Supporting Information

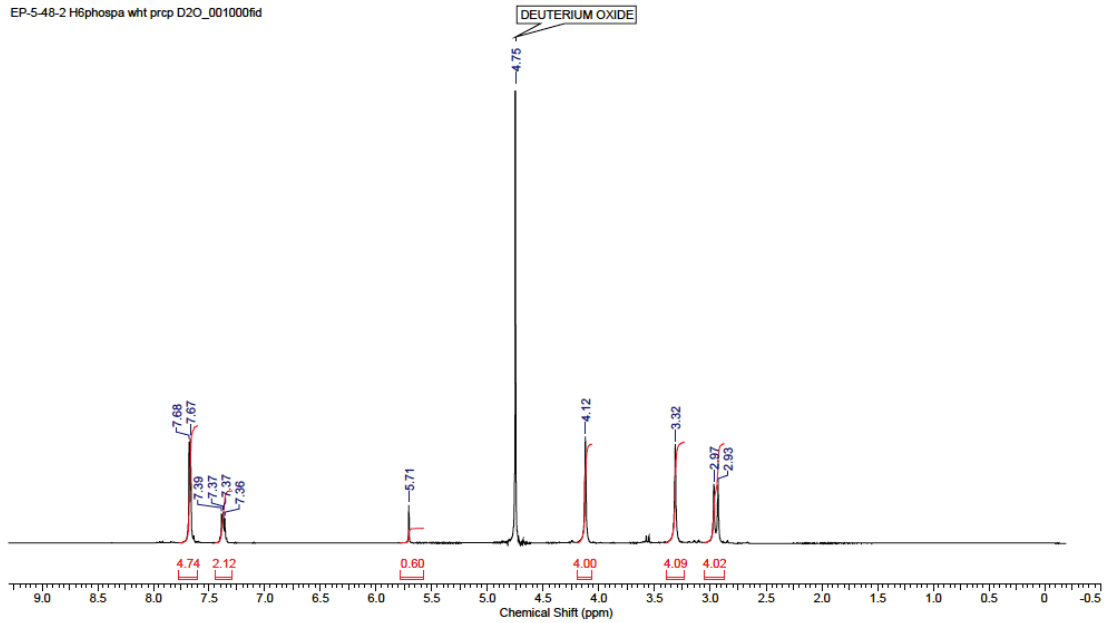
H_6phospa-Trastuzumab: Bifunctional Methylenephosphonate-based Chelator with ^{89}Zr, ^{111}In and ^{177}Lu.

Eric W. Price[†,§], Brian M. Zeglis[‡], Jason S. Lewis[*,‡], Michael J. Adam[*,§], and Chris Orvig[*,†]

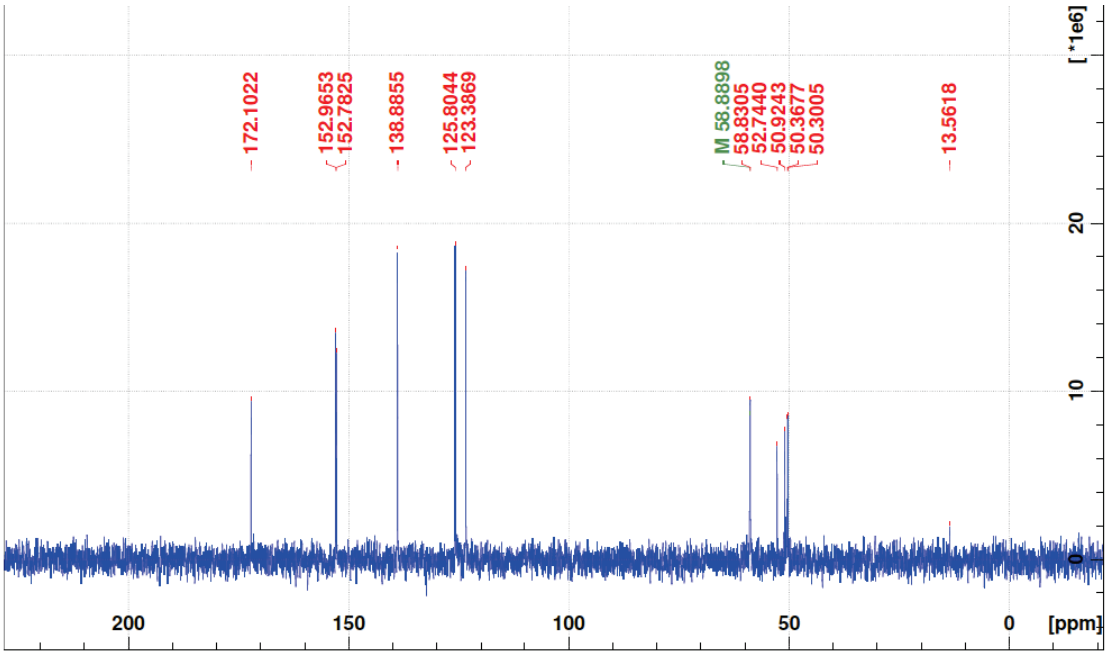
[†]*Medicinal Inorganic Chemistry Group, Department of Chemistry, University of British Columbia, 2036 Main Mall, Vancouver, British Columbia, Canada, V6T 1Z1;*

[§]*TRIUMF, 4004 Wesbrook Mall, Vancouver, British Columbia, Canada, V6T 2A3;*

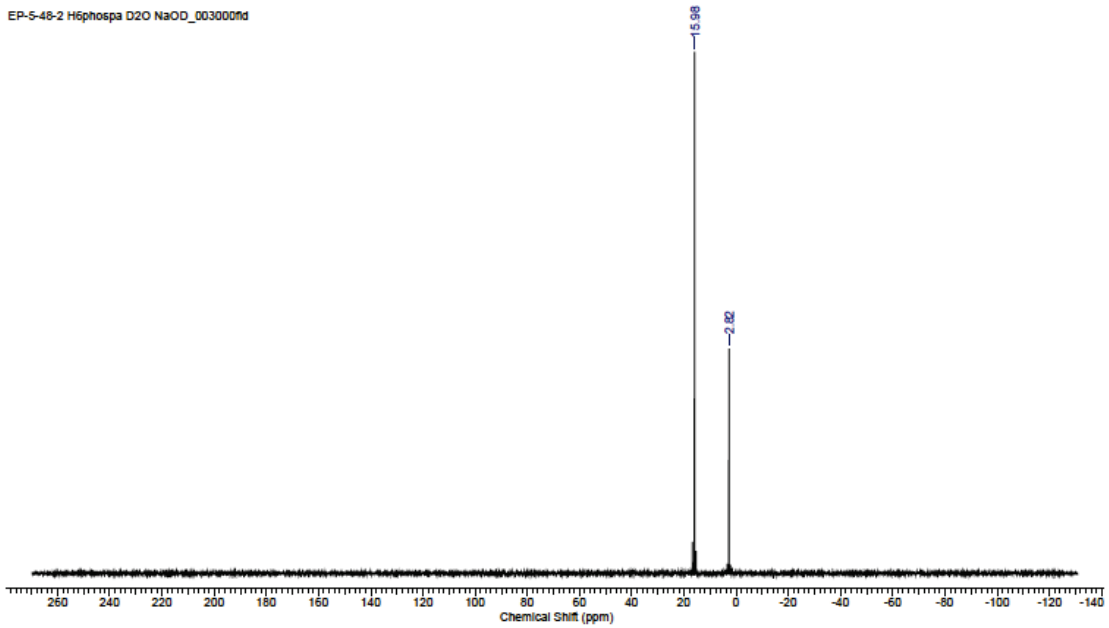
[‡]*Memorial Sloan-Kettering Cancer Center (MSKCC), Memorial Hospital, 1275 York Avenue, New York, New York, 10065, United States of America.*



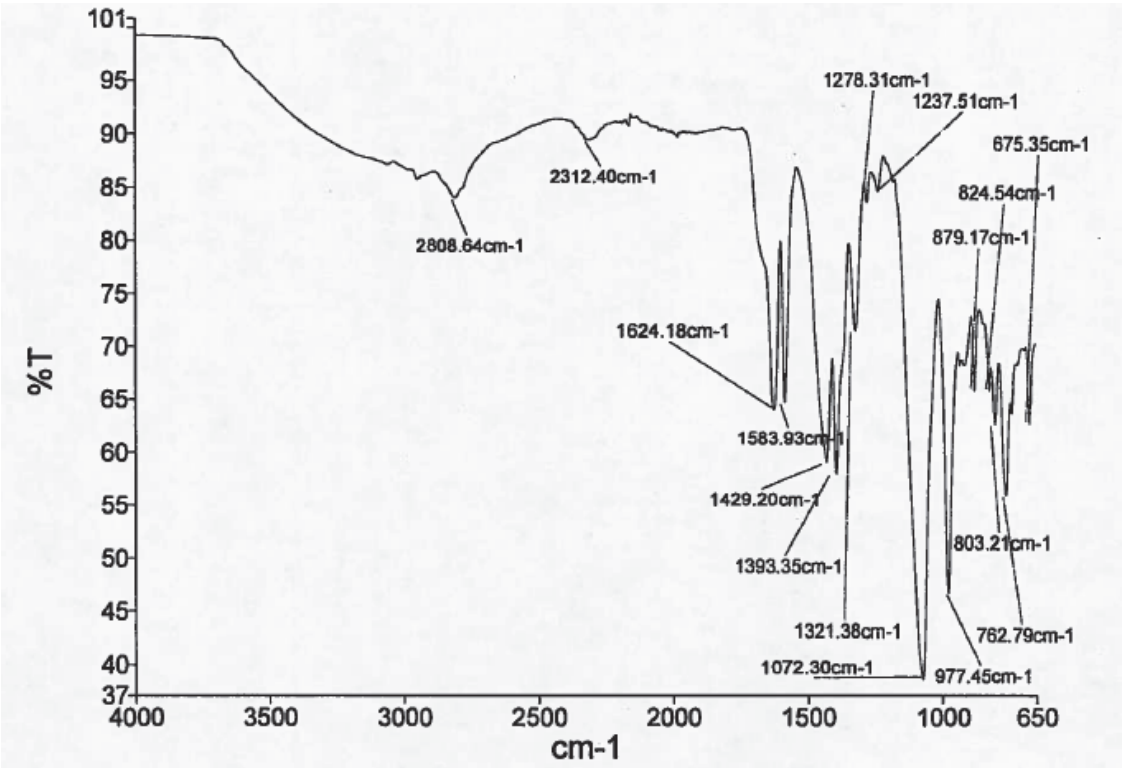
Supplementary Figure S1. ^{1}H NMR spectrum (300 MHz, D_2O, RT) of H_6phospa.



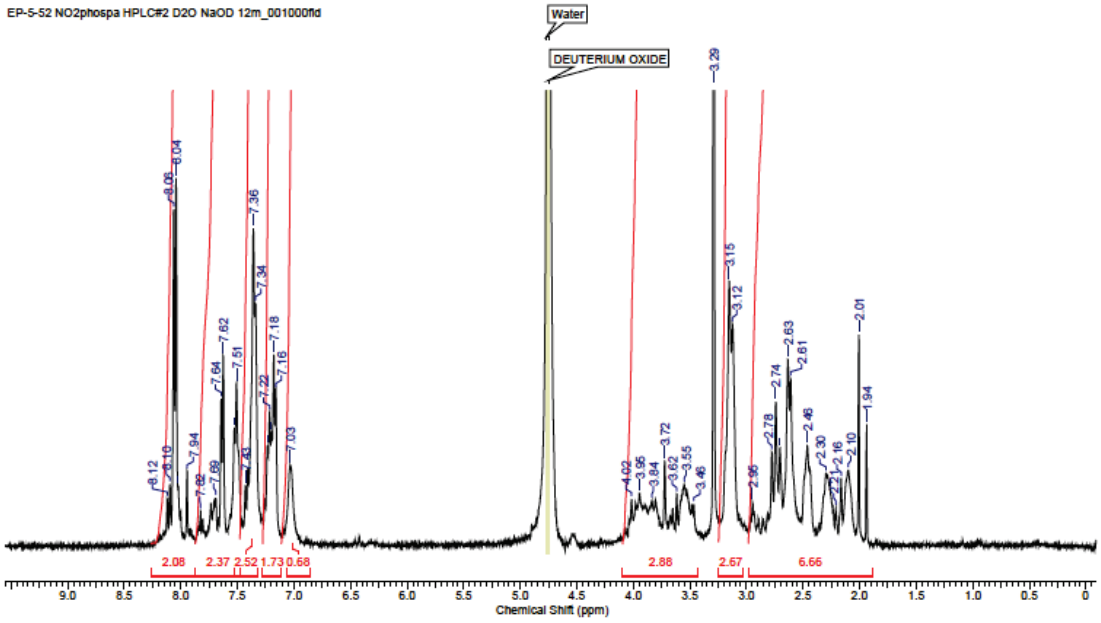
Supplementary Figure S2. ^{13}C NMR spectrum (75 MHz, D_2O, RT) of H_6phospa.



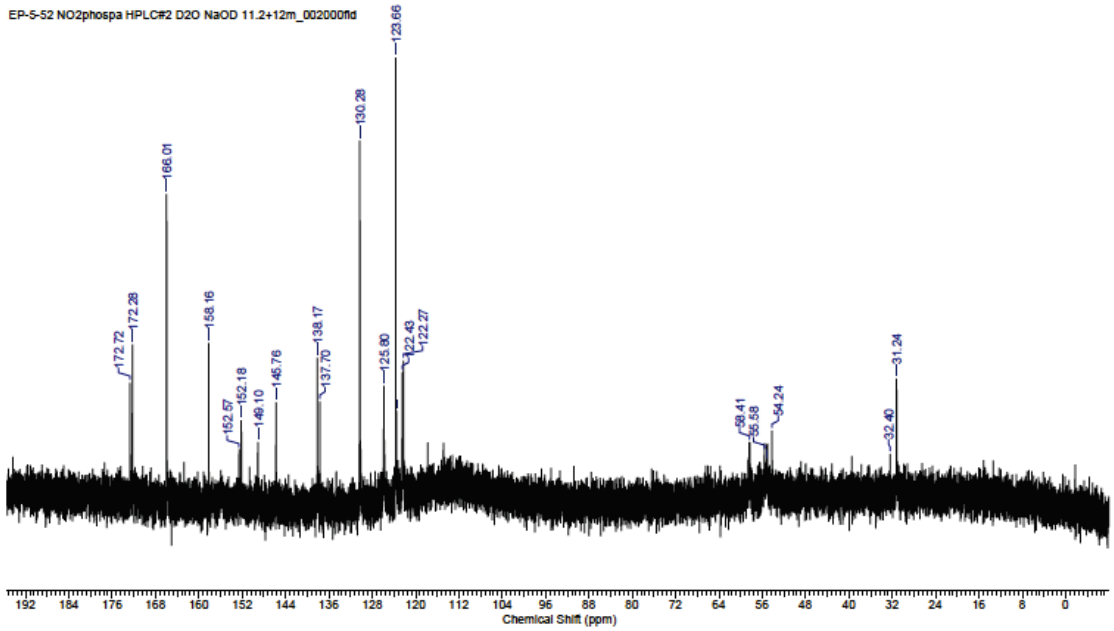
Supplementary Figure S3. $^{31}P\{^{1}H\}$ NMR spectrum (121.5 MHz, D_2O, RT) H_6phospa.



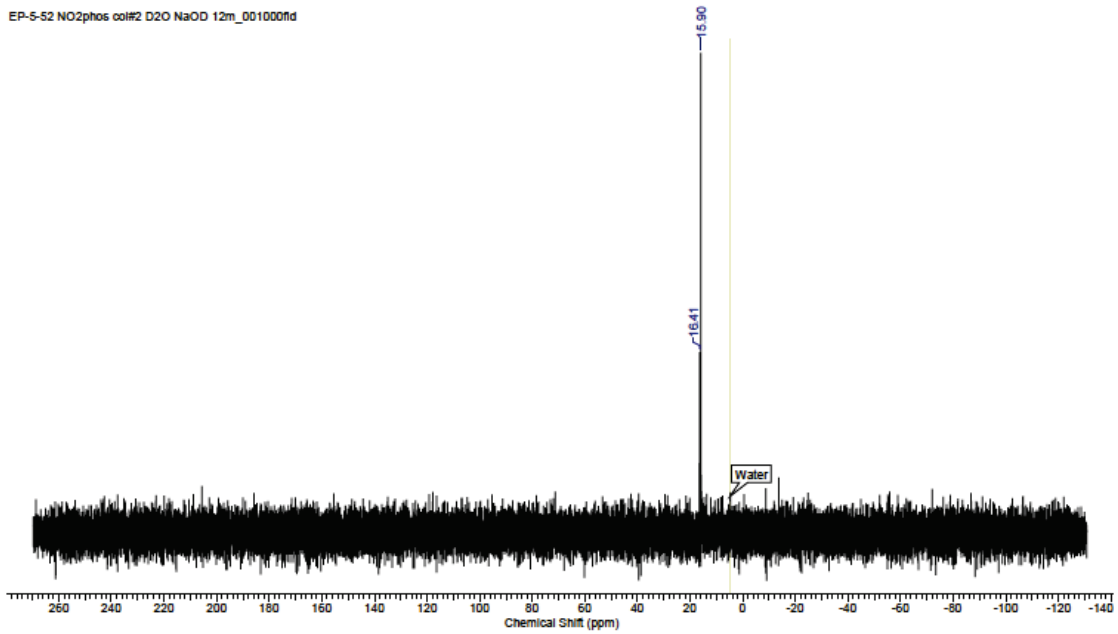
Supplementary Figure S4. ATR-IR spectrum (neat) of H_6phospa.



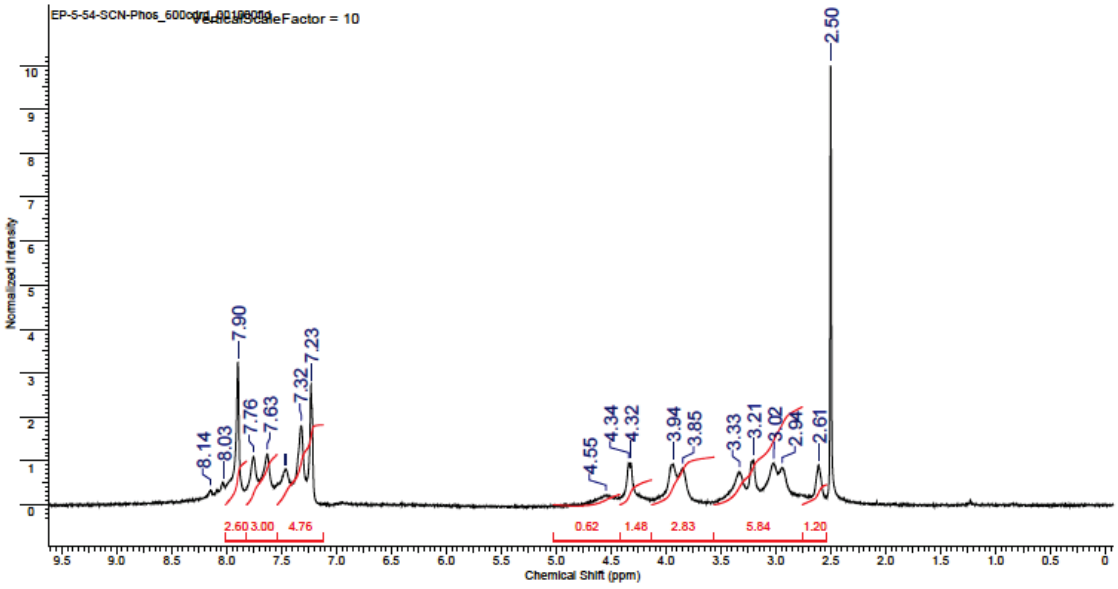
Supplementary Figure S5. ^{1}H NMR spectrum (400 MHz, D_2O, RT) of *p*-NO_2-Bn-H_6phospa



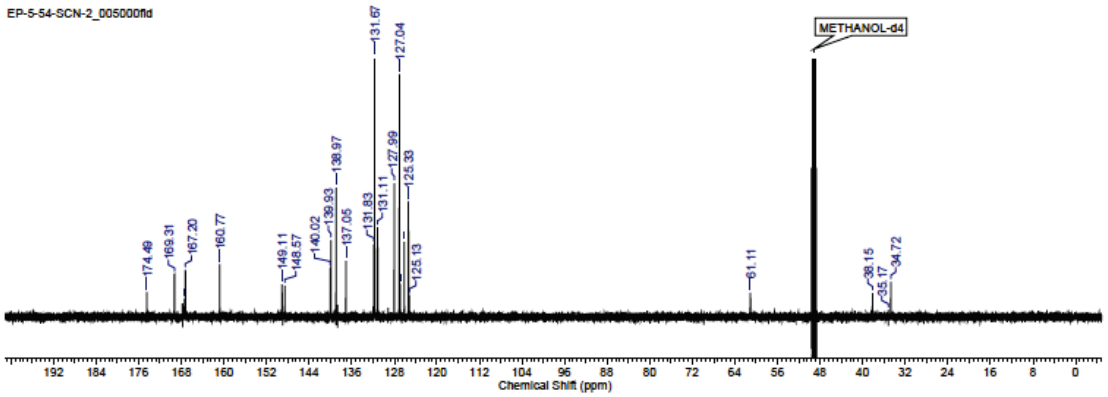
Supplementary Figure S6. ^{13}C NMR spectrum (100 MHz, D_2O, RT) of *p*-NO_2-Bn-H_6phospa



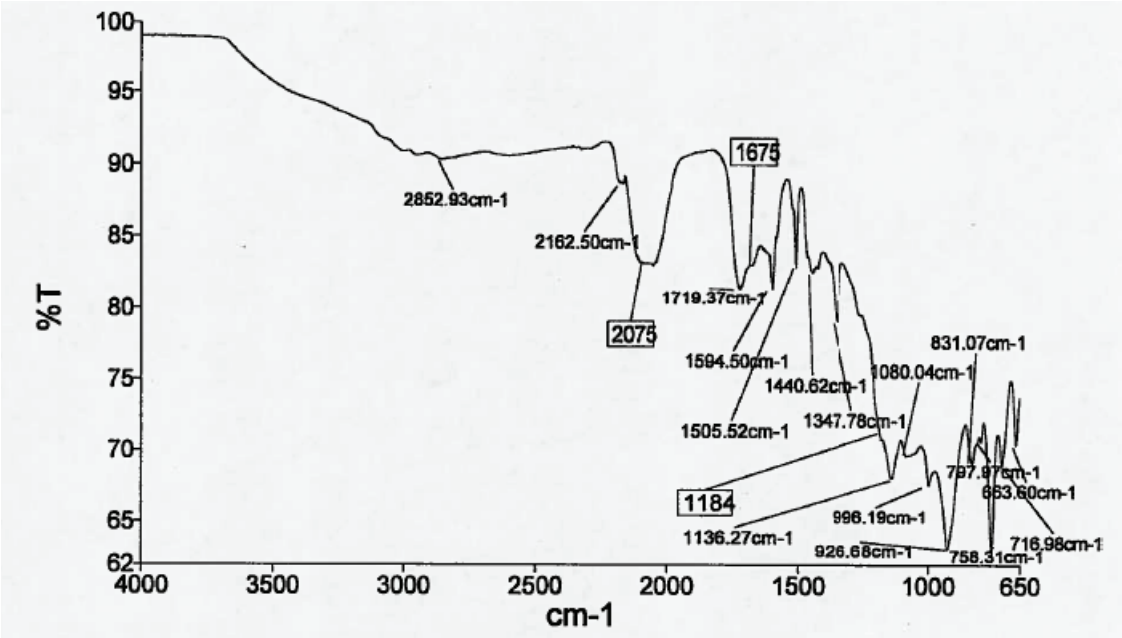
Supplementary Figure S7. $^{31}P\{^{1}H\}$ NMR spectrum (121.5 MHz, D2O, RT) of *p*-NO_2-Bn-H_6phospa.



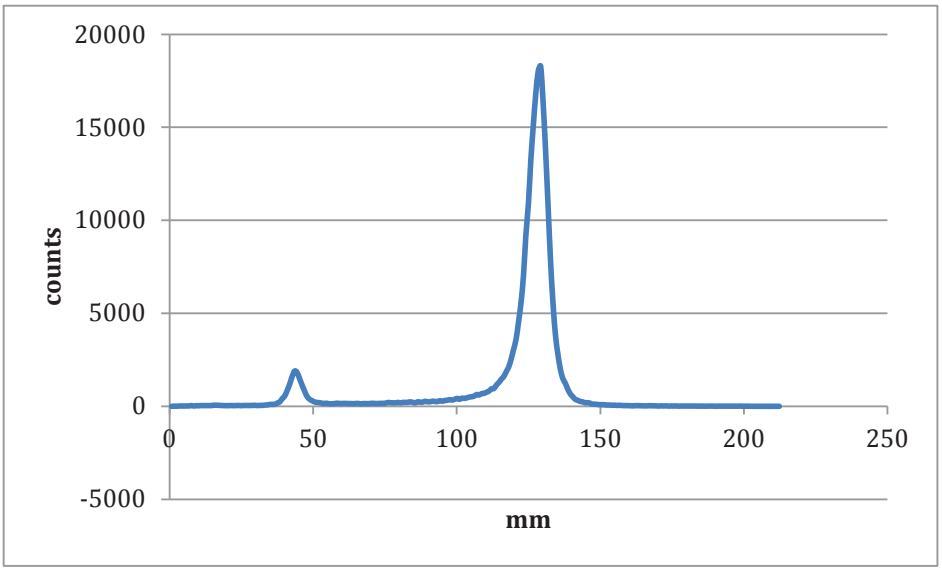
Supplementary Figure S8. ^{1}H NMR spectrum (600 MHz, D2O, RT) of *p*-SCN-Bn-H_6phospa



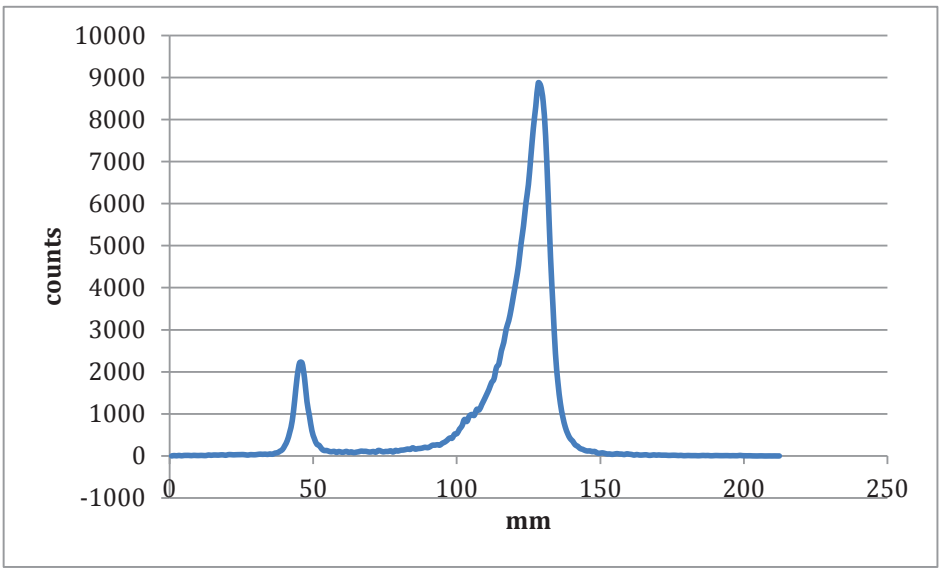
Supplementary Figure S9. ^{13}C NMR spectrum (150 MHz, MeOD, RT) of *p*-SCN-Bn-H_6phospa



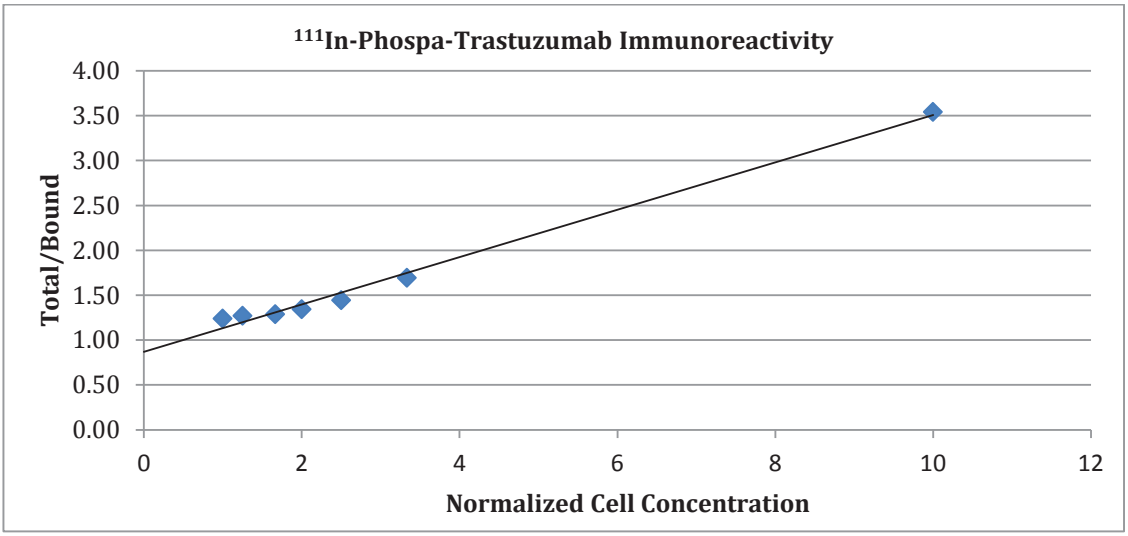
Supplementary Figure S10. ATR-IR spectrum (neat) of *p*-SCN-Bn-H_6phospa.



Supplementary Figure S11. iTLC of ^{89}Zr-phospa-trastuzumab (3.3 chelates per antibody, 80-90 μg of antibody, ~1 mCi of ^{89}Zr) after radiolabeling for 1 hour at room temperature (eluted with 50 mM EDTA, pH 5), showing radiochemical yield of 7%.



Supplementary Figure S12. iTLC of ^{89}Zr-phospa-trastuzumab (3.3 chelates per antibody, 80-90 μg of antibody, ~1 mCi of ^{89}Zr) after radiolabeling for 1 hour at 37 °C (eluted with 50 mM EDTA, pH 5), showing radiochemical yield of 9%.



Supplementary Figure S13. A plot of total/bound ^{111}In radioactivity against (1/[normalized cell concentration]) from *in vitro* immunoreactivity assays with HER2-expressing SKOV-3 cancer cells designed to calculate the immunoreactive fraction of an antibody at infinite antigen levels, showing an immunoreactivty of 97.9 ± 2.6% for ^{111}In-phospa-trastuzumab (n=9). This represents a negligible decrease from the theoretical maximum of 100% assumed for unmodified trastuzumab.