## 1 SUPPLEMENTARY DATA

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3 Figure S1. Diflunisal limits the cytotoxicity of strain Newman and maintains 4 efficacy in cultures with decreased oxygenation. A) To test the efficacy of diffunisal 5 in limiting non-USA300 strains of S. aureus, concentrated supernatants from strain 6 Newman were prepared in the presence or absence of 10 µg/ml diflunisal or vehicle 7 control (DMSO). Percent cell viability is depicted relative to mock intoxication with sterile 8 RPMI. Error bars represent SD. N=10 per group. \*\*\* denotes p<0.001 relative to vehicle 9 control. B) To test the efficacy of diflunisal under hypoxic culture conditions that 10 increase the cytotoxic potential of S. aureus, bacteria were grown in tightly-capped 11 glass Erlenmeyer flasks with a 1:5 volume to flask ratio. MC3T3 murine osteoblastic 12 cells were intoxicated with 30% volume / volume (v/v) of concentrated supernatant (SN) 13 from S. aureus grown as above in the presence of vehicle control (ethanol) or the 14 indicated concentrations of diflunisal. Percent cell viability is depicted relative to mock 15 intoxication with sterile RPMI. Error bars represent SD. N=10 per group and data are 16 representative of two independent trials. \*\*\* denotes p<0.001 relative to vehicle control. 17

## 18 Figure S2. Growth analysis of *S. aureus* cultured in the presence of select

**NSAIDs.** Growth analysis (Optical density at 600nm =  $OD_{600}$ ) of *S. aureus* cultured in glass Erlenmeyer flasks with 1:5 volume to flask ratio, and in the presence of two different vehicle controls (100% ethanol or DMSO) or 10 µg/ml of the indicated NSAIDs. Piroxicam and Ketorolac were dissolved in DMSO, all other compounds were dissolved in ethanol. Error bars represent SD. The average of 3 independent trials is depicted.

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## 25 **Figure S3. Release kinetics of diflunisal-loaded foams**

- Foams containing 10 mM diflunisal were incubated in 50 ml of PBS at 37°C on a mixer.
- 27 Samples were withdrawn for analysis at 4, 8, 24, 32, 48, 56, 72, and 144 hrs post
- incubation. The amount of diflunisal in each eluate was determined by HPLC. Error bars
- 29 represent the SD. N=4 for each timepoint.

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