolitinib

Momelotinib statistically non-inferior to ruxolitinib on spleen \((p=0.011)\)

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

Splenic Response Rate (SRR) defined as ≥ 50% reduction in spleen volume at W24 versus baseline
## Momelotinib Safety: Less Hematologic Toxicity Head-to-Head vs Ruxolitinib

### SIMPLIFY-1

<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>

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

*dose reduction/interruption for thrombocytopenia: Momelotinib = 5.6% Ruxolitinib = 24.5%  
**dose reduction/interruption for anemia: Momelotinib = 1.4% Ruxolitinib = 6.0%
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 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**
>120 subjects; >15 countries
- Durable response data (some patients treated >8 years)
- Long term safety and tolerability data
Momelotinib 2\textsuperscript{nd}-Line Market Opportunity* \\

Diagnosis

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

1\textsuperscript{st}-Line

~70% receive 1\textsuperscript{st}-line treatment

2\textsuperscript{nd}-Line

>75% will need 2\textsuperscript{nd}-line treatment

- >70% of INT-2/High 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

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

Dr. Srdan Verstovsek
June 2019
Improved agreement and commitment from Gilead meaningfully enhances the potential long-term value of momelotinib for Sierra and its stockholders:

- Gilead will become a stockholder in Sierra (~7% post financing)
- The blended annual royalty rates payable to Gilead will be substantially reduced
- Following this amendment, net royalties range from very low double digits (sub-$B) to teens (>B)
- A milestone payment will be eliminated that would be due to Gilead with the initiation of the 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
• Late stage drug development company oriented to potential registration and commercialization
• Momelotinib – differentiated JAKi potentially addressing all three hallmarks of myelofibrosis
  • MOMENTUM Phase 3 in 2L myelofibrosis launched in Q4 2019
• Exploring non-dilutive options to advance DDR assets
• Highly experienced management team with proven track record in drug development
• Strong financial standing:
  • $67.7M in cash and cash equivalents
    (as of September 30, 2019)
  • $103M gross proceeds from recent equity raise; included Vivo Capital, Longitude Capital, OrbiMed and Abingworth
    (closed November 13, 2019)
  • No debt: $5M repaid to SVB in Q4 2019
• Capital structure:
  • Common shares: 10,395,732 outstanding
    (as of January 31, 2020)
  • Series A warrants: to purchase 8,527,524 shares of common stock at exercise price of $13.20; expire January 2025
  • Series B warrants: to purchase 2,574,727 shares of common stock at exercise price of $13.20; expire 75 days post announcement of MOMENTUM topline data; Cash only exercise provision for potential proceeds of ~$34M
  • Stock options: 318,650 outstanding
    (as of January 31, 2020)