**SUPPLEMENTARY DATA**

**Supplementary Figure S1**

SIP(F8):
Sequence of monomer: E V Q L L E S G G G L V Q P G G S L R L S C A A S G F T
F S L F T M S W V R Q A P G K G L E W V S A I S G S G G S T Y Y A D S V K
G R F T I S R D N S K N T L Y L Q M N S L R A E D T A V Y Y C A K S T H L Y
L F D Y W G Q G T L V T V S S G G G G S G G G G S G G G G S G G G G E I V L T Q S P
G T L S L S P G E R A T L S C R A S Q S V S M P F L A W Y Q Q K P G Q A P R
L L I Y G A S S R A T G I P D R F S G S G S G T D F T L T I S R L E P E D F A V
Y Y C Q Q M R G R P P T F G Q G T K V E I K S G G S G G P R A A P E V Y A F
A T P E W P G S R D K R T L A C L I Q N F M P E D I S V Q W L H N E V Q L P
D A R H S T T Q P R K T K G S G F F V F S R L E V T R A E W E Q K D E F I C
R A V H E A A S P S Q T V Q R A V S V N P E S S R R G G **C**

Calculated mass of monomer: 38728

IgG(F8) HC:
E V Q L L E S G G G L V Q P G G S L R L S C A A S G F T F S L F T M S W V R
Q A P G K G L E W V S A I S G S G G S T Y Y A D S V K G R F T I S R D N S K
N T L Y L Q M N S L R A E D T A V Y Y C A K S T H L Y L F D Y W G Q G T L
V T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L V K D Y F P
E P V T V S W N S G A L T S G V H T F P A V L Q S S G L Y S L S S V V T V P
S S S L G T Q T Y I C N V N H K P S N T K V D K K V E P K S S D K T H T S P
P S P A P E L L G G P S V F L F P P K P K D T L M I S R T P E V T C V V V D V
S H E D P E V K F N W Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V
S V L T V L H Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G
Q P R E P Q V Y T L P P S R D E L T K N Q V S L T C L V K G F Y P S D I A V E
W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T V D K S R W Q
Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K

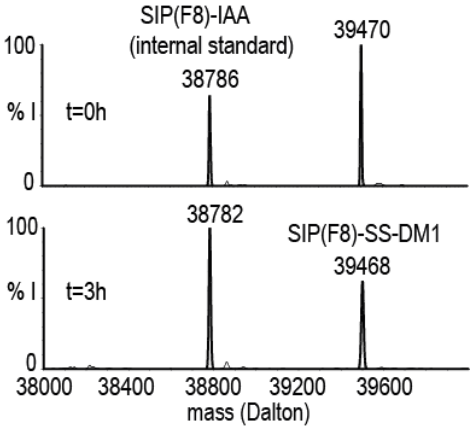
Calculated Mass of Heavy Chain: 48796

IgG(F8) LC:
E I V L T Q S P G T L S L S P G E R A T L S C R A S Q S V S M P F L A W Y Q Q
K P G Q A P R L L I Y G A S S R A T G I P D R F S G S G S G T D F T L T I S R L
E P E D F A V Y Y C Q Q M R G R P P T F G Q G T K V E I K R T V A A P S V F
I F P P S D E Q L K S G T A S V V C L L N N F Y P R E A K V Q W K V D N A L
Q S G N S Q E S V T E Q D S K D S T Y S L S S T L T L S K A D Y E K H K V Y
A C E V T H Q G L S S P V T K S F N R G E **C**

Calculated Mass of Light Chain: 23480

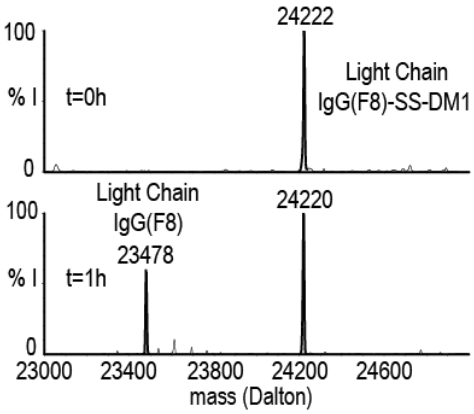
Amino acid sequences and calculated mass of SIP(F8) monomer and IgG(F8) light and heavy chain. Cysteines used for conjugation are highlighted in bold.

**Supplementary figure S2**



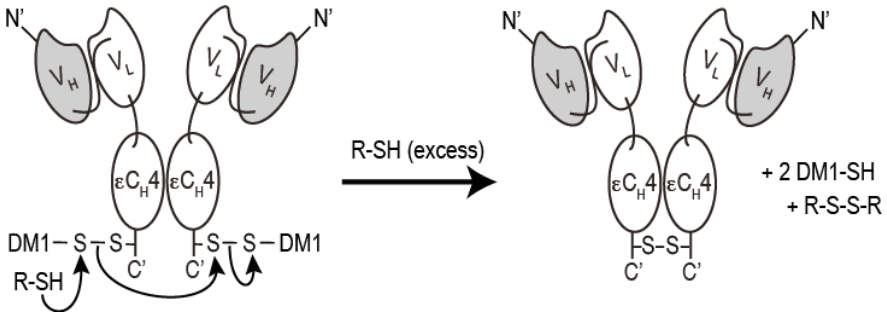

**SIP(F8)-SS-DM1 stability** : ESI-MS spectra of the SIP(F8)-SS-DM1 conjugate after 0 and 3 h of incubation in mice serum in presence of the SIP(F8)-IAA internal standard (Calculated mass = 38784 Da).

**Supplementary figure S3**




**IgG(F8)-SS-DM1 realease test** : ESI-MS spectra of the IgG(F8)-SS-DM1 conjugate after 0 and 1 h of incubation in mice serum in presence of 1mM DTT.

**Supplementary figure S4**




Schematic representation of a proposed mechanism for the formation of disulfide-bonded SIP products, upon cleavage of a first mixed disulfide bond between antibody moiety and DM1-SH drug.

**Supplementary table S1: Biodistribution results**

| | SIP(F8)-SS-DM1 | | | IgG(F8)-SS-DM1 | | |
|---|---|---|---|---|---|---|
| | 3h | 24h | 48h | 3h | 24h | 48h |
| Tumor | 8.18 ± 1.23 | 7.80 ± 1.97 | 3.11 ± 0.52 | 12.18 ± 0.97 | 32.80 ± 1.37 | 24.96 ± 2.61 |
| Liver | 1.84 ± 0.89 | 0.32 ± 0.09 | 0.12 ± 0.01 | 9.74 ± 0.57 | 4.51 ± 0.50 | 2.85 ± 0.18 |
| Lung | 5.33 ± 2.71 | 0.69 ± 0.35 | 0.21 ± 0.15 | 29.23 ± 1.60 | 11.99 ± 2.15 | 5.54 ± 2.73 |
| Spleen | 1.65 ± 0.83 | 0.39 ± 0.12 | 0.11 ± 0.06 | 5.35 ± 2.82 | 3.63 ± 0.27 | 1.13 ± 0.63 |
| Heart | 2.11 ± 0.14 | 0.22 ± 0.04 | 0.07 ± 0.01 | 4.72 ± 4.36 | 3.94 ± 0.58 | 2.73 ± 0.10 |
| Kidney | 9.75 ± 0.12 | 0.42 ± 0.18 | 0.28 ± 0.11 | 13.45 ± 3.69 | 7.08 ± 0.20 | 4.05 ± 1.15 |
| Colon | 0.38 ± 0.33 | 0.08 ± 0.03 | 0.18 ± 0.09 | 4.47 ± 4.37 | 7.36 ± 0.98 | 1.38 ± 0.70 |
| Stomach | 1.71 ± 0.38 | 0.61 ± 0.23 | 0.20 ± 0.18 | 1.36 ± 1.11 | 5.99 ± 0.99 | 3.13 ± 1.37 |
| Blood | 6.62 ± 0.08 | 0.77 ± 0.08 | 0.29 ± 0.03 | 33.49 ± 0.13 | 15.62 ± 2.04 | 9.4 ± 0.89 |

Results of biodistribution experiments, performed in F9 tumor-bearing mice with radioiodinated ADC preparations. Details are presented in the experimental procedures section. Results are expressed as the percent of antibody injected activity per gram of tissue (%IA/g) ± SD