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	1 <sup>st</sup> block (O950 mCTA)			2 <sup>nd</sup> block (HBC Core)		2 <sup>nd</sup> block (CPM Core)		Complete Polymer				
Poly .#	M <sup>1</sup> (kDa)	Ð1	DP <sup>2</sup>	M <sup>1</sup> (kDa)	DP <sup>2</sup>	M <sup>1</sup> (kDa)	DP <sup>2</sup>	M <sup>1</sup> (kDa)	dndc	Block ratio	Ð1	Drug (wt.%)
3	17.5	1.12	18	-	-	-	-	17.5	0.060	-	1.12	-
4	17.5	1.12	18	30.5	56	-	-	48	0.080	1.74	1.27	34
5	17.5	1.12	18	-	-	24.3	32	41.8	0.087	1.39	1.35	30

**Table S1.** Summary of composition, molecular weights, and molar mass dispersity values for diblock copolymers of HBC and CPM prepared from a poly(O950) macroCTA.

As determined by size exclusion chromatography using Tosoh SEC TSK-GEL α-3000 and α-4000 columns
PA) connected in series to an Agilent 1200 Series Liquid Chromatography System (Santa Clara, CA) and Wyatt Technology miniDAWN TREOS, 3 angle MALS light scattering instrument and Optilab TrEX, refractive index detector (Santa Barbara, CA). HPLC-grade DMF containing 0.1 wt% LiBr at 60 °C was used as the mobile phase at a flow rate of 1 mL min<sup>-1</sup>

2. As determined by <sup>19</sup>F NMR in DMSO using a sodium tifluoracetate standard



**Figure S1.** Representative (a) <sup>1</sup>H NMR and (b) <sup>19</sup>F NMR spectrum of poly(O950-*co*-HBC) in CDCl<sub>3</sub> and C<sub>2</sub>D<sub>6</sub>SO respectively with assignment of the characteristic resonances associated with the comonomers. Copolymer composition was determined by comparing the HBC (9H) Boc resonances at  $\delta = 1.52$  ppm to the O950 (3H) methoxy resonance at  $\delta = 3.4$  ppm. <sup>19</sup>F NMR was conducted in C<sub>2</sub>D<sub>6</sub>SO using sodium trifluoroacetate (C<sub>2</sub>F<sub>3</sub>NaO<sub>2</sub>) (0.11 µM) as an internal standard. Integration of the Cipro resonance at  $\delta = -124.5$  ppm (1F) relative to the internal standard at  $\delta = -73.4$  ppm (3F) was used to calculate the final polymer composition



**Figure S2.** RI traces as measured by GPC showing molecular weight distributions of the copolymers (a) poly(O950-*co*-HBC) and (b) poly(O950-*co*-CPM). The RAFT polymerization of the copolymers were conducted in pyridine (blue) and THF (green), respectively, with  $[M]_o:[CTA]_o:[I]_o$  equal to 25:1:0.1, and had a  $M_n$  of 13.1 and 11.8 kDa with a D of 1.08 and 1.09, respectively.



**Figure S3.** Representative NMR spectrums of (a) poly(O950)-*b*-(HBC) and (b) poly(O950)-*b*-(CPM) diblocks in CDCl<sub>3</sub> with assignment of the characteristic resonances associated with the monomers. Diblock copolymer compositions were determined by comparing the HBC (9H) Boc resonances at  $\delta = 1.52$  ppm to the O950 (3H) methoxy resonance at  $\delta = 3.4$  ppm. Additionally, <sup>19</sup>F NMR was conducted in C<sub>2</sub>D<sub>6</sub>SO using sodium trifluoroacetate (C<sub>2</sub>F<sub>3</sub>NaO<sub>2</sub>) (0.22 µM) as an internal standard. Integration of the Cipro resonance at  $\delta = -124.5$  ppm (1F) relative to the internal standard at  $\delta = -73.4$  ppm (3F) was used to calculate the final polymer composition.



**Figure S4**. The peaks associated to (a) free drug elution and representative drug release in serum from example polymer systems, (b) deprotected poly(O950-*co*-HBC) (24 d) and (c) deprotected poly(O950)-*b*-(HBC) (20 d), was isolated using HPLC and confirmed through mass spectroscopy. The appearance of the dominant peak (332.1 m/z) from the polymer samples suggests an appropriate peak selection for monitoring drug release.



**Figure S5**. RAW 264.7 cell viability in the presence of both diblock copolymers was quantified using a MTS assay over a wide polymer dose range (mg/mL). After 24 h, both polymer constructs exhibit a dose dependent toxicity with cell viability measured below 80% with polymer concentrations greater than ca. 1 mg/mL.



**Scheme S1.** Synthesis of (1) butanoic acid, 4-[(4-hydroxyphenyl)methylamino]-4-oxo, 1-(2-methacryloyloxy)ethyl ester, (2) Boc Ciprofloxacin, and resulting prodrug monomers, HBC and CPM.



**Figure S6.** Representative (a) <sup>1</sup>H NMR and (b) mass spectroscopy of synthesized HEMA-Boc-Cipro (HBC) monomer. Proton NMR scans were conducted in CDCl<sub>3</sub> at 300 MHz. Successful preparation of the indicated chemical structure was confirmed by the appearance of resonances associated with the tert-butyl group, residues from 2-hydroxyethyl methacrylate, and the parent drug. Mass spectroscopy was used as supporting data to validate the chemical structure of the resulting product (dominant species) by matching the molecular ion peak for M+H (544.5 m/z) with theoretically expected value 544.6.







**Figure S7.** Representative (a) <sup>1</sup>H NMR and (b) mass spectroscopy of synthesized Ciprofloxacin Phenyl Methacrylate (CPM) monomer. Proton NMR scans were conducted in CDCl<sub>3</sub> at 300 MHz. Successful preparation of the indicated chemical structure was confirmed by the appearance of resonances associated with the tert-butyl group (1), residues from the (aminomethyl) phenolic group (10-13), and the parent drug (2-6). Mass spectroscopy was used as supporting data to validate the chemical structure of the resulting product (dominant species) by matching the molecular ion peak M+H (750.1 m/z) with theoretically expected value 749.8.