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

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PRM-151: Recombinant Human Pentraxin-2 (PTX-2)

- 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

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

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

20 Patients completed 24 weeks

- 5 Patients
- 2 stopped < 72 weeks

13 patients completed 72 weeks

- 9 Patients
- 1 PD
- 5 switched to monthly

- 4 Patients
- 3 stopped < 72 weeks
- 2 stopped < 72 weeks

- 5 switched to monthly
- 1 stopped rux

- 4 Patients
- 5 switched to monthly

- 1 death
- 1 splenectomy

- 1 PD
- 2 deaths

- 1 lack of benefit

- 5 switched to monthly

- 1 stopped rux

- 1 splenectomy

- 1 PD

- 2 deaths

- 1 lack of benefit

- 2 deaths

- 1 PD

- 1 lack of benefit

• 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>
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### 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>
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</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>
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<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>
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<tr>
<td>TOOTH INFECTION</td>
<td>1</td>
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<tr>
<td>SKIN INFECTION</td>
<td>1</td>
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<tr>
<td>HSV INFECTION</td>
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<td>1</td>
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<tr>
<td>HOT FLASHES</td>
<td>1</td>
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<td>1</td>
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<tr>
<td>SWEATING</td>
<td>1</td>
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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)

- Median Hgb (g/L)
- % receiving RBC transfusions

Graph showing changes in median Hgb and percentage of patients receiving RBC transfusions over weeks from baseline to Week 72.
Platelets and Platelet Transfusions

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

- Median PLT (x 10^9/L)
- % pts receiving plt transfusions

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Week 12</th>
<th>Week 24</th>
<th>Week 36</th>
<th>Week 48</th>
<th>Week 60</th>
<th>Week 72</th>
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% of patients with PLT transfusions

Platelets x 10^9/L and
Symptom Improvements

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

Patients with palpable spleen at baseline (n = 10)

Best spleen % Change From Baseline

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 10⁹/L