Supplementary information

Blocking *Borrelia burgdorferi* transmission from infected ticks to non-human primates with a human monoclonal antibody

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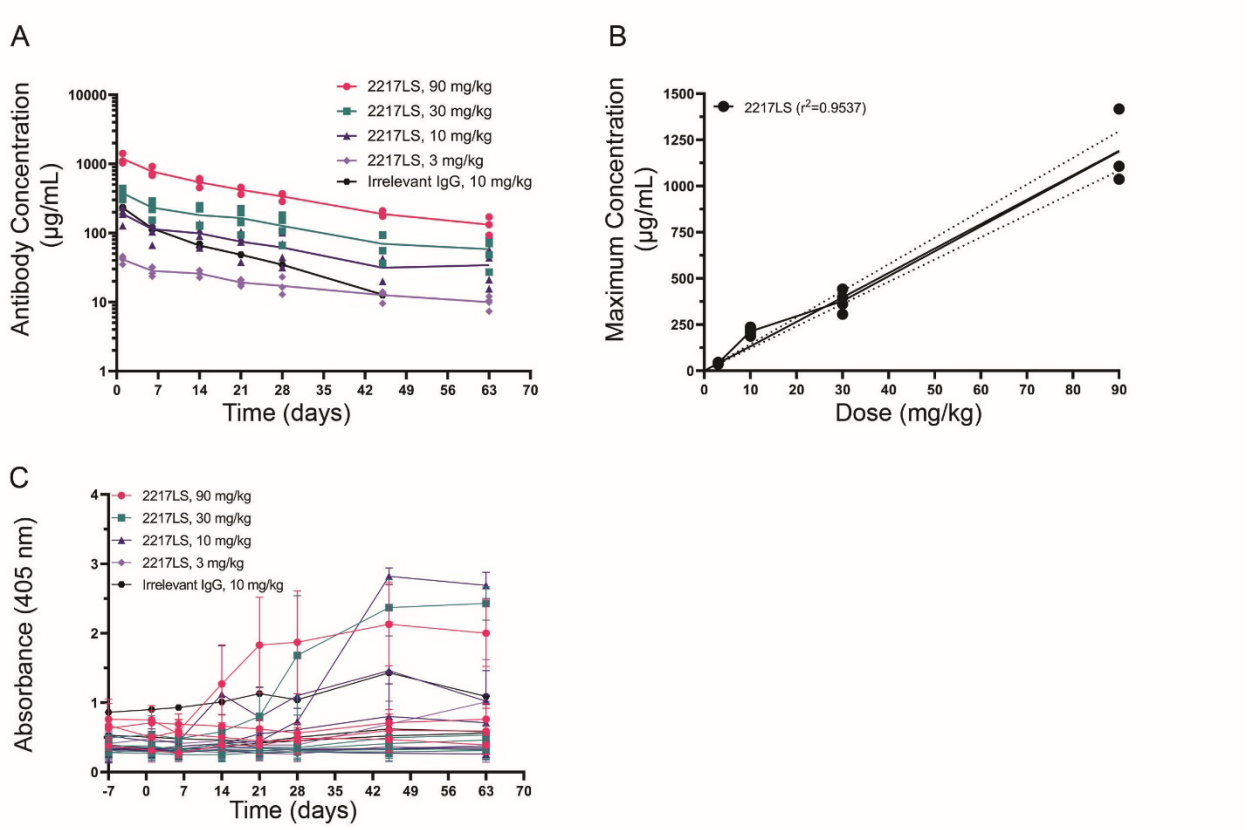
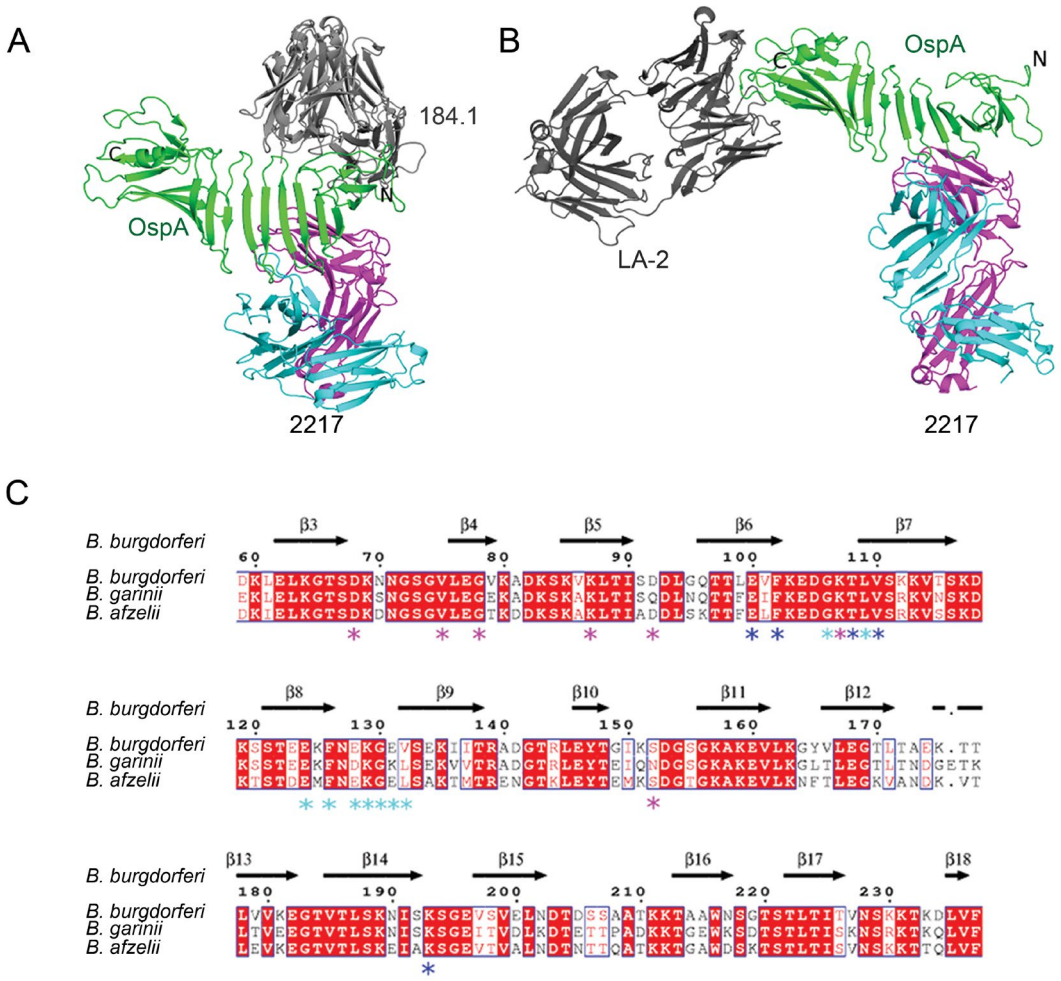


Supplementary Figure 1. Pharmacokinetic data of non-human primates in efficacy model. (A) Observed serum pharmacokinetic profile after a single dose of 2217LS at 3 mg/kg (light purple diamond), 10 mg/kg (dark purple triangle), 30 mg/kg (green square), 90 mg/kg (red circle), and an irrelevant IgG at 10 mg/kg (black circle) as measured by ELISA. (B) Antibody concentration measured 24 hours after injection showed linear correlation (r^2 = 0.9537) between the different 2217LS doses. (C) All animals were screened for anti-drug antibody (ADA) responses by detection of non-human primate IgGs against 2217LS or the irrelevant IgG. Four out of eighteen of the animals showed responses elevated above the baseline and defined as greater than the mean plus three times the standard deviation of the Day -7 values. These animals were distributed among the 10, 30, and 90 mg/kg suggesting that the responses were not concentration dependent. Additionally, two of the animals in the irrelevant IgG group also showed similar ADA responses. Animals exhibiting an ADA response were excluded in the serum pharmacokinetic profile.



Supplementary Figure 2. Sequence alignment of OspA and epitope comparison among 2217, 184,1 and LA-2 . Novel OspA epitope. Superpositioned OspA-2217 complex (cyan and magenta) with (A) OspA-184.1 complex (PDB ID: 1OSP) (gray) and (B) OspA-LA2 complex (PDB ID: 1FJ1) (gray) depicting the different interaction surfaces bound by each Fab. (C) Sequence alignment of the interacting region of OspA from *Borrelia burgdorferi* with OspA from *B. garinii* and *B. afzelii*. Magenta asterisks depict V_L (L1-L3) interacting residues, cyan asterisks depict V_H (H1-H3) interacting residues, and blue asterisks denote interaction with V_L and V_H residues. Secondary structural elements (β-strands 3-18) from OspA (*B. burgdorferi)* bound go Fab 2217 are drawn as black arrows above the sequence and labelled accordingly. Red colored sequence denotes sequence identity and white colored sequence shows reduced sequence similarity. Figure made with ClustalW and ESPript 3.0 (REF 9).

Supplementary Table 1. Detection of *B. burgdorferi* in mice by tissue biopsy[a] observations, DNA (PCR), and seroconversion

Treatment	Animal Number	Observations	PCR	Whole Cell Lysate ELISA
2217 5 mg/kg	111	-	-	-
	112	-	-	-
	113	-	-	-
	114	-	-	-
	115	-	-	-
	186	-	-	-
	187	+ (h, b, e)	+ (h, b, e)	+
	188	-	-	-
	189	-	-	-
	190	-	-	-
	206	-	-	-
	207	-	-	-
	208	-	-	-
	209	-	-	-
	210	-	-	-
2217LS 5 mg/kg	166	-	-	-
	167	-	-	-
	168	+ (h, b, e)	+ (h, b, e)	+
	169	-	-	-
	170	-	-	-
	211	-	-	-
	212	-	-	-
	213	-	-	-
	214	-	-	-
	215	-	-	-

[a] Tissues were collected from the heart (H), bladder (b), ankle (a), and ear (e)

Supplementary Table 2. Crystallographic data collection and refinement statistics

Data Collection	
Complex	OspA-2217
Space group	C2
Cell parameters: *a,b,c* (Å) / □□(°)	173.4, 99.3, 121.6 / 103.5
BNL Beamline	BLL 8.2.2
Resolution range [a,] (Å)	50-3.05 (3.1-3.05)
wavelength (Å)	0.979
No. of reflections	1753894
Average redundancy[a]	3.8(3.8)
Wilson B-factor (Å^2)	73.0
$(I)/(\delta)$[a]	6.9(0.7)
Completeness[a] (%)	99.2(98.6)
R_{merge}[a,b] (%)	7.3(93.7)
$CC^{1/2}$ [a,c]	(0.54)
Refinement	
Bragg spacings [a,] (Å)	48.9-3.05(3.13-3.05)
R[d] / R_{free} [e] (%)	26.9 / 30.5
No. of Protein atoms	10,230
No. of Waters	14
RMSD bond length (Å)	0.003
RMSD bond angle (°)	0.88
Average B-factors Protein atoms (Å^2)	71.7
Average B-factors Water atoms (Å^2)	49.2
Ramachandran favored / allowed[f] (%)	94 / 99
PDB code	7JWG

[a] Values in outermost shell are given in parentheses.
[b] $R_{merge} = (\sum | I_i - \langle I_i \rangle |)/\sum | I_i |$, where I_i is the integrated intensity of a given reflection.
[c] $CC_{1/2} = (1+q^2 s_e^2/\langle I \rangle 2^{-1}$, where s_e denotes the mean error within a half-datase, $CC_{1/2}$ is the correlation coefficient of two split data sets each derived by averaging half of the observations for a given reflection.
[d] $R = \sum | |Fo| - |Fc| | / \sum | |Fo| |$, where Fo and Fc denote observe and calculated structure factors, respectively.
[e] Rfree was calculated using 5% of data excluded from refinement.
[f] Calculated using Molprobity.

Supplementary Table 3. Animal characteristics for cynomolgus monkeys (*Macaca fascicularis*) pharmacokinetic study

Treatment	Animal Number	Sex	Body Weight (kg)	Age (yr)
2217 10 mg/kg	G64M	Male	2.8	2.2
	HAEK	Male	2.8	2.2
	G82F	Male	2.5	2.0
	G83M	Male	2.6	2.0
2217LS 10 mg/kg	G26A	Male	3.3	2.6
	1308073	Male	2.8	3.6
	1311295	Male	2.9	3.3
	1312177	Male	2.6	3.3

Supplementary Table 4. Animal characteristics for Rhesus Macaque (*Macaca mulatta*) efficacy study

Treatment	Animal Number	Sex	Body Weight (kg)	Age (yr)
2217LS 90 mg/kg	RA3840	Female	4.3	3.7
	RA3835	Female	5.0	3.8
	RA3896	Male	4.8	3.7
	RA3901	Male	4.0	3.8
2217LS 30 mg/kg	RA3837	Female	3.7	3.5
	RA3842	Female	4.0	3.7
	RA3898	Male	4.3	3.8
	RA3899	Male	4.2	3.8
	RA3838	Female	3.8	3.5
2217LS 10 mg/kg	G67H	Female	4.8	3.8
	J797	Female	3.8	3.7
	G71F	Female	4.5	3.7
	RA3834	Female	4.6	3.8
	RA3893	Male	4.0	3.6
	RA3897	Male	4.3	3.6
2217LS 3 mg/kg	RA3836	Female	4.7	3.7
	RA3839	Female	4.4	3.7
	RA3869	Male	4.0	3.8
	RA3875	Male	4.2	3.7
Irrelevant IgG 10 mg/kg	G72G	Female	4.0	3.8
	J709	Female	3.8	3.5
	J393	Female	4.5	3.7