RBP-6000 BUPRENORPHINE MONTHLY DEPOT DEMONSTRATES EFFICACY, SAFETY AND EXPOSURE-RESPONSE RELATIONSHIP IN OPIOID USE DISORDER

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RBP-6000 is an investigational new drug, not currently authorized for marketing for any indication.
BACKGROUND

- To achieve opioid blockade
  - from the first dose of treatment and across the entire monthly dosing interval
  - at buprenorphine concentrations that are well-tolerated

- To achieve abstinence and clinically significant control of craving and withdrawal symptoms

- To make abuse and diversion more difficult

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PHASE 3 STUDY (RB-US-13-0001) DESIGN

**Randomization**
(n= 504)

**Screening**

- Induction: 3 days 2-24mg SL

- Stabilization: 4 – 11 days 8-24mg SL

**Treatment Period:**
- 6 double-blind subcutaneous injections
- Weekly urine drug screens and self-reports
- Weekly individualized counseling (IDC)

1. **RBP-6000 300 mg x 2 months/100 mg x 4 months + IDC** (194 subjects)

2. **RBP-6000 300 mg + IDC x 6 months** (196 subjects)

3. **Placebo + IDC x 6 months** (99 subjects, volume-matched equivalent)

**Follow Up**
(option to roll into safety extension)

Week 24/25

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PHASE 3 PRIMARY & SECONDARY ENDPOINTS

**Primary:** CDF of % urine samples negative for opioids + negative self-reports of illicit opioid use (Weeks 5 to 24)

**Key secondary:** ≥80% of urine samples negative for opioids + negative self-reports of illicit opioid use (Weeks 5 to 24)

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*P<0.0001 vs. placebo
Mean COWS (LOCF)

Mean Opiate Craving VAS (LOCF)

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ASSOCIATION BETWEEN PLASMA CONCENTRATIONS OF BUPRENORPHINE, PREDICTED MU-OPIOID RECEPTOR OCCUPANCY AND CLINICAL ENDPOINTS

<table>
<thead>
<tr>
<th>Dose Group</th>
<th>N</th>
<th>C_{min} (ng/mL)</th>
<th>C_{max} (ng/mL)</th>
<th>C_{avg} (ng/mL)</th>
<th>μORO (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>300 mg/100 mg</td>
<td>194</td>
<td>2.74</td>
<td>4.11</td>
<td>3.14</td>
<td>75</td>
</tr>
<tr>
<td>300 mg/300 mg</td>
<td>196</td>
<td>5.11</td>
<td>8.68</td>
<td>6.32</td>
<td>83</td>
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</tbody>
</table>

* Predicted whole brain μ-Opioid Receptor Occupancy corresponding to C_{avg}

Abstinence Rate (Day 169) in Users by Injectable Route

- 300 mg/100 mg: 53%
- 300 mg/300 mg: 69%

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79th Annual Scientific Meeting of the College on Problems of Drug Dependence (CPDD) Meeting, Montreal June 17th-22nd, 2017
SAFETY RESULTS

- No new or unexpected safety findings; generally well-tolerated
- No serious injection site reactions
- 1 subject discontinued treatment due to injection site reaction

<table>
<thead>
<tr>
<th>Occurrence (%)</th>
<th>Placebo + IDC (n=100)</th>
<th>RBP-6000 300/100 mg + IDC (n=203)</th>
<th>RBP-6000 300/300 mg + IDC (n=201)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any TEAE</td>
<td>56.0</td>
<td>76.4</td>
<td>66.7</td>
</tr>
<tr>
<td>Serious TEAE</td>
<td>5.0</td>
<td>2.0</td>
<td>3.5</td>
</tr>
<tr>
<td>TEAE leading to discontinuation</td>
<td>2.0</td>
<td>3.4</td>
<td>5.0</td>
</tr>
<tr>
<td>Any injection site TEAE</td>
<td>9.0</td>
<td>13.8</td>
<td>18.9</td>
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<tr>
<td>Serious injection site TEAE</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Injection site TEAE leading to discontinuation</td>
<td>0</td>
<td>0</td>
<td>0.5</td>
</tr>
</tbody>
</table>

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SUMMARY

- Both dosage regimens of RBP-6000 showed statistically significant differences in percentage abstinence and treatment success vs. placebo.
- Treatment outcomes were consistent across other clinical endpoints including control of craving and withdrawal symptoms.
- Results from the exposure-response analyses predicted a relationship between buprenorphine plasma concentration, predicted whole brain mu-opioid receptor occupancy, abstinence and opioid craving.
- Buprenorphine plasma concentration ≥ 2 ng/mL and mu-opioid receptor occupancy ≥ 70% were observed from the first dose of RBP-6000.
- The safety profile of RBP-6000 was consistent with the known profile of transmucosal buprenorphine, with no unexpected safety findings. Injection site reactions were not treatment-limiting.