Appendix S1: Preparation of RM-PLGA Microspheres

In this experiment, PLGA microspheres were prepared using the double emulsion-solvent evaporation method, with the external phase being the oil phase and the internal phase being the aqueous phase. The preparation method for the external phase is as follows: 25 ml each of liquid paraffin and petroleum ether, along with 10 mg of moxifloxacin, were placed in a 100 ml beaker. A stir bar was added, and the mixture was stirred on a stirrer for 1 hour (at 3000 rpm) to ensure thorough saturation. The mixed solution was then aliquoted into 15 ml centrifuge tubes and centrifuged at 4000 rpm for 15 minutes, after which the supernatant was collected. To 50 ml of the supernatant, 0.1% Span85 (0.049 g) was added dropwise, and the mixture was stirred again in a 100 ml beaker for 50 minutes.

The preparation method for the internal phase was as follows: 150 μl of acetonitrile and 750 μl of isopropanol were added to a 2 ml EP tube, and 80 mg of PLGA (50/50, molecular weight 10,000) was weighed and dissolved in the above solution. The mixture was vortexed for 5 minutes and sonicated for 1 hour. After sonication, 10 mg of moxifloxacin and 1 mg of rifampicin were added to the 80 mg PLGA internal phase solution, followed by vortexing for 10 minutes. Then, 100 μl of dichloromethane was added, and the mixture was vortexed again for 5 minutes to ensure complete dissolution.

Once both the external and internal phases were prepared, 20 ml of the external phase was aliquoted into a 50 ml beaker for shearing. Then, 1 ml of the internal phase was poured into the 20 ml external phase and sheared at 8000 rpm for 30 seconds using a high-speed disperser. The remaining 30 ml of the external phase was then added to the mixed solution, and the mixture was placed on a vortex mixer for 4 hours (at a certain speed). As the vortexing proceeded, the petroleum ether evaporated, and pink microspheres became visible in the solution. The solution was then poured into 15 ml centrifuge tubes and centrifuged for 15 minutes. The supernatant was discarded, and 5 ml of washing solution (a 1:1 mixture of petroleum ether and n-hexane) was added. The mixture was vortexed for 2 minutes and centrifuged for 2 minutes. This washing procedure was repeated three times. Finally, the microspheres were placed in a petri dish and allowed to dry thoroughly for 48 hours.

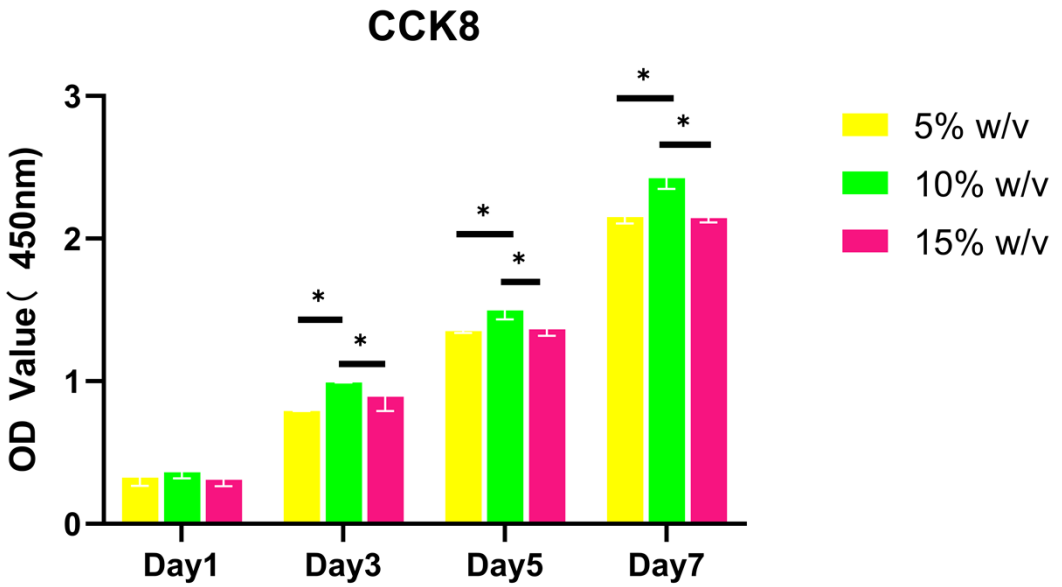

Figure.S1: CCK8 results of cell co-culture with hydrogels at concentrations of 5%, 10%, and 15% (w/v).

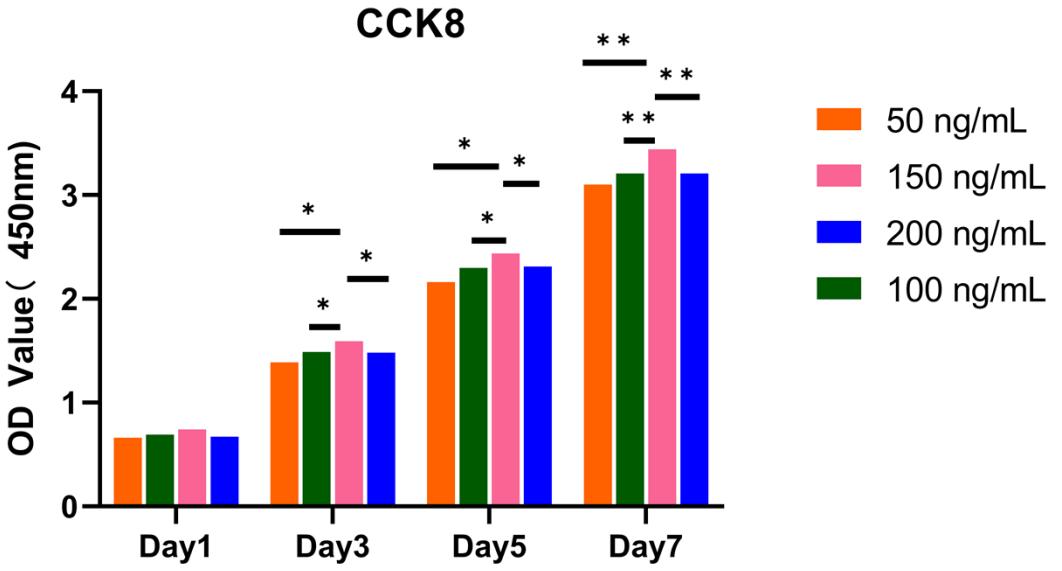

Figure.S2: Results of CCK8 assay for BMP-2 at concentrations of 50, 100, 150, and 200 ng/mL when co-cultured with cells.

Appendix S2: Sustained-release Testing of Drugs

Place the support in a dialysis bag with a relative molecular weight of 3500. Seal the two ends of the dialysis bag and add 1 ml of PBS solution. Put it into a PE tube containing 5 ml of PBS solution, seal the PE tube and incubate it in a constant temperature water bath at 37℃. Take samples at 3h, 6h, 12h, 24h, 2d, 3d, 5d, 7d, 10d, 14d, 21d, and 27d. Each time, take 5 ml of the sample and store it in a sealed container at -20℃ for later testing. Then, add 5 ml of fresh PBS solution to the PE tube. Use a UV spectrophotometer to determine the content of moxifloxacin in the released solution. Release amount = ml/m2 * 100% (ml is the amount of moxifloxacin and rifampicin released by the microsphere in the buffer solution, m2 is the total amount of moxifloxacin and rifampicin in the microsphere).

Appendix S3: Sustained-release Detection of BMP-2

The specific operation steps are as follows: Add 100.00 μl of 0.50 μg/ml capture antibody to each ELISA plate well. Incubate at room temperature overnight. Then remove the liquid in the wells and wash the plates 4 times with 300.00 buffer. Add 300.00 μl blocking buffer to each well and incubate at room temperature for 1 hour. At the end, remove the liquid in the wells and wash the plates 4 times with buffer. Dilute the standard substance with the diluent, and dilute the sample with the diluent. Quickly add 100.00 μl of the standard diluent and the sample diluent to the well plate and incubate at room temperature for 2 hours. Wash the plates as before. Add 1.00 μg/mL capture antibody 100.00 μl to the well plate and incubate at room temperature for 2 hours. Wash the plates 4 times, add 1:2000 diluted Avidin-HRP conjugate to each well and incubate at room temperature for 30 minutes, and then wash the plates again. Finally, add 100.00 L of ABTS liquid substrate to the well plate. Place the well plate in the microplate reader, with the reading wavelength at 405 nm, and the wavelength correction set to 650 nm. Read the optical density (OD) value, draw the standard curve, and calculate the BMP-2 release amount.

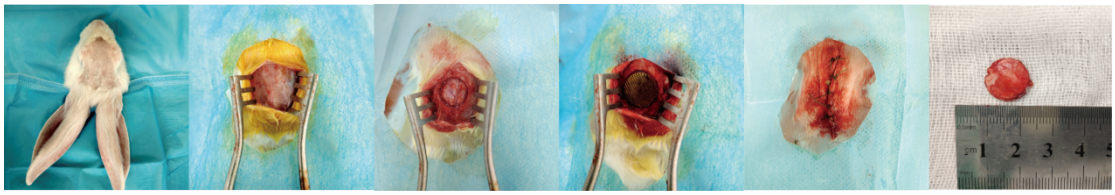

Figure.S3: Schematic diagram illustrating the process of creating an infectious bone defect model at the top of the New Zealand rabbit skull.

Appendix S4: Western-blot Assay for Osteogenesis-related Markers

Take soft tissue samples from the modeling area of SD rats (around the implanted stent), place the obtained soft tissue samples in pre-cooled PBS for rinsing to remove surface blood and impurities. Use scissors to cut the samples into pieces, and add RIPA lysis buffer to the minced samples, along with pre-added protease and phosphatase inhibitors. Centrifuge the lysed samples to remove cell debris and insoluble substances. Carefully aspirate the supernatant and transfer it to a new centrifuge tube. Use the extracted protein samples for Western-blot detection of osteogenic-related markers (Runx2, OST, OPN proteins).

Appendix S5: Quantitative PCR (qPCR) for Detection of Osteogenic Differentiation-related Genes

Soft tissue samples from the modeling area of SD rats (around the implanted stent) were collected. The obtained soft tissue samples were washed in pre-cooled PBS to remove surface blood and impurities. The samples were then cut into pieces using scissors, RNA was extracted and reverse transcribed, and qPCR was used to detect osteogenic differentiation-related genes (Runx2, OST, and OPN genes).

Table S1. The usage of RT-qRCT primers for osteogenesis-related genens.

Genes	Primer sequence	
Runx2	F:5'-ACTCCAAGACCCTAAGAAACCGAT-3'	R: 5'- TGGCTCCTCCCTTCTCAACCTC-3'
OPN	F: 5'- CTCAGAATTCAGCCAGGAGAAC-3'	R: 5'- CCAAACAGGCAAAAGCAAAT-3'
Actin	F: 5'- ACATCCGTAAAGACCTCTATGCC-3'	R: 5'- TACTCCTGCTTGCTGATCCAC-3