Single Ascending Dose Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of Sutezolid in Healthy Adult Subjects

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Supplementary Materials

Supplementary Table S1: Plasma Pharmacokinetic Parameters of PNU-101244

| Parameter            | Cohort 1: (300 mg) | Cohort 2: (600 mg) | Cohort 3: (1200 mg) | Cohort 4: (1800 mg) |
|----------------------|--------------------|--------------------|---------------------|---------------------|
|                      | n  | Mean | SD    | CV%        | n  | Mean | SD    | CV%        | n  | Mean | SD    | CV%        | n  | Mean | SD    | CV%        |
| T_max (h)            | 6  | 2.51 | 0.85  | 33.65      | 6  | 3.17 | 1.17  | 36.92      | 6  | 2.09 | 1.16  | 55.44      | 6  | 3.25 | 1.33  | 40.99      |
| C_max (ng/mL)        | 6  | 24.5 | 7.84  | 31.97      | 6  | 46.9 | 15.8  | 33.59      | 6  | 55.8 | 8.40  | 15.04      | 6  | 85.0 | 33.7  | 39.66      |
| AUClast (h*ng/mL)    | 6  | 117  | 52.7  | 44.95      | 6  | 263  | 142   | 54.23      | 6  | 402  | 129   | 32.18      | 6  | 877  | 262   | 29.94      |
| AUCint (h*ng/mL)     | 3  | 219  | 80.8  | 36.86      | 6  | 330  | 169   | 51.31      | 5  | 562  | 292   | 51.99      | 3  | 1250 | 354   | 28.27      |
| AUCExtrap (%)        | 3  | 42.9 | 23.5  | 54.83      | 6  | 21.3 | 5.95  | 27.95      | 5  | 26.3 | 13.8  | 52.63      | 3  | 17.4 | 4.70  | 27.00      |
| λz (h⁻¹)            | 3  | 0.189| 0.109 | 57.77      | 6  | 0.238| 0.0741| 31.08      | 5  | 0.154| 0.125 | 81.02      | 3  | 0.0596| 0.0315| 52.74      |
| T1/2 (h)             | 3  | 4.91 | 3.37  | 68.73      | 6  | 3.18 | 1.11  | 35.05      | 5  | 10.6 | 10.5  | 98.87      | 3  | 13.6 | 5.57  | 41.04      |
| T_last (h)           | 6  | 7.17 | 2.64  | 36.83      | 6  | 8.67 | 2.73  | 31.53      | 6  | 14.6 | 3.72  | 25.49      | 6  | 14.3 | 3.49  | 24.48      |
| C_last (ng/mL)       | 6  | 14.6 | 3.72  | 25.49      | 6  | 14.6 | 3.72  | 25.49      | 6  | 14.6 | 3.72  | 25.49      | 6  | 14.6 | 3.72  | 25.49      |
Supplementary Table S2: Assessment of Dose Proportionality of PNU-101603 Following Single Dose Administration of Sutezolid

| Dependent Variable | Model Variable | Estimate (β1) | Lower CI<sup>a</sup> | Upper CI<sup>a</sup> | Rho<sub>1</sub><sup>b</sup> |
|-------------------|----------------|--------------|----------------------|----------------------|------------------|
| ln(C<sub>max</sub>) | ln(Dose)       | 0.7217       | 0.5875               | 0.8559               | 2.0087           |
| ln(AUC<sub>last</sub>) | ln(Dose)       | 1.0183       | 0.9071               | 1.1294               | 9.2440           |
| ln(AUC<sub>inf</sub>) | ln(Dose)       | 1.0559       | 0.9334               | 1.1783               | 5.0193           |

Power Model: ln(PK)=ln(β<sub>0</sub>)+β<sub>1</sub>*ln(Dose)+ε, where PK is the pharmacokinetic parameter tested, ln(β<sub>0</sub>) is the y-intercept, β<sub>1</sub> is the slope, and ε is an error term.

<sup>a</sup> 90% confidence intervals (lower and upper).

<sup>b</sup> High/low dose ratio in which dose proportionality can be demonstrated definitely, relative to the lowest dose in the analysis dataset. Rho<sub>1</sub> was calculated as: Rho<sub>1</sub>=(Θ<sub>hl</sub>)<sup>(1/max(1-lower, upper-1))</sup>, in which Θ<sub>hl</sub>=1.333.

Supplementary Table S3: Assessment of Dose Proportionality of PNU-101244 Following Single Dose Administration of Sutezolid

| Dependent Variable | Model Variable | Estimate (β1) | Lower CI<sup>a</sup> | Upper CI<sup>a</sup> | Rho<sub>1</sub><sup>b</sup> |
|-------------------|----------------|--------------|----------------------|----------------------|------------------|
| ln(C<sub>max</sub>) | ln(Dose)       | 0.6348       | 0.4726               | 0.7970               | 1.7254           |
| ln(AUC<sub>last</sub>) | ln(Dose)       | 1.0811       | 0.8575               | 1.3046               | 2.5714           |
| ln(AUC<sub>inf</sub>) | ln(Dose)       | 0.9081       | 0.5601               | 1.2561               | 1.9233           |

Power Model: ln(PK)=ln(β<sub>0</sub>)+β<sub>1</sub>*ln(Dose)+ε, where PK is the pharmacokinetic parameter tested, ln(β<sub>0</sub>) is the y-intercept, β<sub>1</sub> is the slope, and ε is an error term.

<sup>a</sup> 90% confidence intervals (lower and upper).

<sup>b</sup> High/low dose ratio in which dose proportionality can be demonstrated definitely, relative to the lowest dose in the analysis dataset. Rho<sub>1</sub> was calculated as: Rho<sub>1</sub>=(Θ<sub>hl</sub>)<sup>(1/max(1-lower, upper-1))</sup>, in which Θ<sub>hl</sub>=1.333.
Supplementary Figure S1: Individual concentration-versus-time profiles, linear scale.

Supplementary Figure S2: Individual concentration-versus-time profiles, log scale.