Supplementary Information (SI) for Journal of Materials Chemistry B.

Supporting Information for:

A Macrocyclic Gadolinium Contrast Agent Bearing Assembly-dissociable Feature with albumin for Enhanced Magnetic Resonance Imaging and in-vivo Profiles

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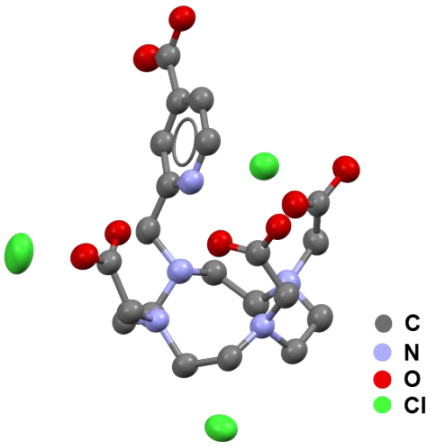

Figure S1. Single crystal X-ray diffraction study of the ligand.

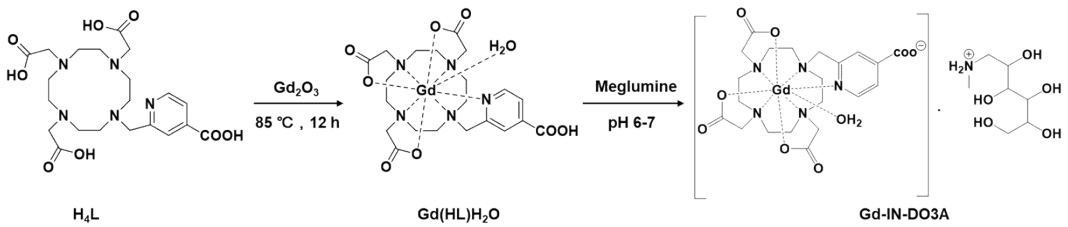

Figure S2. Synthetic route of Gd-IN-DO3A.

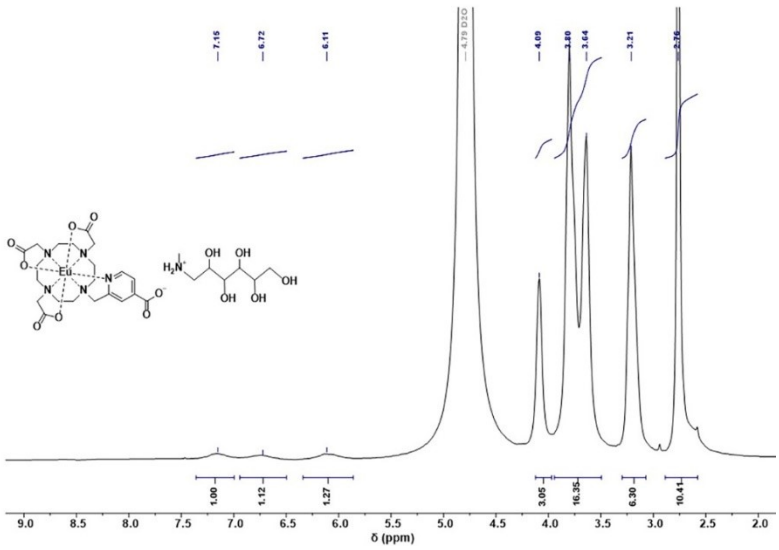

Figure S3. ^{1}H NMR spectrum of Eu-IN-DO3A (D_2O, 400 MHz).

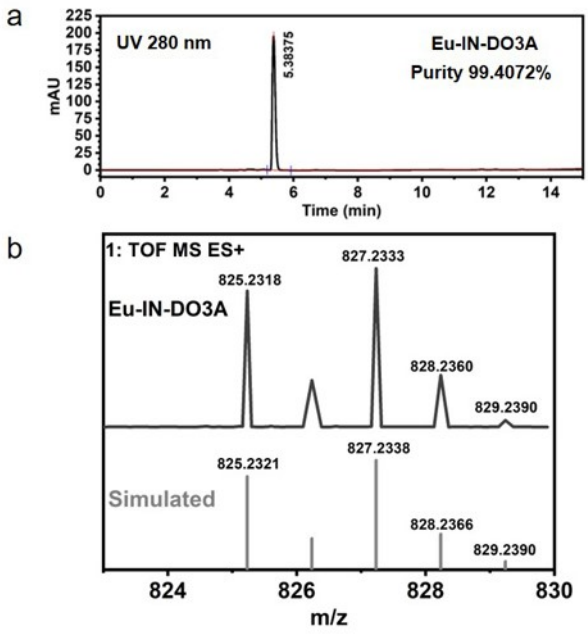

Figure S4. (a) HPLC chromatogram analysis and (b) ESI-MS spectrum of Eu-IN-DO3A.

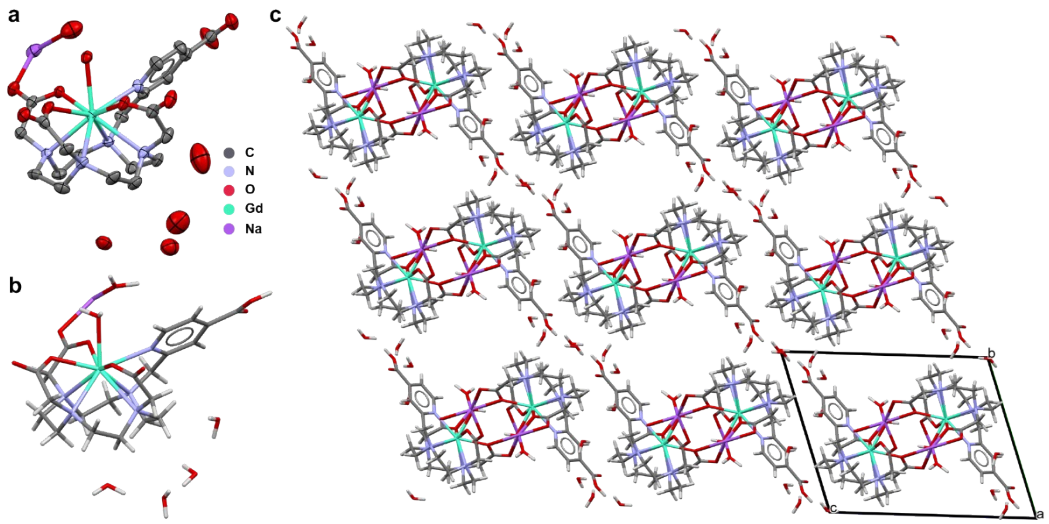

Figure S5. Single crystal X-ray diffraction results for [Gd(L)H_2O]Na(7H_2O). (a) The structural motif is shown at a 50% ellipsoid probability (hydrogen atoms are omitted for clarity). (b) The structure with one coordinated water molecule as well as water molecules in the secondary sphere of Gd. (c) the packing structure along *a* axis.

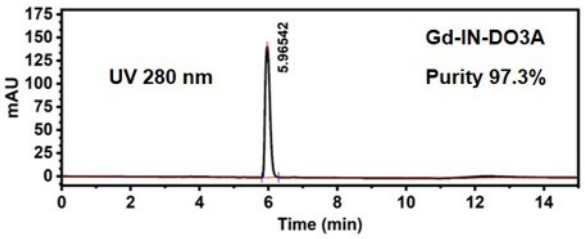

Figure S6. HPLC chromatogram of Gd-IN-DO3A.

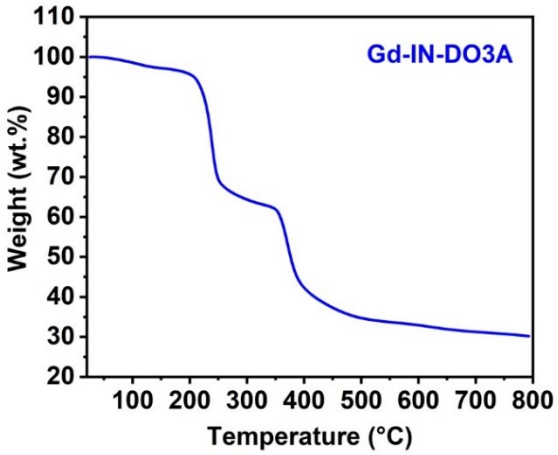

Figure S7. TGA of Gd-IN-DO3A under nitrogen flow.

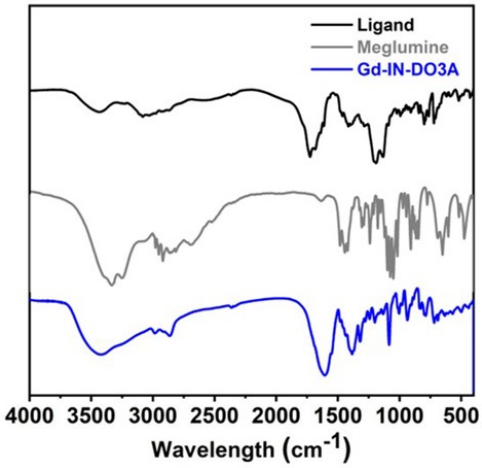

Figure S8. FTIR spectra of the Ligand, meglumine, and as-prepared Gd-IN-DO3A.

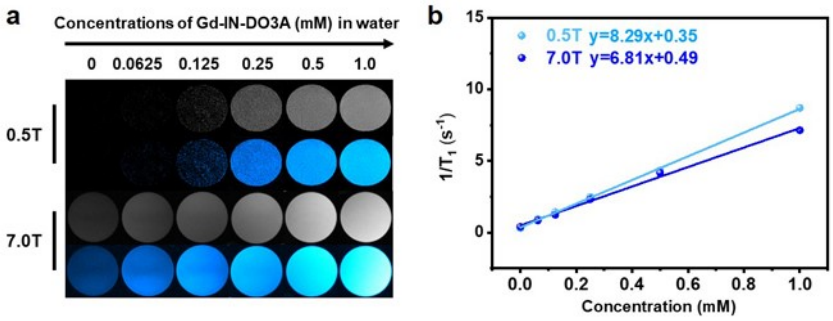

Figure S9. (a) T_1-weighted and color-mapped MR images of the concentration of Gd-IN-DO3A in water at 0.5 T and 7.0 T, respectively. (b) Corresponding relaxivity r_1 ($1/T_1$) versus the concentration of Gd-IN-DO3A.

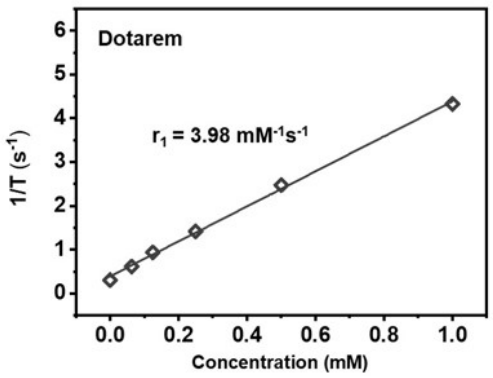

Figure S10. Relaxivity r_1 ($1/T_1$) versus the concentration of Dotarem in water at 0.5 T (32 °C).

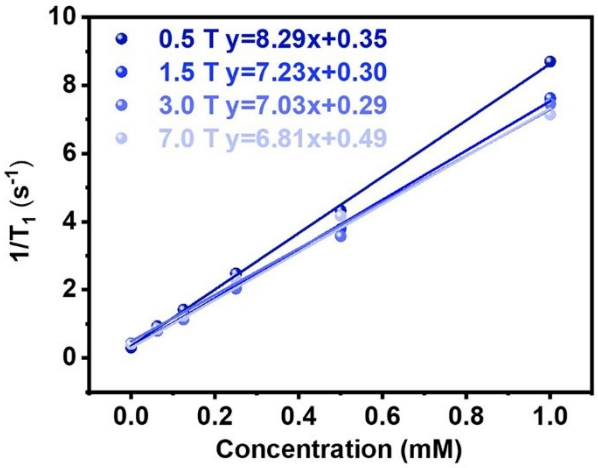

Figure S11. Relaxivity r_1 ($1/T_1$) versus the concentration of Gd-IN-DO3A in water at 0.5 T (32 °C), 1.5 T, 3.0 T, and 7.0 T (25 °C), respectively.

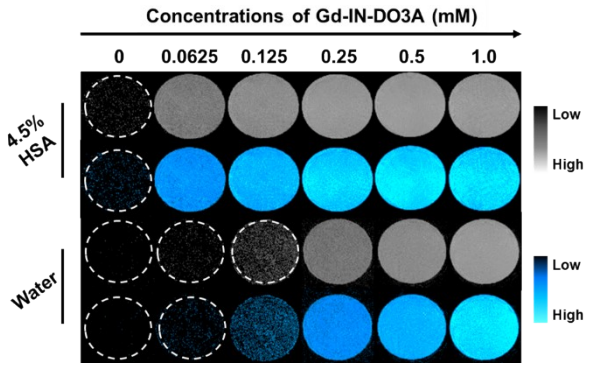

Figure S12. T_1-weighted and color-mapped MR images for the concentration of Gd-IN-DO3A in water and 4.5% HSA solution at 0.5 T (32 °C), respectively.

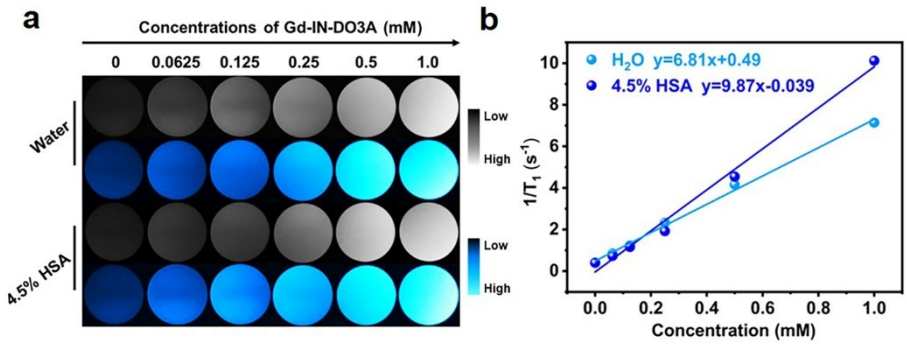

Figure S13. (a) T_1-weighted and color-mapped MR images for the concentration of Gd-IN-DO3A in water and 4.5% HSA solution at 7.0 T, respectively. (b) Corresponding relaxivity r_1 ($1/T_1$) versus the concentrations of Gd-IN-DO3A.

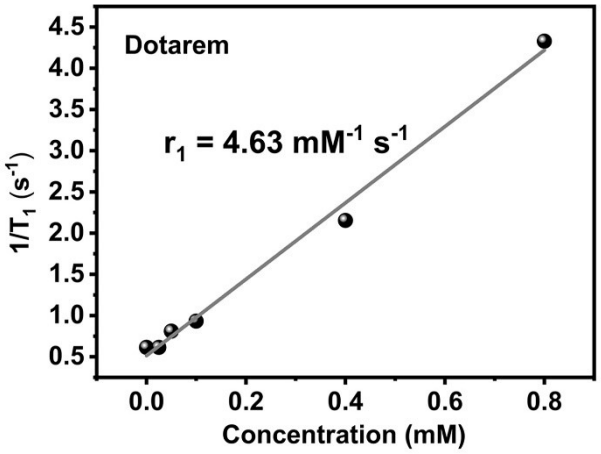

Figure S14. Relaxivity r_1 ($1/T_1$) versus the concentration of Dotarem in 4.5% HSA at 0.5 T (32 °C).

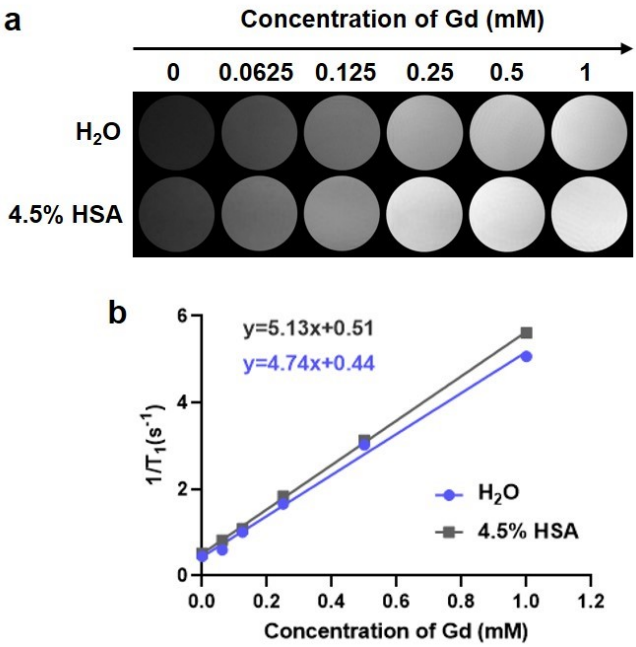

Figure S15. (a) T_1-weighted and color-mapped MR images for various concentrations of Gd-BOPTA in water and 4.5% HSA solution at 7.0 T, respectively. (b) Corresponding relaxivity r_1 ($1/T_1$) versus different concentrations of Gd-BOPTA.

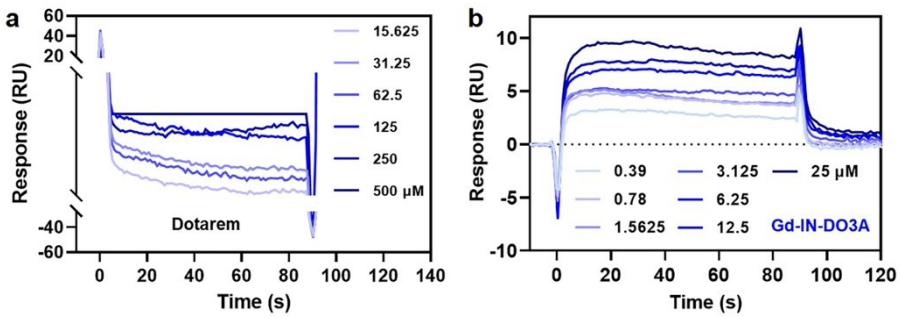

Figure S16. Affinity curves of Dotarem (a) and Gd-IN-DO3A (b) for HSA.

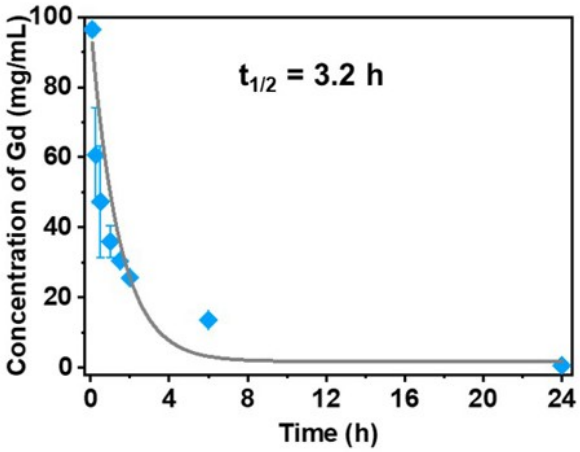

Figure S17. The time-concentration curve in mouse blood after a single dose intravenous administration of 0.1 mmol Gd/kg.

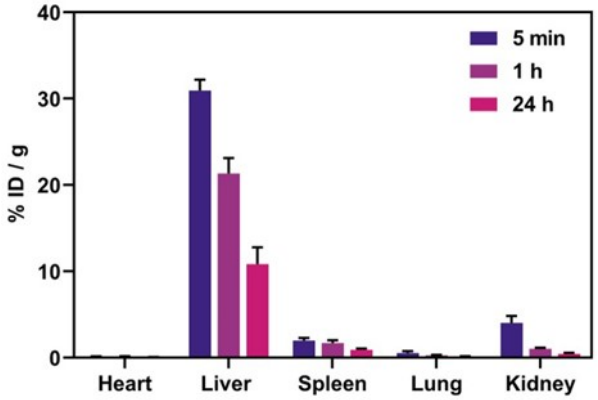

Figure S18. Biodistribution of Gd-IN-DO3A in normal BALB/c mice at 5 min, 1 h, and 24 h after injection at a dose of 0.1 mmol Gd/kg.

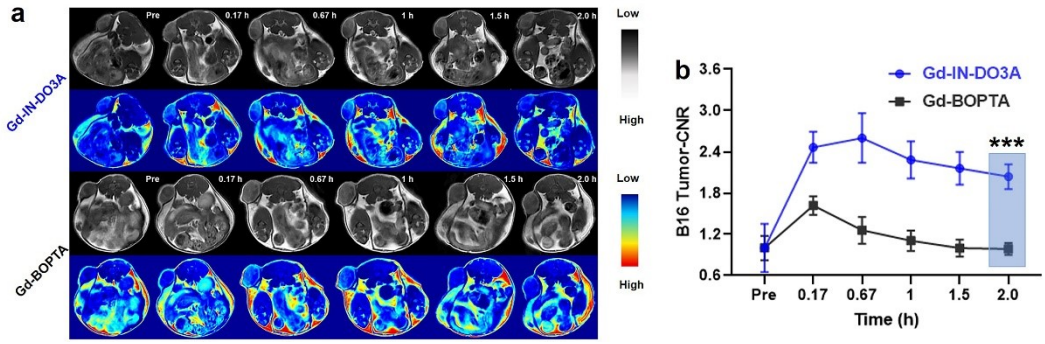

Figure S19. Axial T_1-weighted images of B16 tumor-bearing mouse acquired at 3.0 T (a) and the corresponding plots of the contrast-to-noise ratio (CNR) versus time for the above images. (Date are shown as means ± SD, n = 3, ***$p < 0.001$.)

Table S1. The parameters of crystalline structure for the ligand.

Parameter	ligand
Empirical formula	$C_{23}H_{47.5}Cl_{2.5}N_5O_{17}$
Formula weight	754.78
Crystal system	triclinic
Space group	P-1
***a* (Å)**	10.6702(8)
***b* (Å)**	10.6772(8)
***c* (Å)**	15.2565(12)
***β* (°)**	83.071(3)
***V* (Å^3)**	1715.6(2)
Z	2
***D*$_c$ (g/cm^3)**	1.461
***μ* (mm^{-1})**	1.858
***F*(000)**	798.0
GOF on F^2	1.103
***R*$_1$[a], *wR*$_2$[b] [*I* >2 *σ*(*I*)]**	R_1 = 0.0862, wR_2 = 0.2536
$\Delta\rho_{max}/\Delta\rho_{min}$ (e/Å^3)	0.47/-0.69
CCDC	2515628

[a] $R_1 = \Sigma||F_0| - |F_c||/\Sigma|F_0|$. [b] $wR_2 = [\Sigma w(F_0^2 - F_c^2)^2/\Sigma w(F_0^2)^2]^{1/2}$

Table S2. The parameters of crystalline structure for [NaGd(L)H_2O]($7H_2O$).

Parameter	ligand
Empirical formula	$C_{21}H_{42}GdN_5NaO_{17}$
Formula weight	816.83
Crystal system	triclinic
Space group	P-1
***a* (Å)**	9.1685(19)
***b* (Å)**	12.758(3)
***c* (Å)**	15.540(3)
***β* (°)**	85.709(7)
***V* (Å^3)**	1694.2(6)
Z	2
***D*$_c$ (g/cm^3)**	1.601
***μ* (mm^{-1})**	2.046
***F*(000)**	828.0
GOF on F^2	0.962
***R*$_1$[a], *wR*$_2$[b] [*I* >2 *σ*(*I*)]**	R_1 = 0.0469, wR_2 = 0.0968
Δ*ρ*$_{max}$/Δ*ρ*$_{min}$ (e/Å^3)	1.70/-0.94
CCDC	2515627

[a] $R_1 = \Sigma||F_0| - |F_c||/\Sigma|F_0|$. [b] $wR_2 = [\Sigma w(F_0^2 - F_c^2)^2/\Sigma w(F_0^2)^2]^{1/2}$

Table S3. Major pharmacokinetic parameters derived by two-compartmental modeling after intravenous administration of Gd-IN-DO3A complex (0.1 mmol Gd /kg) in healthy mice.

Parameter	Unit	Value
$AUC_{(0-t)}$	mg/L·h	403.057
$AUC_{(0-\infty)}$	mg/L·h	404.490
$t_{1/2z}$	h	3.229
T_{max}	h	0.083
CL_z	L/h/kg	0.039
C_{max}	mg/L	113.450

$AUC_{(0-t)}$ and $AUC_{(0-\infty)}$ area under the curve. $t_{1/2z}$: elimination half-life. T_{max}: peak time. CL_z: clearance. C_{max}: peak concentration.