Table S1: List of PK studies of IGIV and anti-D Ig performed in pregnant women

Autor/Reference	Number of subjects	Gestational age (Wks) at first dosing	Body weight (Kg)	Route & Dose	PK sampling	Product name
Ensom et al. 2011[26]	12	First trimester	60.3-87	IV; 0.5-1 g/kg	4 post-dose samples	Gamimune or Gamunex
Ensom et al. 2011[26]	10	Second trimester	64.2- 77.2	IV;0.5-1 g/kg	4 post-dose samples	Gamimune or Gamunex
Sidiropoulos et al.1986[11]	11	Second trimester	Estimated*	IV; 1x12 gm and 5x24 gm	One sample	Sandoglobulin
Sidiropoulos et al.1986[11]	16	Third trimester	Estimated*	IV; 1x12 gm & 5x24 gm	One sample	Sandoglobulin
Bichler et al. 2003[25]	14	Third trimester	71.2	IV & IM; 300 ug	Extensive	Anti-D IgG (Rhophylac)
MacKenzie et al. 2006[28]	43	Third trimester	68.8-74.2	IM: 100 ug	Extensive	Anti-D IgG
Tiblad et al. 2012[27]	16	Third trimester	80.1	IM; 250 ug	Extensive	Anti-D IgG (Rhesonativ)

*Estimated using body weight equations based on the gestational weeks of pregnancy (Abduljalil et al. 2012)[34]

Table S2: Equations used for development of minimal PBPK Model

Equation	Initial condition
$\frac{dCp}{dt}$=[Clymph · L – Cp · L1 · (1 –σ1) – Cp · L2 · (1 –σ2) – Cp · CLp]/Vp	Cp(0)= Dose/Vp

$\frac{dCtight}{dt}$=[Cp · L1 · (1 −σ1) − Ctight · L1 · (1 −σL)]/Vtight	Ctight(0)=0
$\frac{dCleaky}{dt}$=[Cp · L2 · (1 −σ2) − Cleaky · L2 · (1 −σL)]/Vleaky	Cleaky(0)=0
$\frac{dClymph}{dt}$=[Ctight · L1 · (1 −σL) + Cleaky · L2 · (1 −σL) − Clymph · L]/Vlymph	Clymph(0)=0

;where C_p is IgG concentration in V_p (plasma volume), C_{tight} and C_{leaky} are antibodies interstitial fluids (ISF) concentrations in tissues tight (V_{tight}) and leaky (V_{leaky}). The pregnancy related physiological compartments such as placenta and fetus are incorporated in the leaky compartment of the mPBPK model. The The L is total lymph flow equal to the sum of L_1 and L_2, the lymph flow for V_{tight} and V_{leaky}. The σ1 and σ2 are vascular reflection coefficients for V_{tight} and V_{leaky}. The σL is the lymphatic capillary reflection coefficient, which is assumed to be 0.2.

Table S3: Parameters used for development and evaluation of mPBPK model for Anti-D IgG in pregnant women

	Parameters for pregnant women in third trimester
Plasma volume (L)	3.67
Leaky tissue volume (L)	4.37*(BW/70)
Tight tissue volume (L)	8.11*(BW/70)
Lymph volume (L)	5.2*(BW/70)
Total lymph flow (L/ day)	2.9*(BW/70)
Lymphatic capillary reflection coefficient	0.2
Vascular reflection coefficient*	σ_1= 0.99 σ_2= 0.81
Clearance (L/day)	0.259*(BW/70)^0.75

*σ_1 & σ_2 indicate reflection coefficient of tight and leaky tissues, respectively.

The reflection coefficients and clearance are estimated with %CV <10% using PK data of anti-D Ig following intravenous administration in pregnant women (Bichler et al. 2003)[25].

Figure S1: Schematic representation of the minimal PBPK (mPBPK) model framework, including model inputs and outputs used for characterizing the pharmacokinetics of IGIV and anti-D Ig in nonpregnant and pregnant women. The mPBPK model categorizes tissues into leaky compartments (liver, kidney, heart, and other highly vascularized organs) and tight compartments (muscle, skin, adipose tissue, and brain) based on vascular permeability characteristics. For pregnancy applications, placenta and fetus were incorporated into the leaky tissue compartment to account for pregnancy-related physiological changes.

Model Input

- Physiology
- Biochemical
- Dosing

Model Output

- Conc. vs time
- PK parameters
- Dosing optimization

