**Supplementary Materials**

Direct Comparison of Chol-siRNA Polyplexes and Chol-DsiRNA Polyplexes Targeting STAT3 in a Syngeneic Murine Model of TNBC

Zhen Ye 2, Mai Mohamed Abdelmoaty 2,3, Stephen M. Curran 2, Shetty Ravi Dyavar 4,#, Devendra Kumar 2, Yazen Alnouti 2, Don W. Coulter 5, Anthony T. Podany 4, Rakesh K. Singh 1,6, Joseph A. Vetro 1,2,\*

1 Center for Drug Delivery and Nanomedicine and 2Department of Pharmaceutical Sciences, College of Pharmacy, University of Nebraska Medical Center, Omaha, Nebraska 68198, USA

3 Therapeutic Chemistry Department, Pharmaceutical and Drug Industries Research Division, National Research Centre, Giza, Egypt

4 Department of Pharmacy Practice, College of Pharmacy, University of Nebraska Medical Center, Omaha, Nebraska 68198, USA

5 Department of Pediatrics, Division of Pediatric Hematology/Oncology, Department of Radiation Oncology, J. Bruce Henriksen Cancer Research Laboratories, University of Nebraska Medical Center, Omaha, NE 68198-2168, USA

6 Department of Pathology and Microbiology, University of Nebraska Medical Center, Omaha, NE 68198-5900, USA

# Current address: Adicet Bio, Inc., 200 Constitution Dr, Menlo Park, CA, 94025

\* Correspondence: jvetro@unmc.edu; Tel.: 402-559-9359



**Figure S1.** **Representative Distributions of Chol-siCTRL Polyplex and Chol-DsiCTRL Polyplex Diameters.** Average diameters of Chol-siCTRL Polyplexes and Chol-DsiCTRL Polyplexes ± SD (n=3 independent sample measurements) were determined in 0.1 M HEPES, pH 7.4 by nanoparticle tracking analysis (NTA). A plot of accumulated percent of total Chol-siRNA Polyplexes (grey circles) or Chol-DsiRNA Polyplexes (grey squares) at each diameter (y-axis) vs. ln diameter (x-axis) was then fit against a cumulative Gaussian (percent) model using GraphPad Prism 9 to determine a best-fit mean (dashed red line for Chol-siCTRL Polyplexes and solid red line for Chol-DsiCTRL Polyplexes) and standard deviation from the lognormal curve.Data for Chol-DsiCTRL Polyplexes taken from [2].

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**Figure S2.** **Effect of Inactive Chol-siCTRL Polyplexes and Chol-DsiCTRL Polyplexes on the growth of primary syngeneic murine 4T1 breast tumors after repeated i.v. treatments.** Vehicle alone (white triangles) or vehicle containing an equimolar does of inactive Chol-siCTRL (white circles) or inactive Chol-DsiCTRL (white squares) complexed with PLL[30]-PEG[5K] at the indicated N/P ratio was injected into the tail veins of female BALB/c mice (black arrows) bearing a single subcutaneous 4T1 breast tumor (30 to 50 mm3). Average daily tumor volumes ±SD (n=5 mice) were then determined by 3D surface scanning and compared at each time point by Multiple t-tests. Data for Vehicle and Chol-DsiCTRL Polyplexes taken from [2].