**PILOT COMPARATIVE BIOAVAILABILITY STUDY DESIGN**

**Methodology:** Two period, two sequence, cross-over, block randomized pilot study on healthy volunteers in fasting conditions. Hospitalization of subjects until 24 hours post administration.

**Products administered:**
- **TEST:** one film-coated tablet of 35 mg Sodium Risedronate formulation of INSCB – CNRS, Montpellier, France;
- **REFERENCE:** one film-coated tablet of 35 mg, ACTONEL® from Procter & Gamble Pharmaceuticals GmbH.

**Blood samplings:** collected before dose (0.0) and at 0.25, 0.50, 1.00, 2.50, 3.00, 4.50, 5.00, 6.00, 10.00, 12.00, 18.00, 24.00, 48.00 and 168.00 hours post dose, after each administration.

**Statistical methods:**
- **Diagnosis and selection criteria:** Male & female, healthy volunteers, aged 18-45, body mass index within 19-25.75.
- **Dose and mode of administration:** per os one film-coated tablet of 35 mg with 200 ml of low carbonated water.
- **Duration of treatment:** One day per period.
- **Criteria for Evaluation:** Risedronate Chi-square; AUC 0-1 (as primary), T max (as secondary).

**Safety:** Laboratories data / Vital signs / Adverse events

**Statistical methods:**
- **Comparison of pharmacokinetic parameters between Test and Reference:** ANOVA after logarithmic transformation, classic 95% confidence intervals for the intra-individual ratio and Schuirmann two-one sided parametric Test.
- **Test Willson Signed-Rank Test;** T max / AUC test
- **Descriptive statistics:** arithmetic mean, geometric mean, standard deviation, median, range.

---

**RESULTS**

**Pharmacokinetic parameters:**
- **Comparative Bioavailability of BP-ODDS / INSCB Risedronate 35 mg vs ACTONEL® 35 mg.**

**Comparative Bioavailability of the primary parameters (test name: Class I vs. I):**
- **Parameter:** AUC 0-t / AUC 0-inf / C max / T max
- **Statistics:**
  - Test / Reference
  - AUC 0-t
  - AUC 0-inf
  - C max
  - T max

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Test Value</th>
<th>Reference Value</th>
<th>CV (%)</th>
<th>SD 70180</th>
<th>0.130</th>
<th>185129</th>
<th>232037</th>
<th>12.888</th>
<th>69.712</th>
<th>63.163</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC 0-t</td>
<td>23737.630</td>
<td>218.0</td>
<td>10.7</td>
<td>651.240</td>
<td>0.000</td>
<td>63013.69</td>
<td>803333.08</td>
<td>27.070</td>
<td>358.407</td>
<td>519.256</td>
</tr>
<tr>
<td>AUC 0-inf</td>
<td>63013.69</td>
<td>218.0</td>
<td>10.7</td>
<td>651.240</td>
<td>0.000</td>
<td>63013.69</td>
<td>803333.08</td>
<td>27.070</td>
<td>358.407</td>
<td>519.256</td>
</tr>
<tr>
<td>C max</td>
<td>3529.70</td>
<td>218.0</td>
<td>10.7</td>
<td>651.240</td>
<td>0.000</td>
<td>63013.69</td>
<td>803333.08</td>
<td>27.070</td>
<td>358.407</td>
<td>519.256</td>
</tr>
<tr>
<td>T max</td>
<td>46.00</td>
<td>218.0</td>
<td>10.7</td>
<td>651.240</td>
<td>0.000</td>
<td>63013.69</td>
<td>803333.08</td>
<td>27.070</td>
<td>358.407</td>
<td>519.256</td>
</tr>
</tbody>
</table>

**Comparative coefficients of variation (CV) of the primary pharmacokinetic parameters**
- **Parameter:** Test / Reference
- | Test Value | Reference Value | CV (%) |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC 0-t</td>
<td>100.00</td>
<td>100.00</td>
</tr>
<tr>
<td>AUC 0-inf</td>
<td>100.00</td>
<td>100.00</td>
</tr>
<tr>
<td>C max</td>
<td>100.00</td>
<td>100.00</td>
</tr>
<tr>
<td>T max</td>
<td>100.00</td>
<td>100.00</td>
</tr>
</tbody>
</table>

**SAFETY:** no serious adverse events.

---

**CONCLUSION**

**The film coated tablet of Bisphosphonate Osteotropic Drug Delivery System (BP-ODDS) developed by INSCB is supra-bioavailable when compared to the reference marketed product Actonel® with a factor ranging from 300 % for the AUC to a factor of almost 500 % for C max.**

**BP-ODDS tablets or capsules offer an alternative route of administration to bisphosphonate products currently marketed, covering an unmet need for oral bisphosphonates in oncology. BP-ODDS is an effective and potentially safer alternative to bisphosphonate intravenous infusions which could offer the following advantages:**

- Improved quality of life
- Flexibility in the dosing regimen
- Improved compliance