Supporting Information

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Figure caption:

Fig. S1. Particle size distributions of the optimized Riv-NPs measured by Dynamic light scattering

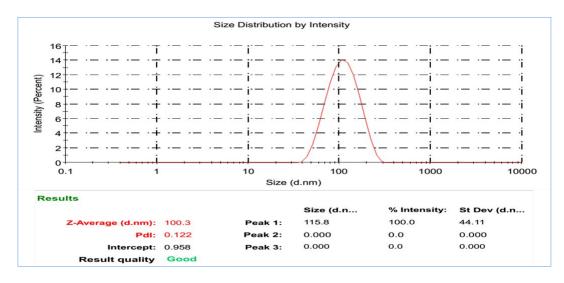


Fig. S1. Particle size distributions of the optimized Riv-NPs measured by Dynamic light scattering

 $\textit{Table S1. Molecular weight of diblock copolymers synthetized with different PCL/mPEG\ ratio.}$

| Polymer code | feeding ratio (ε-CL / M-PEG , w/w) | Mn PEG | DPpgL | Mnpgl | Mn _{PCL} / Mn _{PEG} | Copolymer Mn (Da) |
|--------------|--|---------------|-------|-------|--|----------------------|
| Pol 1 | 1 | 5000 | 37.7 | 4525 | 0.9 | 9525 |
| Pol 2 | 2 | 5000 | 89.3 | 10722 | 2.1 | 15721 |
| Pol 3 | 3 | 5000 | 130.5 | 15661 | 3.1 | 20660 |
| Pol 4 | 5 | 5000 | 196.9 | 23625 | 4.7 | 28625 |

Table S2. Kinetic analysis of drug release

| Goodness of fit | Zero- order | First-order | Higuchi | Korsmeyer- Peppas | Hixson- Crowell | Weibull |
|--------------------|----------------|-------------|---------|----------------------|--------------------|---------|
| Rsqr_adj | -1.457 | 0.974 | 0.465 | 0.864 | 0.475 | 0.996 |
| AIC | 123.27 | 68.62 | 104.97 | 89.42 | 104.74 | 45.58 |
| MSC | -1.07 | 3.49 | 0.46 | 1.76 | 0.48 | 5.41 |

Table S3. HPLC method validation in rat plasma and brain

| | Quality control | Nominal concentration (ug/ml) | day | Intra-day (n=3) | | Inter-day (n=9) | |
|--------|--------------------|-------------------------------|-----|-----------------|--------------|-----------------|--------------|
| | | | | RSD (%) | Accuracy (%) | RSD (%) | Accuracy (%) |
| plasma | | | 1 | 6.5 | 111.6 | | |
| | LQC | 0.08 | 2 | 11.5 | 98.1 | 11.1 | 102.4 |
| | | | 3 | 12.3 | 97.5 | | |
| | | | 1 | 5.4 | 100.7 | | |
| | MQC | 1 | 2 | 4.3 | 98.9 | 5.6 | 102.2 |
| | | | 3 | 4.8 | 107.1 | | |
| | | | 1 | 3.1 | 103.2 | | |
| | HQC | 3 | 2 | 4.0 | 102.6 | 5.9 | 99.5 |
| | | | 3 | 1.8 | 92.6 | | |
| brain | | | 1 | 8.6 | 106.8 | | |
| | LQC | 0.1 | 2 | 4.7 | 110.9 | 8.1 | 107.0 |
| | | | 3 | 11.5 | 103.2 | | |
| | | | 1 | 3.6 | 107.4 | | |
| | MQC | 1 | 2 | 7.7 | 95.8 | 7.9 | 101.2 |
| | | | 3 | 9.3 | 100.4 | | |
| | | | 1 | 2.9 | 99.3 | | |
| | HQC | 3 | 2 | 5.4 | 101.4 | 3.5 | 100.9 |
| | | | 3 | 2.3 | 102.1 | | |