Supplementary data:



Scheme 1

5

Scheme 2

Fig. S1 Synthetic route for HA Nano 1 (Scheme 1) and HA Nano 2-3 (Scheme 2).



Fig. S2 ¹**H NMR spectra** in D₂O of the graft polymers **d-f** compared to those of the starting material: **a**, HA; **b**, HA-DBCO; **c**, azide-terminated pNiPAM; **d**, HA Nano 3; **e**, HA Nano 2; and **f**, HA Nano 1. The specific assignments of the proton NMR

5 resonance peaks are for HA (δ 2.00 ppm (1)), DBCO (δ 2.71 (3) and 7.67 ppm (2)), PEG (δ 3.61 ppm (8)) and pNiPAM (δ 1.13 (7), 1.56 (5, 6), and 3.88 (4) ppm).



Fig. S3 General overview of the HA graft polymer and control (empty, PBS, and commercial HA at 20 °C) injection profiles generated using a **a**, 23G and, **b**, 29G needle-syringe system at 20 °C. An empty syringe, commercial HA and PBS were used as the controls. **c** Conoral evention of the HA graft polymer injection profiles

5 used as the controls. c, General overview of the HA graft polymer injection profiles generated using a 29G needle at 37 °C. (n = 3, mean ± s.d.).

3



Fig. S4 Elastic (G') and viscous (G") moduli expressed in Pascal (Pa) as a function of the time at 37 °C (0.9 % (w/v) commercial HA and hyaluronidase 55 U·mL⁻¹ in PBS).



Fig. S5 Cumulative *in vitro* drug release profile of dexamethasone from a saline solution, commercial HA, HA Nano 1-2 at 37 °C (n = 3, mean ± s.d.). After 28 h, the polymer matrix was hydrolyzed by heating (121 °C), and the remaining content of 4 dexamethasone was measured.



Fig. S6 Mitochondrial activity of human fibroblast-like synoviocytes exposed to HA
Nano 1 at the concentrations used in *in vivo* trials, as well as HA Nano 2 (n = 3, mean ± s.d.).



Fig. S7 Representative paraffin-embedded tissue sections of bone marrow from the knee at 2 months after OA induction. Autofluorescence of tissues (blue), and fluorescence of HA and HA Nano 1 (red). HA and HA Nano 1 are denoted by white arrows. Scale has = 40 µm

5 arrows. Scale bar = 40 μ m.