### Supplementary Material

#### Supplementary Table 1. Changes in vital sign parameters between baseline and the half-day laboratory classroom visit (safety analysis population).

| Parameter                        | PRC-063 dose |
|----------------------------------|--------------|
|                                  | 25 mg/day (N=5) | 35 mg/day (N=9) | 45 mg/day (N=30) | 55 mg/day (N=61) | 70 mg/day (N=59) | 85 mg/day (N=43) | 100 mg/day (N=32) | All doses (N=239) |
| Weight (kg)                      |              |                |                  |                  |                  |                  |                  |                   |
| Mean                             | +0.82        | -0.34          | -1.02            | -0.57            | -1.36            | -0.59            | -1.80            | -0.95             |
| Standard deviation               | 2.21         | 2.45           | 2.66             | 2.32             | 4.00             | 1.63             | 2.55             | 2.83             |
| Systolic blood pressure (mmHg)   |              |                |                  |                  |                  |                  |                  |                   |
| Mean                             | +2.2         | +6.8           | +2.1             | +5.0             | +3.6             | +4.8             | +2.4             | +3.9              |
| Standard deviation               | 10.13        | 12.08          | 10.52            | 10.90            | 11.36            | 10.05            | 9.73             | 10.64             |
| Diastolic blood pressure (mmHg)  |              |                |                  |                  |                  |                  |                  |                   |
| Mean                             | +4.2         | +6.9           | +3.0             | +3.5             | +3.3             | +2.2             | +4.7             | +3.4              |
| Standard deviation               | 9.23         | 4.83           | 7.43             | 8.52             | 8.73             | 6.81             | 6.65             | 7.79              |
| Heart rate (beats/min)           |              |                |                  |                  |                  |                  |                  |                   |
| Mean                             | -5.0         | +4.7           | +7.8             | +3.1             | +3.2             | +0.8             | +4.8             | +3.4              |
| Standard deviation               | 4.58         | 12.79          | 9.78             | 12.30            | 9.79             | 11.34            | 11.17            | 11.12             |
**Supplementary Table 2.** Clinically significant vital sign and electrocardiogram abnormalities during the open-label dose-optimization period and the double-blind treatment period (safety analysis population).

| Vital signs, n (%) | 25 mg/day | 35 mg/day | 45 mg/day | 55 mg/day | 70 mg/day | 85 mg/day | 100 mg/day | All doses | Placebo |
|-------------------|-----------|-----------|-----------|-----------|-----------|-----------|------------|----------|---------|
| **Open-label dose-optimization period** |           |           |           |           |           |           |            |          |         |
| Weight decreased  | 1 (0.4)   | 1 (0.4)   | 1 (0.4)   | 1 (0.5)   | 0         | 0         | 0          | 4 (1.4)  | –       |
| Heart rate increased | 0        | 1 (0.4)   | 3 (1.2)   | 1 (0.5)   | 0         | 0         | 0          | 5 (1.8)  | –       |
| Systolic blood pressure increased | 0        | 0         | 1 (0.4)   | 1 (0.5)   | 0         | 0         | 0          | 2 (0.7)  | –       |
| Diastolic blood pressure increased | 3 (1.1) | 1 (0.4)   | 2 (0.8)   | 0         | 0         | 0         | 0          | 6 (2.1)  | –       |
| **Double-blind treatment period** |           |           |           |           |           |           |            |          |         |
| Heart rate increased | 0        | 0         | 0         | 0         | 0         | 0         | 0          | 0         | 1 (0.8) |
| Systolic blood pressure increased | 0        | 0         | 0         | 0         | 0         | 0         | 0          | 0         | 1 (0.8) |
| Blood pressure increased | 0        | 0         | 0         | 0         | 0         | 1 (4.5)   | 0          | 1 (0.8)  | 0       |
| **Electrocardiogram, n (%)** |           |           |           |           |           |           |            |          |         |
| **Open-label dose-optimization period** |           |           |           |           |           |           |            |          |         |
| Tachycardia        | 0         | 2 (0.7)   | 0         | 1 (0.5)   | 2 (1.3)   | 1 (1.2)   | 0          | 6 (2.1)  | –       |
| Palpitations       | 1 (0.4)   | 0         | 1 (0.4)   | 1 (0.5)   | 0         | 0         | 0          | 3 (1.1)  | –       |
| Bradycardia        | 0         | 0         | 0         | 0         | 0         | 1 (1.2)   | 0          | 1 (0.4)  | –       |
| Sinus tachycardia  | 0         | 0         | 0         | 0         | 1 (0.6)   | 0         | 0          | 1 (0.4)  | –       |

*There were no clinically significant electrocardiogram abnormalities during the double-blind treatment period.