Schematic Example Observe Observe Cp Simulate > Predict another dosing Observe Observe body weight 2. Input Predict energy Predict estimation intake Observe Predict Observe biophase receptor Predict Observe Observe dose occupancy conc. 3. Estimate unobserved state

Supplementary Figure 6. Fundamental operations on model representations of the biomarker chain. The AZD1979 case study considers two fundamental computational operations on model representations of the biomarker chain: traditional forward simulation and input estimation. By complementing these two operations with estimation of an unobserved biomarker causally preceded and followed by observed biomarkers, a set of three fundamental computational operations is established. We believe that user-friendly software tools for these three operations constitute one important factor for improving quality and increasing speed in the data analysis of drug discovery programmes.