PRM-151 in Myelofibrosis: Durable Efficacy and Safety at 72 Weeks

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**Hypothesis:**
Reduction of bone marrow fibrosis will restore hematopoiesis and improve cytopenias

- PTX-2 (•) is an endogenous regulator of tissue repair
- PTX-2 binds to damaged tissue (●) and monocytes/macrophages
- PTX-2 prevents and reverses fibrosis in pre-clinical models
- PTX-2 levels are low in MF patients
  - Also low in patients with renal, pulmonary and liver fibrosis
PRM-151G-101 Stage 1 and Extension

27 Patients Enrolled

- Monthly PRM-151 10 mg/kg IV
  - 7 patients
  - 1 PD
  - 1 lack of benefit

- Weekly PRM-151 10 mg/kg IV
  - 8 patients
  - 1 PD
  - 2 deaths

- Monthly PRM-151 10 mg/kg IV + ruxolitinib
  - 6 patients
  - 1 death
  - 1 splenectomy

- Weekly PRM-151 10 mg/kg IV + ruxolitinib
  - 6 patients
  - 1 death

20 Patients completed 24 weeks

- Monthly PRM-151 10 mg/kg IV
  - 5 patients
  - 2 stopped < 72 weeks

- Weekly PRM-151 10 mg/kg IV
  - 5 patients
  - 5 switched to monthly
  - 1 stopped rux

- Monthly PRM-151 10 mg/kg IV + ruxolitinib
  - 6 patients
  - 3 stopped < 72 weeks

- Weekly PRM-151 10 mg/kg IV + ruxolitinib
  - 4 patients
  - 5 switched to monthly
  - 2 stopped < 72 weeks

13 patients completed 72 weeks

- Monthly PRM-151 10 mg/kg IV
  - 9 patients

- Weekly PRM-151 10 mg/kg IV
  - 5 patients

- Monthly PRM-151 10 mg/kg IV + ruxolitinib
  - 4 patients

- Weekly PRM-151 10 mg/kg IV + ruxolitinib
  - 4 patients

- 20 Patients completed 24 weeks

- 13 patients completed 72 weeks

- 24 week treatment period
  - Patients with clinical benefit may continue beyond 24 weeks

- PRM-151 + RUX: stable RUX dose ≥3 months with no decrease in splenomegaly for ≥ 4 weeks

- No eligibility restrictions for anemia, thrombocytopenia, leukopenia, or spleen size
## Patient Demographics (n=13)

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age, Years (range)</td>
<td>60 (51-76)</td>
</tr>
<tr>
<td>Median Years Since Diagnosis (range)</td>
<td>2 (0-9)</td>
</tr>
<tr>
<td>DIPSS Stage(^1) (n, %) Intermediate 1/Intermediate 2</td>
<td>6/7 (46/54)</td>
</tr>
<tr>
<td>Fibrosis Grade by central pathologist s (n, %) MF 3/2/1</td>
<td>5/6/2 (38/46/15)</td>
</tr>
<tr>
<td>Median number of prior therapies (#, range)</td>
<td>2 (0-6)</td>
</tr>
<tr>
<td>Mean weeks since last prior therapy, pts not on rux (#, range)</td>
<td>20 (3-60)</td>
</tr>
<tr>
<td>Prior or current JAK Inhibitor (n, %)</td>
<td>9 (69)</td>
</tr>
<tr>
<td>Mean duration of ongoing RUX, Years (range)</td>
<td>1.5 (0.6-2.2)</td>
</tr>
<tr>
<td>Hgb &lt; 100 g/L (n, %)</td>
<td>5 (38)</td>
</tr>
<tr>
<td>Patients receiving RBC transfusions (n, %)</td>
<td>5 (38)</td>
</tr>
<tr>
<td>Platelets &lt;50 x 10(^9)/L (n, %)</td>
<td>5 (38)</td>
</tr>
<tr>
<td>Platelets &lt; 100 x 10(^9)/L (n, %)</td>
<td>9 (69)</td>
</tr>
<tr>
<td>Patients receiving Platelet transfusions (n, %)</td>
<td>4 (31)</td>
</tr>
<tr>
<td>Patients with palpable spleen (n, %)</td>
<td>10 (77)</td>
</tr>
<tr>
<td>Mean MPN-SAF Total Symptom Score(^2) (#, range)</td>
<td>20 (4-47)</td>
</tr>
</tbody>
</table>

### All Possibly Related Adverse Events Through 72 Weeks (n=13)

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANKLE SWELLING</td>
<td>1</td>
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<td></td>
<td>1</td>
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<tr>
<td>DIARRHEA</td>
<td>1</td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>ANEMIA</td>
<td></td>
<td></td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>COUGH NONPRODUCTIVE</td>
<td>1</td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>HYPERURICEMIA</td>
<td>1</td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>BLURRED VISION</td>
<td>1</td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>FATIGUE</td>
<td>2</td>
<td></td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>TOOTH INFECTION</td>
<td>1</td>
<td></td>
<td></td>
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<tr>
<td>SKIN INFECTION</td>
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<tr>
<td>HSV INFECTION</td>
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<td>1</td>
<td>1</td>
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<tr>
<td>HOT FLASHES</td>
<td>1</td>
<td></td>
<td></td>
<td>1</td>
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<tr>
<td>SWEATING</td>
<td>1</td>
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</tbody>
</table>

6 SAEs in 4 patients - none related: wound infection, multiple fractures, bladder rupture, bowel obstruction, focal pneumonia, and unspecified infection
Bone Marrow Fibrosis Improvement as Measured by WHO Criteria

- Response assessment by central hematopathologists blinded to patient, treatment and time point. WHO MF Response = % of patients with ≥1 grade reduction in MF score at any time point
- Reduction in BM fibrosis was associated with normalization of bone marrow architecture: Normal erythroid clustering, Normal or decreased myeloid:erythroid ratio, Fewer paratrabecular megakaryocytes
Hemoglobin and RBC Transfusions

Patients with baseline Hgb < 100 g/L who completed ≥ 72 weeks (n=5)
Platelets and Platelet Transfusions

Patients with Baseline Platelets < 100 x 10^9/L who completed ≥ 72 weeks (n=9)
Symptom Improvements

MPN-SAF TSS Best % Change from Baseline (n=13)

TSS % Change from Baseline

PRM-151 alone
PRM-151 + RUX

Baseline TSS
Spleen Reductions

Patients with palpable spleen at baseline (n = 10)

Best spleen % Change From Baseline

-120 -100 -80 -60 -40 -20 0

PRM-151 alone

PRM-151 + RUX

*1 patient had no improvement
Conclusions

• 13 patients have completed 72 weeks of PRM-151 treatment

• Reductions in bone marrow fibrosis have been accompanied by
  – Median increase in Hgb in patients with baseline Hgb < 100 g/L
  – Decreased RBC transfusions
  – Median increase in PLT in patients with baseline PLT < 100 x 10^9/L
  – Decreased PLT transfusions
  – > 50% reduction in symptoms in 62% of patients
  – > 50% reduction in splenomegaly in 2 patients on PRM-151 alone

• PRM-151 was well-tolerated
  – 13 related adverse events, 11 Grade 1
  – 6 SAEs, none related
Next Steps

• Stage 2 of this adaptive study is now enrolling:
  • Single agent PRM-151 Q4W x 36 weeks: blinded randomization to 1 of 3 doses
  • Patients may continue beyond 36 weeks in open label extension
  • Eligibility
    – DIPSS Intermediate -1, Intermediate-2, or High Risk
    – WHO Grade 2 or 3 myelofibrosis
  • Patients not candidates for ruxolitinib based on:
    – EITHER Hgb < 100 g/L, requiring ≥ 2 units RBC in prior 12 weeks, and intolerance of or inadequate response to ruxolitinib
    – AND/OR Platelet count < 50 x 10^9/L