Building Momentum for Patients with Myelofibrosis

Q2 2020
SAFE HARBOR STATEMENT

Except for statements of historical fact, any information contained in this presentation may be a forward-looking statement that reflects the Company’s current views about future events and are subject to risks, uncertainties, assumptions and changes in circumstances that may cause events or the Company’s actual activities or results to differ significantly from those expressed in any forward-looking statement. In some cases, you can identify forward-looking statements by terminology such as "may", "will", "should", "plan", "predict", "expect," "estimate," "anticipate," "intend," "goal," "strategy," "believe," and similar expressions and variations thereof. Forward-looking statements may include statements regarding the Company’s business strategy, cash flows and funding status, potential growth opportunities, preclinical and clinical development activities, the timing and results of preclinical research, clinical trials and potential regulatory approval and commercialization of product candidates. Although the Company believes that the expectations reflected in such forward-looking statements are reasonable, the Company cannot guarantee future events, results, actions, levels of activity, performance or achievements. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including those described under the heading “Risk Factors” in documents the Company has filed with the SEC. These forward-looking statements speak only as of the date of this presentation and the Company undertakes no obligation to revise or update any forward-looking statements to reflect events or circumstances after the date hereof.

Certain information contained in this presentation may be derived from information provided by industry sources. The Company believes such information is accurate and that the sources from which it has been obtained are reliable. However, the Company cannot guarantee the accuracy of, and has not independently verified, such information.

TRADEMARKS:

The trademarks included herein are the property of the owners thereof and are used for reference purposes only. Such use should not be construed as an endorsement of such products.
Etiology of Myelofibrosis: A Disease of Dysregulated JAK-STAT Signaling

• Myelofibrosis (MF) primarily driven by dysregulated JAK-STAT signaling leading to clonal proliferation in the bone marrow

• Progressive fibrosis reduces hematopoietic capacity of the marrow (anemia), triggering extramedullary hematopoiesis in the spleen (splenomegaly)

• Constitutive activation of JAK-STAT signaling & progressive fibrosis creates both local and systemic pro-inflammatory cytokine profile (constitutional symptoms); drives production of hepcidin, the master iron regulator

• Elevated hepcidin restricts iron availability for erythropoiesis, further reducing red blood cell (RBC) production (anemia)

• These factors coalesce leading to the classic disease hallmarks of anemia, constitutional symptoms and splenomegaly
Myelofibrosis Biology: JAK1, JAK2 & ACVR1 Drive Myelofibrosis Disease Hallmarks

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

**Splenomegaly**
Clonal proliferation leading to extramedullary hematopoiesis and burdensome splenomegaly

**Functional Iron Deficiency Anemia**
Aberrant activation of hepcidin transcription via hyperactivated ACVR1 signaling resulting in profound functional iron deficiency anemia
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
>1 YEAR AFTER DIAGNOSIS

ANEMIA
Bone marrow cancer that significantly impairs red blood cell production

45% 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

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

64%
46%
34%
Unmet Needs in Myelofibrosis: Inadequate Current Treatment Options for Anemia

• Approved MF agents (ruxolitinib and fedratinib) offer certain benefits for splenomegaly and symptoms, but fail to address – actually, worsen - anemia and thrombocytopenia

• Anemia in myelofibrosis is multifactorial (hypersplenism, ineffective erythropoiesis, hemolysis, functional iron deficiency, chronic inflammation, etc.)

• Multiple options have been deployed to attempt to manage MF anemia; none are approved or have been shown demonstrably effective:
  • Danazol
  • ESAs
  • Steroids
  • IMiDs

• In the absence of an effective therapeutic option, frequent, chronic red blood cell (RBC) transfusions are employed as the default form of anemia management in MF

• Optimal MF therapeutic would provide robust and sustained benefits for anemia, constitutional symptoms and splenomegaly
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

>10 years
on treatment for several patients
Myelofibrosis Biology:
Momelotinib Uniquely Inhibits All Three Disease Drivers

**Improve Constitutional Symptoms**
Decreased inflammation and aberrant cytokine signaling improves constitutional symptoms

**Improve Splenomegaly**
Reduced extramedullary hematopoiesis improves splenomegaly

**Increase Hemoglobin**
Decreased hepcidin transcription via ACVR1 inhibition restores iron homeostasis and increases hemoglobin leading to array of anemia benefits
Myelofibrosis Anemia: High Hepcidin & Severe Anemia Predict Poor Survival

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

Hepcidin predicts poor survival in myelofibrosis

- Transfusion-dependent
- Transfusion-independent

Nicolosi M et al; Leukemia. 2018
Elena et al; Haematologica. 2011
Momelotinib-mediated inhibition of ACVR1 markedly decreases hepcidin. Results in plasma iron elevation leading 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, higher odds of being transfusion free

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

**SPLENOPEGALY**
Only JAKi to show equivalent splenic response to ruxolitinib in 1st-line
Building MOMENTUM for Patients with Myelofibrosis

LAUNCHED Q4 2019
Now Recruiting Globally!
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

**Primary Endpoint**

Week 24

Day 1

**Double-Blind Treatment**

Momelotinib 200 mg daily + Placebo

Danazol* 600 mg daily + Placebo

**Open Label/Crossover**

Momelotinib 200 mg daily

*Spleen progression (Momelotinib 200mg)

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

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.
MOMENTUM Phase 3 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 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

* 99% powered; p<0.05
** >90% powered; p<0.05
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

Primary Endpoint 99% Powered

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
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)

≥ 12 Week Transfusion Independence Response Rate*

Transfusion Independence 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

**SIMPLIFY-1**

Remarkable Reduction in Need for Transfusions

9.3x ✓

Odds of *not being transfused* on momelotinib compared to ruxolitinib

(p < 0.0001)

*Data from Sierra’s post-hoc analyses of SIMPLIFY-1 & SIMPLIFY-2 studies*
• Duration of transfusion independence (TI) response in S1 was determined by a KM analysis of time to loss of TI*

• Analysis demonstrated that the median time to loss of TI was not reached for momelotinib-treated patients, with a follow up period exceeding 3 years

*Loss of TI was defined by the requirement for RBC transfusion or hemoglobin < 8.5 g/dL at any time
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

**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>

* *dose reduction/interruption for thrombocytopenia: Momelotinib = 5.6% Ruxolitinib = 24.5%*  
** *dose reduction/interruption for anemia: Momelotinib = 1.4% Ruxolitinib = 6.0%*

<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
Momelotinib Market Opportunity*

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

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

1\textsuperscript{st}-Line
~70% receive 1\textsuperscript{st}-line treatment
• ~25% of Int/High risk myelofibrosis patients are transfusion dependent at diagnosis

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

*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 (Oct 2019) meaningfully enhanced the potential long-term value of momelotinib for Sierra and its stockholders:

- Gilead became 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
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 2\textsuperscript{nd}-line myelofibrosis launched in Q4 2019
- Highly experienced management team with proven track record in drug development
- Strong financial standing:
  - $133.5M in cash and cash equivalents (as of March 31, 2020)
  - Key investors include Vivo Capital, Longitude Capital, OrbiMed and Abingworth
  - Topline data warrant: Expires 75 days post-announcement; Potential ~$34M in additional funding