

# 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                             | <b>Cohort 1:<br/>(300 mg)</b>  |       |       |       | <b>Cohort 2:<br/>(600 mg)</b>  |        |        |       |
|---------------------------------------|--------------------------------|-------|-------|-------|--------------------------------|--------|--------|-------|
|                                       | n                              | Mean  | SD    | CV%   | n                              | Mean   | SD     | CV%   |
| <b>T<sub>max</sub> (h)</b>            | 6                              | 2.51  | 0.85  | 33.65 | 6                              | 3.17   | 1.17   | 36.92 |
| <b>C<sub>max</sub> (ng/mL)</b>        | 6                              | 24.5  | 7.84  | 31.97 | 6                              | 46.9   | 15.8   | 33.59 |
| <b>AUC<sub>last</sub> (h*ng/mL)</b>   | 6                              | 117   | 52.7  | 44.95 | 6                              | 263    | 142    | 54.23 |
| <b>AUC<sub>inf</sub> (h*ng/mL)</b>    | 3                              | 219   | 80.8  | 36.86 | 6                              | 330    | 169    | 51.31 |
| <b>AUC<sub>Extrap</sub> (%)</b>       | 3                              | 42.9  | 23.5  | 54.83 | 6                              | 21.3   | 5.95   | 27.95 |
| <b>λ<sub>z</sub> (h<sup>-1</sup>)</b> | 3                              | 0.189 | 0.109 | 57.77 | 6                              | 0.238  | 0.0741 | 31.08 |
| <b>T<sub>1/2</sub> (h)</b>            | 3                              | 4.91  | 3.37  | 68.73 | 6                              | 3.18   | 1.11   | 35.05 |
| <b>T<sub>last</sub> (h)</b>           | 6                              | 7.17  | 2.64  | 36.83 | 6                              | 8.67   | 2.73   | 31.53 |
| <b>C<sub>last</sub> (ng/mL)</b>       | 6                              | 14.6  | 3.72  | 25.49 | 6                              | 14.3   | 3.49   | 24.48 |
| Parameter                             | <b>Cohort 3:<br/>(1200 mg)</b> |       |       |       | <b>Cohort 4:<br/>(1800 mg)</b> |        |        |       |
|                                       | n                              | Mean  | SD    | CV%   | n                              | Mean   | SD     | CV%   |
| <b>T<sub>max</sub> (h)</b>            | 6                              | 2.09  | 1.16  | 55.44 | 6                              | 3.25   | 1.33   | 40.99 |
| <b>C<sub>max</sub> (ng/mL)</b>        | 6                              | 55.8  | 8.40  | 15.04 | 6                              | 85.0   | 33.7   | 39.66 |
| <b>AUC<sub>last</sub> (h*ng/mL)</b>   | 6                              | 402   | 129   | 32.18 | 6                              | 877    | 262    | 29.94 |
| <b>AUC<sub>inf</sub> (h*ng/mL)</b>    | 5                              | 562   | 292   | 51.99 | 3                              | 1250   | 354    | 28.27 |
| <b>AUC<sub>Extrap</sub> (%)</b>       | 5                              | 26.3  | 13.8  | 52.63 | 3                              | 17.4   | 4.70   | 27.00 |
| <b>λ<sub>z</sub> (h<sup>-1</sup>)</b> | 5                              | 0.154 | 0.125 | 81.02 | 3                              | 0.0596 | 0.0315 | 52.74 |
| <b>T<sub>1/2</sub> (h)</b>            | 5                              | 10.6  | 10.5  | 98.87 | 3                              | 13.6   | 5.57   | 41.04 |
| <b>T<sub>last</sub> (h)</b>           | 6                              | 16.7  | 8.16  | 48.99 | 6                              | 29.3   | 6.41   | 21.85 |
| <b>C<sub>last</sub> (ng/mL)</b>       | 6                              | 11.9  | 1.27  | 10.69 | 6                              | 11.8   | 1.56   | 13.21 |

**Supplementary Table S2: Assessment of Dose Proportionality of PNU-101603 Following Single Dose Administration of Sutezolid**

| Dependent Variable       | Model Variable | Estimate ( $\beta_1$ ) | Lower CI <sup>a</sup> | Upper CI <sup>a</sup> | Rho1 <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:  $\ln(\text{PK}) = \ln(\beta_0) + \beta_1 * \ln(\text{Dose}) + \varepsilon$ , where PK is the pharmacokinetic parameter tested,  $\ln(\beta_0)$  is the y-intercept,  $\beta_1$  is the slope, and  $\varepsilon$  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:  $\text{Rho}_1 = (\Theta_H)^{1/\max(1-\text{lower}, \text{upper}-1)}$ , in which  $\Theta_H = 1.333$ .

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

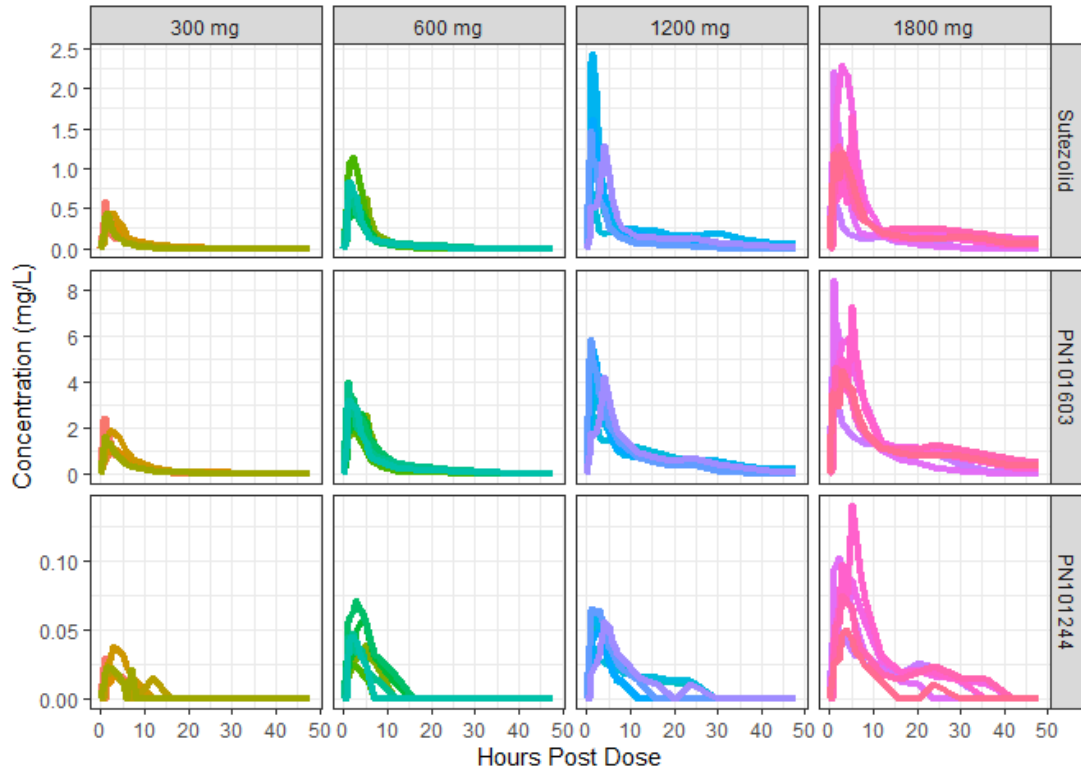
| Dependent Variable       | Model Variable | Estimate ( $\beta_1$ ) | Lower CI <sup>a</sup> | Upper CI <sup>a</sup> | Rho1 <sup>b</sup> |
|--------------------------|----------------|------------------------|-----------------------|-----------------------|-------------------|
| ln(C <sub>max</sub> )    | 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:  $\ln(\text{PK}) = \ln(\beta_0) + \beta_1 * \ln(\text{Dose}) + \varepsilon$ , where PK is the pharmacokinetic parameter tested,  $\ln(\beta_0)$  is the y-intercept,  $\beta_1$  is the slope, and  $\varepsilon$  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:  $\text{Rho}_1 = (\Theta_H)^{1/\max(1-\text{lower}, \text{upper}-1)}$ , in which  $\Theta_H = 1.333$ .

**Supplementary Figure S1: Individual concentration-versus-time profiles, linear scale.**



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

