Supplemental Information

Figure S1. *In vivo* fluorescence images of intratibial osteosarcoma tumor-bearing NSG mice at t=0 (pre-injection), 0.1, 6, 12, 24, 48, 72, 96, 120, 144, and 168 hr after tail-vein injection of Cy5.5-labeled HPMA-CHP. Mice were implanted with Saos-2 cells in the right proximal tibia and grown for 4 weeks prior to administration of polymer conjugate or peptide. Yellow dashed oval indicates location of osteosarcoma tumor. Experiment was performed with N=6, with five animals pictured here and the sixth animal in Figure S4.

НРМА-СНР



Min 3.00 × 10⁸ Max 1.00 × 10⁹ **Figure S2.** *In vivo* fluorescence images of intratibial osteosarcoma tumor-bearing NSG mice at t=0 (pre-injection), 0.1, 6, 12, 24, 48, 72, 96, 120, 144, and 168 hr after tail-vein injection of Cy5.5-labeled HPMA-^SCHP. Mice were implanted with Saos-2 cells in the right proximal tibia and grown for 4 weeks prior to administration of polymer conjugate or peptide. Yellow dashed oval indicates location of osteosarcoma tumor. Experiment was performed with N=6, with five animals pictured here and the sixth animal in Figure S4.

HPMA-^sCHP



Radiant Efficiency $(\frac{p/sec/cm^2/sr}{\mu W/cm^2})$ Color Scale Min 3.00 × 10⁸ Max 1.00 × 10⁹

Figure S3. *In vivo* fluorescence images of intratibial osteosarcoma tumor-bearing NSG mice at t=0 (pre-injection), 0.1, 6, 12, 24, 48, 72, 96, 120, 144, and 168 hr after tail-vein injection of Cy5.5-labeled CHP. Mice were implanted with Saos-2 cells in the right proximal tibia and grown for 4 weeks prior to administration of polymer conjugate or peptide. Yellow dashed oval indicates location of osteosarcoma tumor. Experiment was performed with N=6, with five animals pictured here and the sixth animal in Figure S4.

CHP



Efficiency $(\frac{p/sec/cm^2/sr}{\mu W/cm^2})$ Color Scale Min 3.00 × 10⁸ Max 1.00 × 10⁹

Figure S4. *In vivo* fluorescence images of intratibial osteosarcoma tumor-bearing NSG mice at t=0 (pre-injection), 0.1, 6, 12, 24, 48, 72, 96, 120, 144, and 168 hr after tail-vein injection of Cy5.5-labeled HPMA-CHP (1), HPMA-^SCHP (2), and CHP (3). Mice were implanted with Saos-2 cells in the right proximal tibia and grown for 4 weeks prior to administration of polymer conjugate or peptide. Yellow dashed oval indicates location of osteosarcoma tumor. Experiment was performed with N=6, with one animal from each group pictured here, and the other five animals pictured in Figures S1-S3.



Figure S5. Fluorescence images of harvested tumor-bearing leg (1), heart (2), lungs (3), liver (4), kidneys (5), spleen (6), and stomach and intestines (7) from mice bearing osteosarcoma tumors in the right proximal tibia, at 168 hrs after tail-vein injection of Cy5.5-labeled HPMA-CHP. (N=6).

HPMA-CHP









Epi-Fluorescence

- 1: Tumor-bearing leg
- 2: Heart
- 3. Lungs
- 4. Liver

- 5. Kidneys
- 6. Spleen
- 7. Stomach and Intestines

 $\begin{array}{l} \text{Color Scale} \\ \text{Min 2.00} \times 10^8 \\ \text{Max 5.00} \times 10^8 \end{array}$

Figure S6. Fluorescence images of harvested tumor-bearing leg (1), heart (2), lungs (3), liver (4), kidneys (5), spleen (6), and stomach and intestines (7) from mice bearing osteosarcoma tumors in the right proximal tibia, at 168 hrs after tail-vein injection of Cy5.5-labeled HPMA-^sCHP. (N=6).

HPMA-^sCHP









Epi-

- 1: Tumor-bearing leg
- 2: Heart
- 3. Lungs
- 4. Liver

- 5. Kidneys
- 6. Spleen
- 7. Stomach and Intestines

Color Scale Min 2.00 × 10⁸ Max 5.00 × 10⁸ **Figure S7.** Fluorescence images of harvested tumor-bearing leg (1), heart (2), lungs (3), liver (4), kidneys (5), spleen (6), and stomach and intestines (7) from mice bearing osteosarcoma tumors in the right proximal tibia, at 168 hrs after tail-vein injection of Cy5.5-labeled CHP. (N=6).

СНР











- 2: Heart
- 3. Lungs
- 4. Liver

- 5. Kidneys
- 6. Spleen
- 7. Stomach and Intestines

Radiant Efficiency $\frac{p/sec/cm^2/sr}{\mu W/cm^2}$) Color Scale Min 2.00 × 10⁸

Max 5.00×10^8

Epi-Fluorescence

0.8

Table S1. Pearson correlation coefficient r values for accumulation at 168 hr (S_{168}) and maximum accumulation (S_{max}) values of HPMA-CHP, HPMA-^SCHP, and CHP with respect to each bone morphometric parameter. Parameters with a Pearson r value with absolute value greater than or equal to 0.7 are highlighted in yellow.

	Pearson r					
	HPMA-CHP (n=6)		HPMA- ^s CHP (n=5)		CHP (n=6)	
	S_{168}	S _{max}	S_{168}	S _{max}	S_{168}	S _{max}
Volume of total bone	-0.3923	-0.6804	0.7871	0.671	0.4037	-0.3692
Volume of cortex	-0.4141	-0.7189	0.7976	0.6922	0.4754	-0.3111
Volume of intra-trabecular region	-0.24	-0.2062	0.3245	0.6696	0.3111	-0.1285
Volume of trabecular bone	0.1938	0.3112	0.6041	0.3749	-0.4575	-0.6859
Volume of total trabecular tissue	-0.2261	-0.1698	0.4861	0.7205	0.2097	-0.2433
Volume of whole tissue	-0.4129	-0.6177	0.7947	0.7675	0.4802	-0.3657
Total volume of trabecular tissue	-0.406	-0.613	0.7942	0.7664	0.4752	-0.3655
Bone volume of trabecular tissue	-0.3923	-0.6804	0.7871	0.671	0.4037	-0.3692
Bone surface area of trabecular tissue	-0.7268	-0.7096	0.7618	0.8189	0.03658	-0.6661
Bone volume fraction of trabecular tissue	-0.04029	-0.2892	0.5884	0.2841	-0.0007015	-0.1353
Bone surface density of trabecular tissue	0.006045	0.3614	-0.1909	0.1318	-0.7932	-0.2273
Specific bone surface of trabecular tissue	0.02375	0.3857	-0.5734	-0.1746	-0.4753	-0.06563
Cortical porosity	0.7704	0.6553	0.8166	0.7423	-0.1723	-0.1056
Pore number of cortex	-0.3459	-0.01768	0.7805	0.7647	-0.2758	-0.8352
Total pore volume of cortex	0.5889	0.2791	0.8057	0.7111	0.1064	-0.2187
Average pore volume of cortex	0.7374	0.2145	-0.449	-0.6687	0.4582	0.854
Pore density of cortex	0.01089	0.5116	0.7735	0.8001	-0.541	-0.818