PSI-7977 PROTON and ELECTRON: 100% Concordance of SVR4 with SVR24 in HCV GT1, GT2 & GT3


Abstract #7

GS-7977 (formerly PSI-7977) is a specific nucleotide analog inhibitor of HCV NS5B

- Safe and well-tolerated in clinical studies
- Once-daily, with or without food
- Potent antiviral activity with broad HCV genotype coverage with or without IFN in treatment-naive patients
  - ELECTRON genotype 2/3: 100% SVR¹
  - ELECTRON genotype 1: 100% RVR²
  - PROTON genotype 1: 91% SVR³
  - PROTON genotype 2/3: 94% SVR⁴
- High barrier to resistance

Background

**Introduction**

- GS-7977 400 mg + peginterferon (PEG) + ribavirin (RBV) provided 91% SVR in treatment-naive patients with genotype 1 HCV infection (PROTON trial)
  - 24-week regimen: 12 weeks GS-7977/PEG/RBV + 12 weeks PEG/RBV

- Given the high response rates, the next objective was to evaluate whether a total of 12 weeks of therapy could achieve the same results.

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**Atomic Study Design**

- **Group A**
  - N = 52
  - GS-7977 + PEG + RBV

- **Group B**
  - N = 125*
  - GS-7977 + PEG + RBV

- **Group C**
  - N = 155†
  - GS-7977 + PEG + RBV

- Patients with HCV genotype 1 were randomized 1:2:3 into 1 of 3 open-label arms.
- Stratified by:
  - IL28B genotype (CC vs non-CC)
  - HCV RNA at screening (≤ vs >800,000 IU/mL)
- HCV RNA analyzed by TaqMan® HCV Test 2.0 (LOD: 15 IU/mL)

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*Of the 125 patients enrolled in Arm B, 16 were genotype 4 or 6.
†5 of the 155 patients were not re-randomized at week 12.

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90% of Patients Achieved SVR12: GS-7977 + PEG/RBV 12-Week Regimen

- 94% of patients in Arm A who reached follow up Week 12 were <LOD

Electron Study Design

- GS-7977 +RBV
- GS-7977 +PEG + RBV
- GS-7977 + PEG + RBV
- GS-7977 + PEG + RBV (GT 2/3 Treatment-Naïve)
- GS-7977 + RBV (GT 1 Null Responders)
- GS-7977 + RBV (GT 1 Treatment-Naïve)
- GS-7977 + RBV (GT 2/3 Treatment-Experienced)

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On Treatment Viral Suppression

- GS-7977 + RBV + PEG for 8 week in GT2/3 naives
- GS-7977 + RBV 12 weeks in GT1 nulls
- GS-7977 + RBV for 12 weeks in GT1 naives
- GS-7977 + RBV for 12 week in GT2/3 experienced

Patients with HCV RNA <LOD Over Time n/N (%)

<table>
<thead>
<tr>
<th></th>
<th>GT 2/3 Treatment-naive 8 wks (n=10)</th>
<th>GT 1 Null Responders 12 wks (n=10)</th>
<th>GT 1 Treatment-naive 12 wks (n=25)</th>
<th>GT 2/3 Treatment-experienced 12 wks (n=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 1</td>
<td>6/10 (60)</td>
<td>1/10 (10)</td>
<td>8/24 (33)</td>
<td>8/25 (32)</td>
</tr>
<tr>
<td>Week 2</td>
<td>10/10 (100)</td>
<td>7/10 (70)</td>
<td>17/24 (71)</td>
<td>21/25 (84)</td>
</tr>
<tr>
<td>Week 4</td>
<td>10/10 (100)</td>
<td>10/10 (100)</td>
<td>25/25 (100)</td>
<td>25/25 (100)</td>
</tr>
<tr>
<td>EOT</td>
<td>10/10 (100)</td>
<td>9/9 (100)</td>
<td>25/25 (100)</td>
<td>21/21 (100)</td>
</tr>
<tr>
<td>SVR 4</td>
<td>10/10 (100)</td>
<td>1/9 (11)</td>
<td>25/25 (88)</td>
<td>12/15 (80)*</td>
</tr>
<tr>
<td>SVR 12</td>
<td>10/10 (100)</td>
<td>Quantum Per protocol 59% SVR 4</td>
<td></td>
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</tr>
</tbody>
</table>

* 1 subject relapsed at the SVR8 time point after having previously achieved SVR4
Patients Included in Analysis (N = 259)

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Week 0</th>
<th>Week 12</th>
<th>Week 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 1</td>
<td>GS-7977 + PEG + RBV</td>
<td>n = 45 (ATOMIC)</td>
<td>GS-7977 ± PEG ± RBV</td>
</tr>
<tr>
<td>Genotype 1</td>
<td>GS-7977 + PEG + RBV</td>
<td>n = 41 (PROTON)</td>
<td>PEG + RBV</td>
</tr>
<tr>
<td>Genotype 2/3</td>
<td>GS-7977</td>
<td>n = 10 (ELECTRON)</td>
<td></td>
</tr>
<tr>
<td>Genotype 2/3</td>
<td>GS-7977 + RBV</td>
<td>n = 10 (ELECTRON)</td>
<td></td>
</tr>
<tr>
<td>Genotype 2/3</td>
<td>GS-7977 + PEG + RBV</td>
<td>n = 51 (ELECTRON, PROTON)</td>
<td></td>
</tr>
</tbody>
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99%-100% Concordance

<table>
<thead>
<tr>
<th></th>
<th>Concordance of SVR4 with SVR12</th>
<th>Concordance of SVR4 with SVR24</th>
</tr>
</thead>
<tbody>
<tr>
<td>All regimens</td>
<td>249/251 (99%)</td>
<td>107/107 (100%)</td>
</tr>
<tr>
<td>Regimens containing PEG</td>
<td>233/235 (99%)</td>
<td>91/91 (100%)</td>
</tr>
<tr>
<td>Regimens not containing PEG</td>
<td>16/16 (100%)</td>
<td>16/16 (100%)</td>
</tr>
</tbody>
</table>

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