

## Supplemental Materials

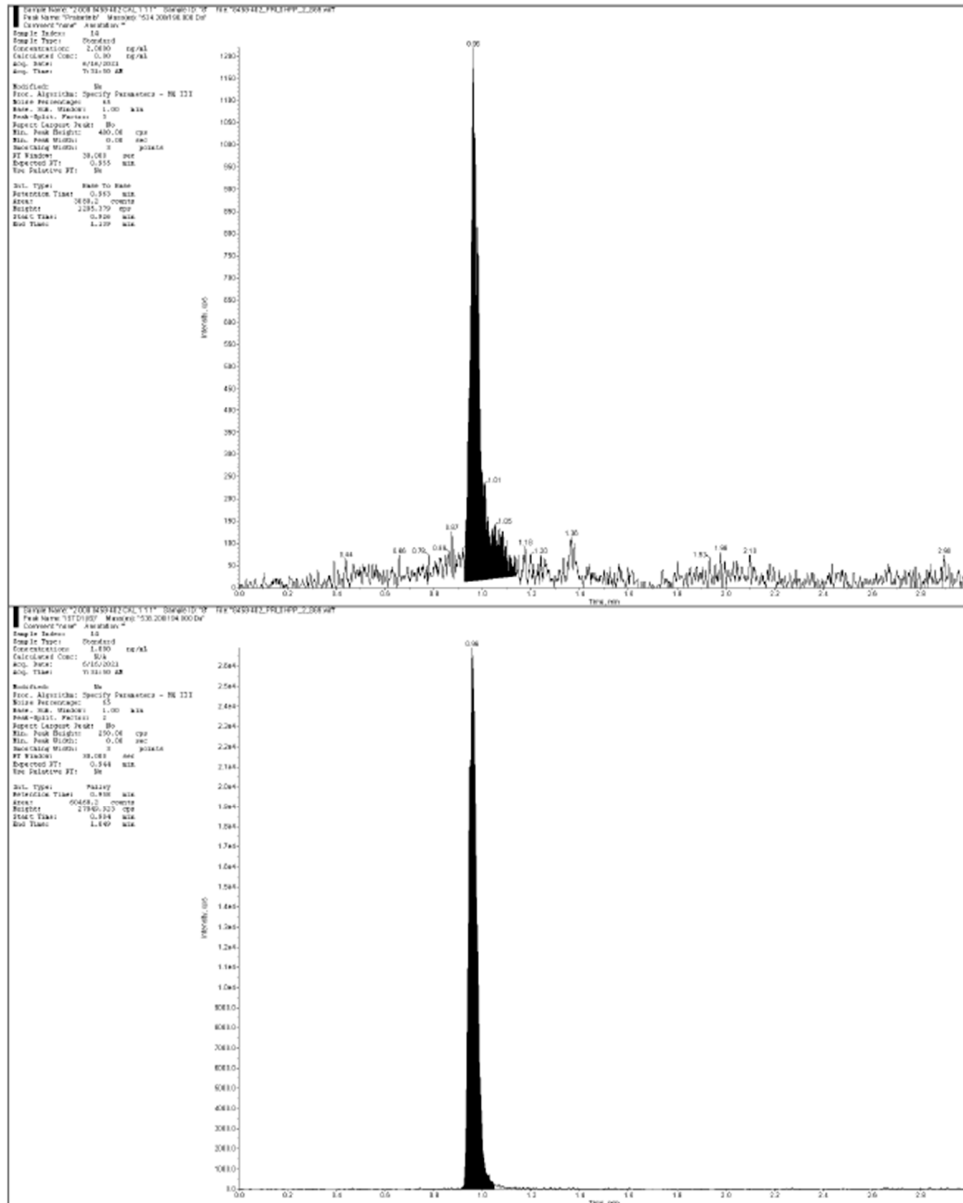
### Supplementary Material S1: Details on validated liquid chromatography-tandem mass spectrometry assay to measure the concentration of pralsetinib in human plasma.

- Curve range: 2.00 (LLOQ) to 2000 (ULOQ) ng/mL.
- Inter-Assay Accuracy (%Bias): 1.3% to 5.0%
- Inter-Assay Precision (%RSD): 4.5% to 8.9%
- Matrix effect:

| Nominal con. of 2 ng/mL, 6 individual blank matrix spiked at the LLOQ level |      |      |      |      |      |      |
|---|------|------|------|------|------|------|
| Result (ng/mL)  | 1.84 | 2.06 | 1.97 | 1.66 | 1.88 | 1.94 |
| Bias (%)  | -8   | 3    | -1.5 | -17  | -6   | -3   |

- Recovery: LQC: 84.9%,  
LMQC: 83.3%,  
MQC: 90.5%,  
HQC: 84.1%
- Matrix bench-top stability: 24 hours at room temperature
- Matrix free-thaw stability: 5 cycles at -10°C to -30°C, 5 cycles at -60°C to -80°C.
- Matrix frozen stability: 750 days at -10°C to -30°C, 750 days at -60°C to -80°C.

- Representative chromatograms:





### Chromatogram of a 2000 ng/mL Calibration Standard (Upper Limit of Quantification)





**Figure S1. Regression analysis of pralsetinib pharmacokinetic parameters. Scatterplots of total AUC<sub>0-∞</sub> (A), C<sub>max</sub> (B), unbound AUC<sub>0-∞</sub> (C), unbound C<sub>max</sub> (D) versus screening Child-Pugh total score are presented.** There was no evidence of a relationship between total and unbound AUC and C<sub>max</sub>. The Spearman's ranks coefficient indicated very weak correlations between total and unbound AUC or C<sub>max</sub> and Child-Pugh total score. Additionally, the p-values for the slopes ranged from 0.35 to 0.90.

