

**Supplementary File S4:** Representative ion chromatograms of ibrutinib (IBR), dihydrodiol ibrutinib (DIB), and their respective internal standards  $^2\text{H}_5$ -ibrutinib ( $^2\text{H}_5$ -IBR) and  $^2\text{H}_5$ -dihydrodiol ibrutinib ( $^2\text{H}_5$ -DIB). (A), IBR in the level 1 calibration sample (2.27 nmol/L), (B)  $^2\text{H}_5$ -IBR in the level 1 calibration sample, (C) IBR in a blank sample, (D)  $^2\text{H}_5$ -IBR in a blank sample, (E) DIB in the level 1 calibration sample (2.11 nmol/L), (F)  $^2\text{H}_5$ -DIB in the level 1 calibration sample, (G) DIB in a blank sample, (H)  $^2\text{H}_5$ -DIB in a blank sample.

