Supplementary Materials:

Figures

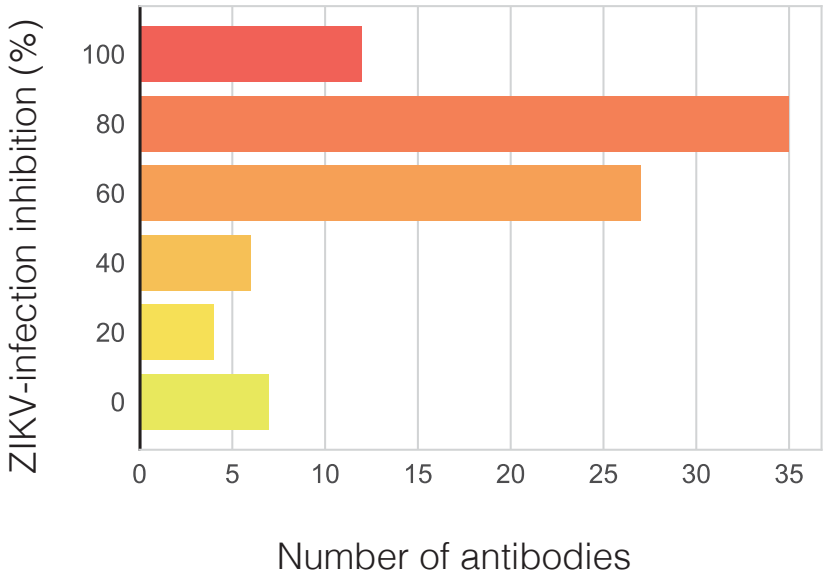

Fig. S1.
Plasmablast-derived human mAbs neutralize ZIKV *in vitro*. Ninety-one mAbs generated from a ZIKV-infected patient were screened for ZIKV-neutralization potency using a Vero cell infectivity assay and enumerated by FRNT. The percentage of ZIKV foci reduced in the presence of 1 μg ml^{-1} of mAb, compared to isotype control mAb, was defined as the percent inhibition.

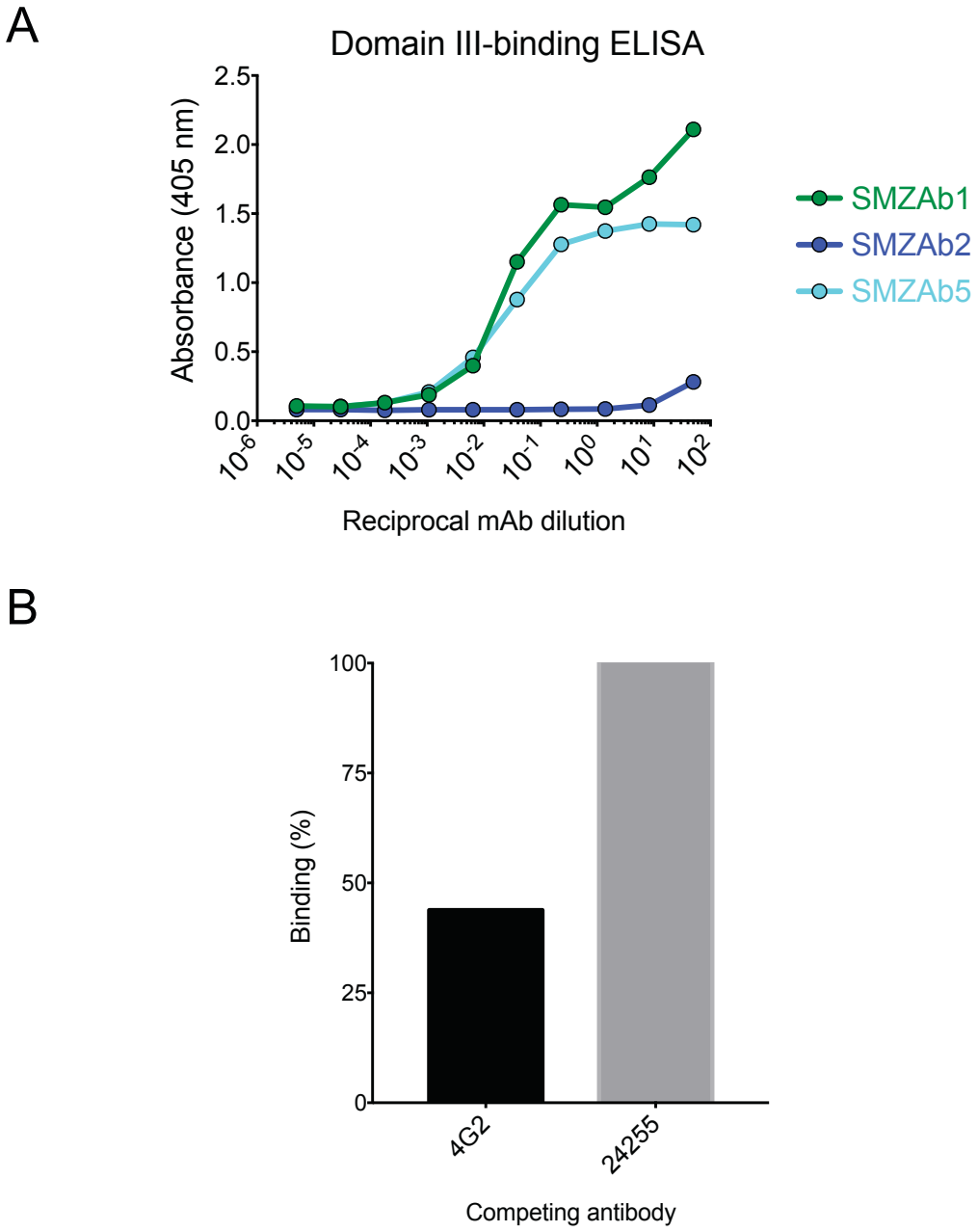

Fig. S2.
Epitope mapping. SMZAb1, SMZAb2, and SMZAb5 ZIKV E protein epitope specificity was evaluated. (**A**) mAbs with domain III specificity, SMZAb1 and SMZAb5, were identified by a domain III binding ELISA. (**B**) SMZAb2 epitope specificity was determined by a fusion loop-specific mAb competition assay with pre-incubation of 4G2, a fusion loop (domain II)-specific mAb, with ZIKV E protein prior to the addition of SMZAb2. Percent reduction of the binding of SMZAb2 to ZIKV E protein in the presence of 4G2 was calculated compared to pre-incubation with a previously characterized domain III-binding mAb, ADI24255.

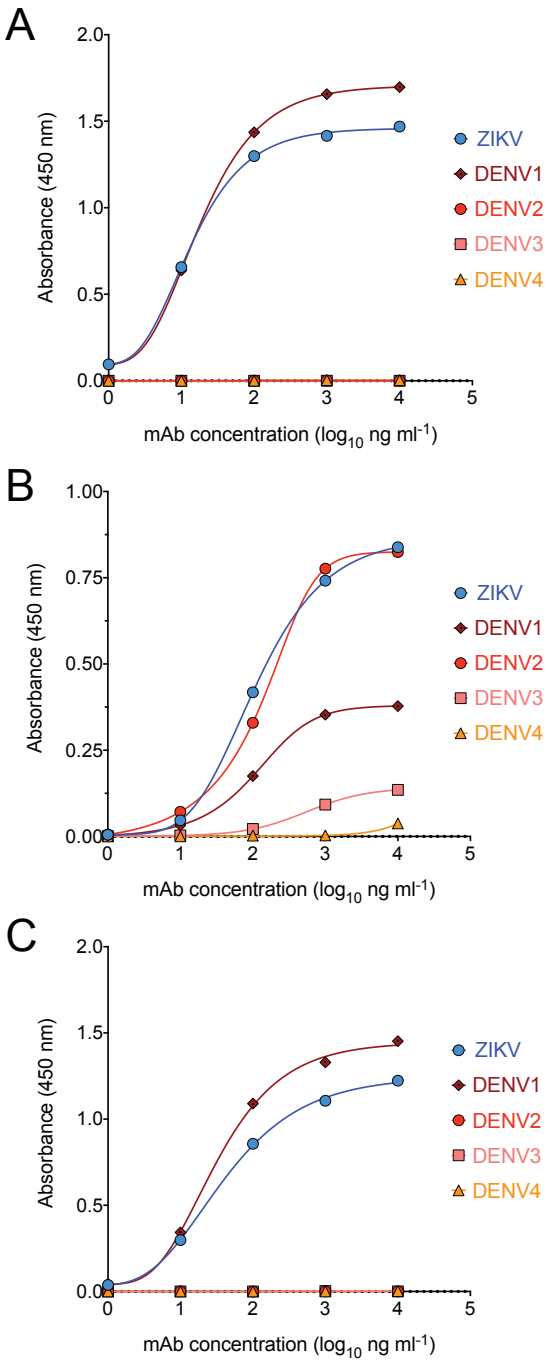

Fig. S3.

Binding of SMZAb1, SMZAb2, SMZAb5 to whole ZIKV or DENV was evaluated by virus-capture ELISA using 4G2. (**A**) SMZAb1, (**B**) SMZAb 2, (**C**) SMZAb5 binding to ZIKV and DENV.

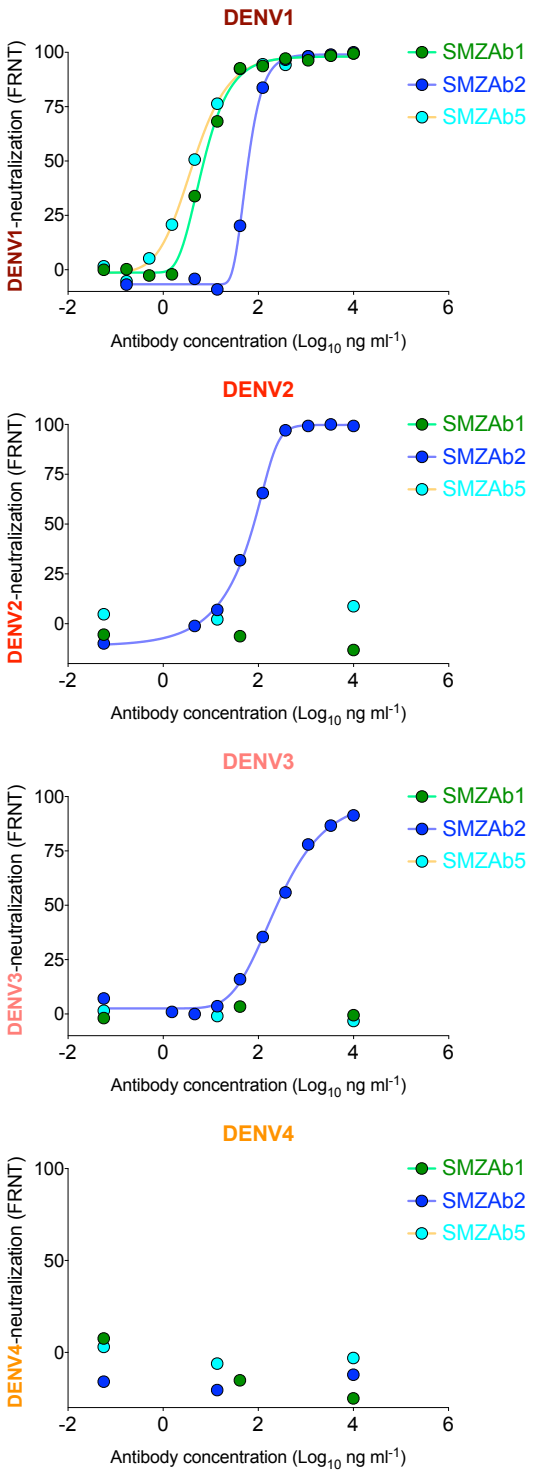

Fig. S4.
DENV-neutralization by SMZAbs. SMZAb1, SMZAb2, and SMZAb5 neutralize a subset of DENV serotypes *in vitro*. mAbs were screened for DENV-neutralization potency using the FRNT infectivity assay with (**A**) DENV1, (**B**) DENV2, (**C**) DENV3, and (**D**) DENV4. Lines represent nonlinear regression curves for mAbs with neutralization activity.

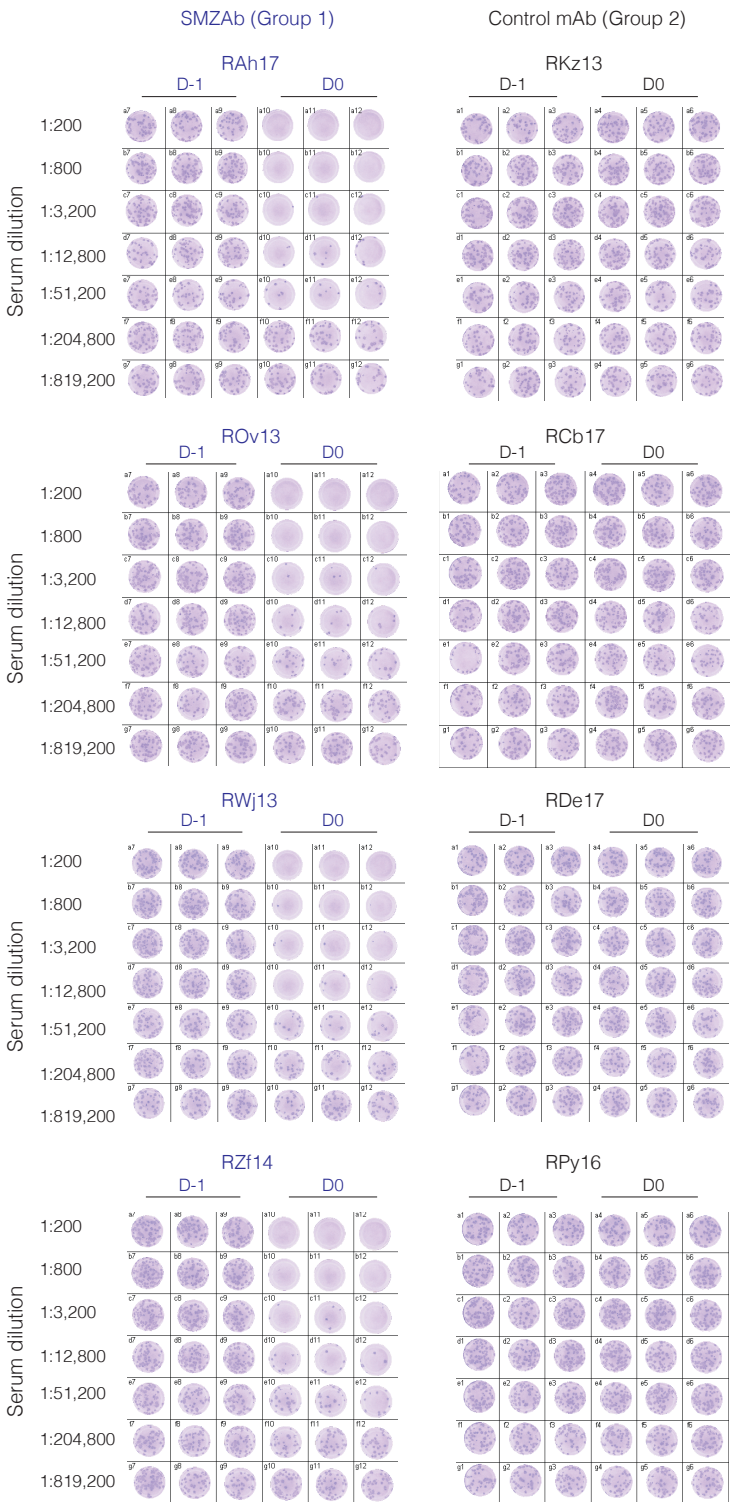

Fig. S5.
ZIKV-neutralizing activity post mAb infusion (FRNT).

Table S1.
SMZAb amino acid sequences

SMZAb1 heavy chain
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYGMSWVRQAPGKGLQWVSGISSIDDSKY
YADSVKGRFTISRDNSKNTLYLQMNSLTVADTALYYCGKDRVARGFGELLDSWGQGTL
VTVSS

SMZAb1 light chain
AIRMTQSPSTLSASVGDRVTITCRASQSINSWLAWFQQKPGKAPKLLMFRASNLHTGVP
SRFSGSGSGTEFTLTISSLQPDDFATYYCQHYYSYPWTFGQGTKVEIK

SMZAb2 heavy chain
EVQLVQSGAEVKKPGSSVKVSCKAPGGTFSSYAMSWVRQAPGQGPEWVGGIVPVYGT
SRYAQKFQGRGTITADESTSTVYLELSSLRSEDTALYYCARVRYYGSGTYYGGDAFDF
WGQGTMVTVSS

SMZAb2 light chain
QTVVTQEPSFSVSPGGTVTLTCGLTSDSVSIHLYPSWYQQTPGQAPRALIYNTNTRSSGV
PDRFSGSILGNKAALTITGAQADDESVYFCVVYMGSGIWVFGGGTKLTVL

SMZAb5 heavy chain
EVQLLESGGGLVQPGGSLRLSCAASGFTFRDYGMSWVRQAPGKGLEWVSAISSIDDSTY
YAASVRGRFTISRDNSKNTLDLQMNSLRAEDTAVYFCAKDRSTRGFGELLNYWGQGTL
VTVSS

SMZAb5 light chain
AIRMTQSPSTLSASVGDRVTITCRASQNINSWLAWYQQKPGKAPNLLIYKASSLESGVPL
RFSGSGSGTEFTLTISRLQPDDFATYYCQHYYSYPWTFGQGTKVEIK

Table S2.
Neutralization of ZIKV strains and DENV serotypes by SMZAbs ($FRNT_{50}$ µg ml^{-1}).

Virus	SMZAb1	SMZAb2	SMZAb3
ZIKV Paraiba	0.014	0.12	0.005
ZIKV Uganda	None	0.37	None
ZIKV Panama	0.37	0.37	1.11
ZIKV Honduras	0.12	0.37	0.12
ZIKV Cambodia	0.12	0.12	0.12
ZIKV Puerto Rico	0.12	0.12	1.11
ZIKV Senegal	None	0.12	10
DENV 1	0.014	0.12	.005
DENV 2	None	0.12	None
DENV 3	None	0.37	None
DENV 4	None	None	None

Table S3.
ZIKV Paraiba/2015-neutralization by SMZAbs prior to infusion.

Antibody ID	$PRNT_{50}$ (ng ml^{-1})
SMZAb1	12
SMZAb2	147
SMZAb5	8

Table S4.
Study animals

Animal ID	Group	Sex	Date of birth	Weight (kg)
RAh17	Group 1 (SMZAb cocktail)	Female	5/22/15	3.5
RCb17	Group 1 (SMZAb cocktail)	Male	4/19/15	3.2
RDe17	Group 1 (SMZAb cocktail)	Male	5/3/15	3.1
RPy16	Group 1 (SMZAb cocktail)	Female	3/19/15	3.5
RKz13	Group 2 (Control mAb)	Male	5/1/10	15.1
ROv13	Group 2 (Control mAb)	Male	4/17/10	14.3
RWj13	Group 2 (Control mAb)	Female	5/5/09	8.9
RZf14	Group 2 (Control mAb)	Female	6/16/10	8.6

Table S5.
Viral titers (Log_{10} PFU ml^{-1}) in serum post ZIKV-challenge.

	Group 1 (SMZAb cocktail)				**Group 2 (Control mAb)**			
Day	**Rah17**	**RCb17**	**RDe17**	**RPy16**	**Rkz13**	**ROv13**	**RWj13**	**RZf14**
Pre-challenge	<0.7	<0.7	<0.7	<0.7	<0.7	<0.7	<0.7	<0.7
0	<0.7	<0.7	<0.7	<0.7	<0.7	<0.7	<0.7	<0.7
2	<0.7	<0.7	<0.7	<0.7	**2.9**	**2.4**	**2.9**	**2.6**
3	<0.7	<0.7	<0.7	<0.7	**2.9**	**2.7**	**2.8**	**3.2**
4	<0.7	<0.7	<0.7	<0.7	**2.3**	**2.4**	**1.9**	**2.8**
7	<0.7	<0.7	<0.7	<0.7	<0.7	<0.7	<0.7	<0.7
14	<0.7	<0.7	<0.7	<0.7	<0.7	<0.7	<0.7	<0.7
21	<0.7	<0.7	<0.7	<0.7	<0.7	<0.7	<0.7	<0.7

Table S6.
Viral titers (vRNA copies ml^{-1}) in serum post ZIKV-challenge.

	Group 1 (SMZAb cocktail)				**Group 2 (Control mAb)**			
Day	**Rah17**	**RCb17**	**RDe17**	**RPy16**	**Rkz13**	**ROv13**	**RWj13**	**RZf14**
0	<43	<43	<43	<43	<43	<43	<43	<43
2	<43	<43	<43	<43	**2.14E+05**	**1.32E+04**	**1.91E+05**	**7.74E+03**
3	<43	<43	<43	<43	**4.73E+05**	**8.84E+04**	**4.06E+05**	**1.24E+05**
4	<43	<43	<43	<43	**3.77E+04**	**1.29E+04**	**2.07E+04**	**7.71E+04**
7	<43	<43	<43	<43	<43	<43	**1.30E+02**	<43
14	<43	<43	<43	<43	<43	<43	<43	<43
21	<43	<43	<43	<43	<43	<43	<43	<43