**Supplemental digital content 3: NONMEM code for the model differential equations**

The following text is the model equations and differential equations from the NONMEM control file to describe the model. Variable naming is not exactly the same as in the manuscript.

ABP-700 differential equations

KDP=QCO/VD ; abp-700 from depot to arterial

KAD=(QP1+QP2+QND)/VA ; abp-700 arterial to distribution

KCO=QCO/VV ; abp-700 venous to arterial

KA0=CL/VA ; abp-700 arterial clearance

KND=QND/VA ; abp-700 art/ven nondistributive

KAP1=QP1/VA ; abp-700 arterial to periph1

KAP2=QP2/VA ; abp-700 arterial to periph2

KP1V=QP1/VP1 ; abp-700 periph1 to venous

KP2V=QP2/VP2 ; abp-700 periph2 to venous

Metabolite differential equations are prefixed with M

MKDP ; metabolite from depot to arterial

MKAD=(MQP1+MQND)/MVA ; metabolite arterial to distribution

MKCO=MQCO/MVV ; metabolite venous to arterial

MKA0=MCL/MVA ; metabolite arterial clearance

MKND=MQND/MVA ; metabolite art/ven nondistributive

MKAP1=MQP1/MVA ; metabolite arterial to periph1

MKP1V=MQP1/MVP1 ; metabolite periph1 to venous

MRATI=300.31/350.80 ; mass ratio due to different molecular weights

Full model differential equations

DADT(1) = -KDP\*A(1) ; abp-700 depot

DADT(2) = -KAD\*A(2) +KCO\*A(3) +KDP\*A(1) -KA0\*A(2) ; abp-700 arterial

DADT(3) = -KCO\*A(3) +KP1V\*A(4) +KP2V\*A(5) +KND\*A(2) ; abp-700 venous

DADT(4) = KAP1\*A(2) -KP1V\*A(4) ; abp-700 periph 1

DADT(5) = KAP2\*A(2) -KP2V\*A(5) ; abp-700 periph 2

DADT(6) = -MKDP\*A(6) +KA0\*A(2)\*MRATI ; metabolite depot

DADT(7) = -MKAD\*A(7) +MKCO\*A(8) +MKDP\*A(6)-MKA0\*A(7) ; metabolite arterial

DADT(8) = -MKCO\*A(8) +MKP1V\*A(9) +MKND\*A(7) ; metabolite venous

DADT(9) = MKAP1\*A(7) -MKP1V\*A(9) ; metabolite periph 1

DAPRED=A(2)/VA ; Arterial concentration

DADT(10) = KE0\*(DAPRED - A(10)) ; BIS suppression effect site

DADT(11) = KE2\*(DAPRED - A(11)) ; BIS excitation effect site

DADT(12) = KEM\*(DAPRED - A(12)) ; MOAAS effect site

Observable concentrations

AAPRED=A(2)/VA ; abp-700 arterial concentration

AVPRED=A(3)/VV ; abp-700 venous concentration

MAPRED=A(7)/MVA ; metabolite arterial concentration

MVPRED=A(8)/MVV ; metabolite venous concentration