TNX-4800: A Long-Acting, Bactericidal, Human Monoclonal Antibody to Prevent Lyme Disease in the U.S.

NASDAQ: TNXP November 24, 2026



PO6173 Nov. 16, 2026 1690

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Certain statements in this presentation are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995 including those relating to the Company's expected financial performance, the Company's anticipated cash runway, the Company's expected timelines regarding its clinical and preclinical programs, expected enrollment in the Company's clinical trials, expected adoption by the medical community and patients of the Company's products, the expected outcome of litigation, and expected timelines regarding the Company's manufacturing processes. These statements may be identified by the use of forward-looking words such as "anticipate," "believe," "forecast," "estimate," "expect," and "intend," among others. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, risks related to the failure to successfully launch and commercialize TONMYA® and any of our approved products; risks related to the failure to obtain FDA clearances or approvals and noncompliance with FDA regulations; risks related to the timing and progress of clinical development of our product candidates; our need for additional financing; uncertainties of patent protection and litigation; uncertainties of government or third-party payer reimbursement; limited research and development efforts and dependence upon third parties; and substantial competition. As with any pharmaceutical under development, there are significant risks in the development, regulatory approval and commercialization of new products. Tonix does not undertake an obligation to update or revise any forward-looking statement. Investors should read the risk factors set forth in the Company's Annual Report on Form 10-K for the year ended December 31, 2025, as filed with the SEC on March 12, 2026, and periodic reports filed with the SEC on or after the date thereof. Tonix does not undertake an obligation to update or revise any forward-looking statement. All of Tonix's forward-looking statements are expressly qualified by all such risk factors and other cautionary statements. The information set forth herein speaks only as of the date thereof.

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TNX-4800 Summary

- TNX-4800 is a long-acting borreliacidal, human monoclonal antibody (mAb) with an engineered crystallizable fragment (Fc) domain for an extended half-life that targets outer surface protein A (OspA) of *Borrelia burgdorferi*
  - *Borrelia burgdorferi* causes 99.9% of Lyme disease cases in the U.S.
- There are currently no marketed U.S. Food and Drug Administration (FDA)-approved vaccines or prophylactics to protect against Lyme disease
- TNX-4800 was studied in a Phase 1, randomized, double-blind, sequential dose-escalation study (NCT04863287) evaluating safety, tolerability, pharmacokinetics (PK), and immunogenicity in healthy adult participants
- Pending FDA agreement on the final protocol, the Company is planning an adaptive Phase 2 TRAIL field study to evaluate the safety, efficacy, and tolerability of TNX-4800 in preventing Lyme disease in adult participants from Lyme-endemic areas
  - Planned 2028 cohort: balance of efficacy cohort. Enrollment may extend into 2029 if needed
- TNX-4800 is being developed as a prophylactic to be administered subcutaneously in the spring with a booster after ~12 weeks (Day 85), which is expected to provide protection within 2 days for at least 6 months*

*Primary efficacy endpoint through 6 months.
Key secondary efficacy endpoints through weeks 12 and 38.

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Healthcare Providers (HCPs) and Patients Want Rapid Protection Against Lyme disease[1]

- HCPs and consumers surveyed see a significant need for a Lyme vaccine or prophylaxis. Most residents and travelers surveyed consider Lyme disease severe
- An estimated 476,000 people are diagnosed and treated for Lyme disease each year in the United States
- TNX-4800 targets protection within two days, with two seasonal doses intended to provide at least six months of protection. Human preventive efficacy remains to be established

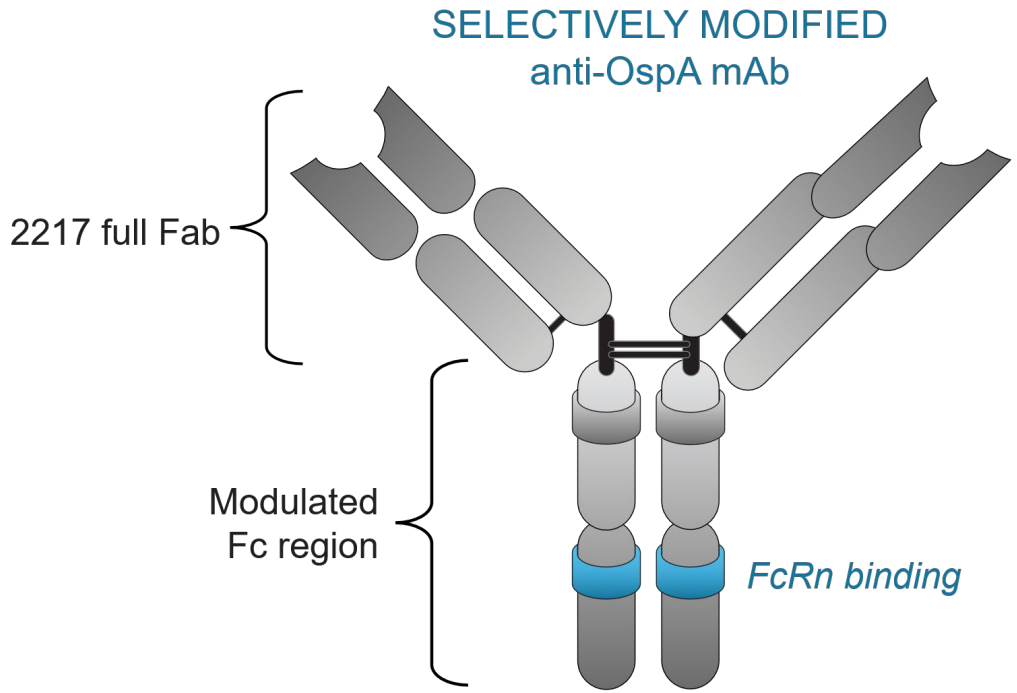
1. Source: Trinity market research commissioned by Tonix in Q3'26.

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About TNX-4800, a Long-acting anti-OspA Monoclonal Antibody

TNX-4800 (formerly 2217LS) is a long-acting borreliacidal, human mAb with an engineered Fc domain for an extended half-life that targets OspA of *Borrelia burgdorferi*[1,2]



LS substitutions maintain C1q binding and function and augment FcRn binding for extended half-life

1. Schiller ZA, et al. *J Clin Invest.* 2021;131(11):e144843.
2. Wang Y, et al. *J Infect Dis.* 2016;214(2):205-211.

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TNX-4800 Characteristics

- TNX-4800 is being developed as a prophylactic to be administered subcutaneously in the spring with a booster after ~3 months (Day 85), which is expected to provide protection within 2 days for at least 6 months*
  - Each 450 mg SC dose will be divided into 2 injections of 1.5 mL volume with 225 mg each
  - TNX-4800 is designed for rapid protection without a multidose vaccine priming series; clinical efficacy has not yet been established
- TNX-4800 acts inside the tick to kill *Borrelia* and block the differentiation and transmission of *Borrelia*
- Nonclinical efficacy studies (mice and non-human primates) provide evidence that TNX-4800 mean serum levels ≥15 µg/ml resulted in a protection of animals from infection with *B. burgdorferi*-infected nymphs
- Phase 1 study of TNX-4800 showed no significant clinical or laboratory safety signals:
  - Serum TNX-4800 was measurable at the earliest sampling time of 48 hours, indicating rapid absorption
  - TNX-4800 was generally well tolerated in the Phase 1 study in healthy participants
  - The PK of TNX-4800 were typical of a human IgG1 with an Fc domain mutation that extends half-life
- TNX-4800 is a mAb measured in concentration “µg/mL” in serum, which is different from the polyclonal antibody responses to vaccines that are measured in “titers”
- TNX-4800 serum concentration enables direct PK-driven exposure targeting

*Primary efficacy endpoint through 6 months.
Key secondary efficacy endpoints through weeks 12 and 38.

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Addressing the Significant Public Health Challenge of Lyme Disease in the U.S.

- ✓ Phase 1 study complete, showing favorable safety, tolerability, immunogenicity, and pharmacokinetics
- ✓ Phase 2 adaptive field study planning and manufacturing of investigational product underway for 1Q 2027

TNX-4800 Upcoming Milestones



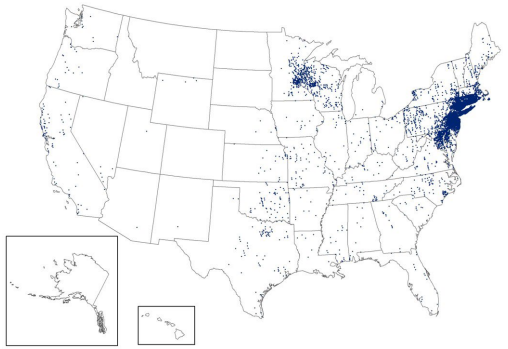
Manufacturing Investigational Product for Human Studies Currently on Track for 1Q 2027

Plan to Initiate Adaptive Phase 2 Field Study, Pending FDA Agreement on Final Protocol

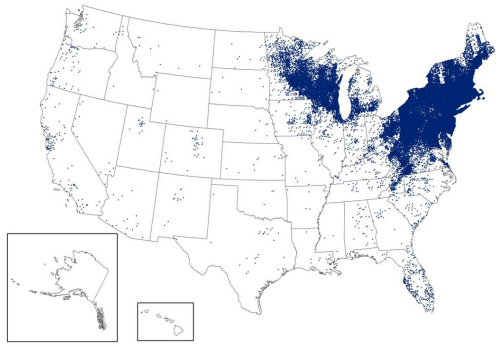
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Lyme Disease: Epidemiology in the U.S.

The range of Lyme disease is expanding[1]



1995

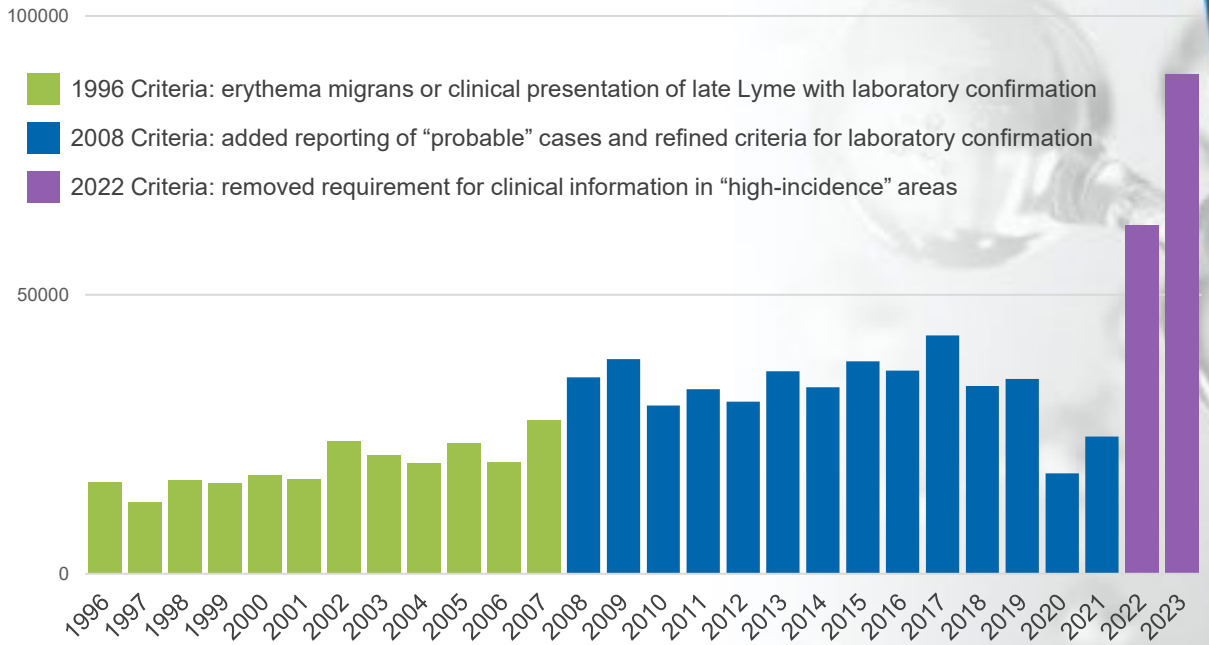


2023

Images from CDC NNDSS

Lyme disease is reported most often in the Northeast and Midwest, with 95% of cases coming from “high-incidence” areas[1]

Lyme disease is an increasing problem[2]



The actual prevalence of Lyme disease is estimated to be 8 to 12 times higher than reported.[3] In 2022, more sensitive surveillance criteria resulted in a 67% increase in reported cases[2]

1. U.S. Centers for Disease Control and Prevention. National Notifiable Diseases Surveillance System; maps. February 11, 2025. Accessed July 18, 2025. https://www.cdc.gov/lyme/data-research/facts-stats/surveillance-data-1.html.
2. U.S. Centers for Disease Control and Prevention. National Notifiable Diseases Surveillance System; graphs: annual cases. February 11, 2025. Accessed July 18, 2025. https://www.cdc.gov/lyme/data-research/facts-stats/surveillance-data-1.html
3. Rodino KG, et al. *J Clin Microbiol*. 2025:e0080723.

CDC=Centers for Disease Control and Prevention; NNDSS=National Notifiable Diseases Surveillance System.

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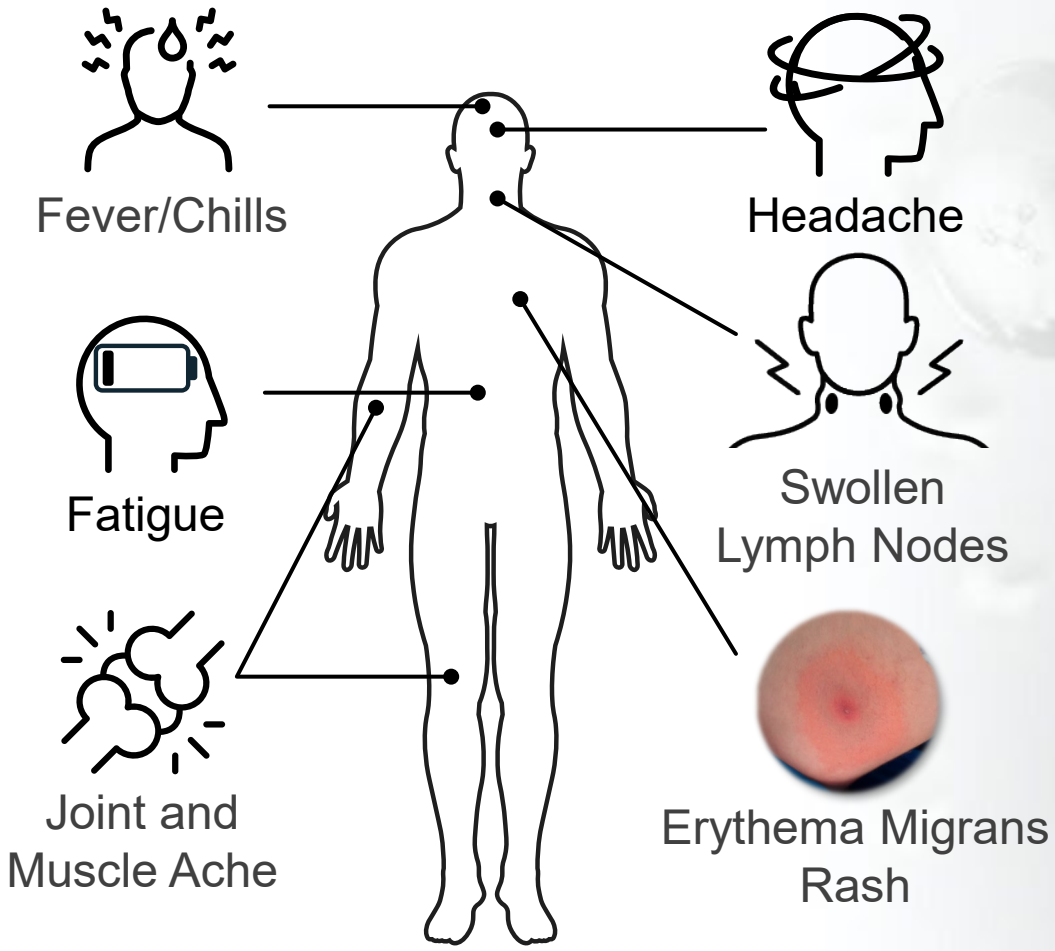
Clinical Presentation: Acute Lyme Disease

There are 3 stages of Lyme disease: early, early disseminated, and late[1]

Early, or acute, Lyme disease has many signs or symptoms[1,2]

Erythema migrans rash is a hallmark symptom of early Lyme disease, occurring in 70% to 80% of people[1,2]

- Begins at site of tick bite and expands up to 12 inches in diameter
- Development is delayed, with an average of 7 days after bite
- Sometimes has a “bull’s-eye” appearance

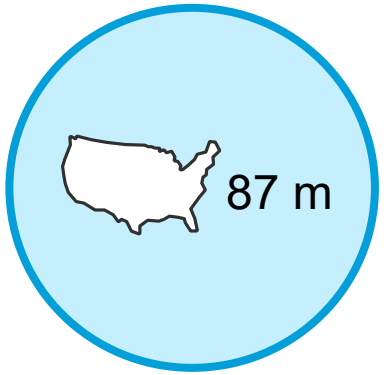


1. Cleveland Clinic. Updated August 16, 2022. Accessed July 18, 2025. https://my.clevelandclinic.org/health/diseases/11586-lyme-disease.
2. U.S. Centers for Disease Control and Prevention. May 15, 2024. Accessed July 18, 2025. https://www.cdc.gov/lyme/signs-symptoms/index.html.

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Current Landscape for Lyme Disease Prophylaxis and Treatment



U.S. population where Lyme disease is endemic is estimated to be 87 million[1]



Recommendations for pre-exposure prevention focus on tick bite avoidance. No vaccine is currently on the market[2-5]



Presently available post-exposure prophylaxis is limited to antibiotic regimens, typically doxycycline.[6] Extended use of antibiotics has recognized side effects[5]



Approximately 10-20% of Lyme disease patients experience long-term sequelae including Post-Treatment Lyme Disease Syndrome (PTLDS)[6,7]

1. Kugeler KJ, et al. *Emerg Infect Dis.* 2021;27(2):616-619.
2. U.S. Centers for Disease Control and Prevention. May 15, 2024. Accessed July 18, 2025. https://www.cdc.gov/lyme/signs-symptoms/index.html.
3. https://www.idsociety.org/practice-guideline/lyme-disease.
4. Chan PA, et al.. *Sex Transm Dis*. 2023 50(11):701-712.
5. Lantos PM et al, *Clinical Infectious Diseases*, 72,(1) 2021, Pages e1–e48.
6. Zafar K, et al. *Front Microbiol*. 2024;15:1459202.
7. Melia M.T.*N Engl J Med.* 2016;374:1277–1278.

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Lyme Disease in the U.S. and Europe Involves Different *Borrelia Species*



- **>99.9% of cases caused by *B. burgdorferi sensu stricto (s.s.)*[1,2]**
  - U.S. *B. burgdorferi* minimal genetic variability[3]
  - Incidence is seasonal in summer months[3]



- **Caused by a diverse group of Borrelia species[1]**
  - Species include *B. afzelii, B. garinii, and B. bavariensis*
  - Lyme disease “Season” varies, based on country and climate

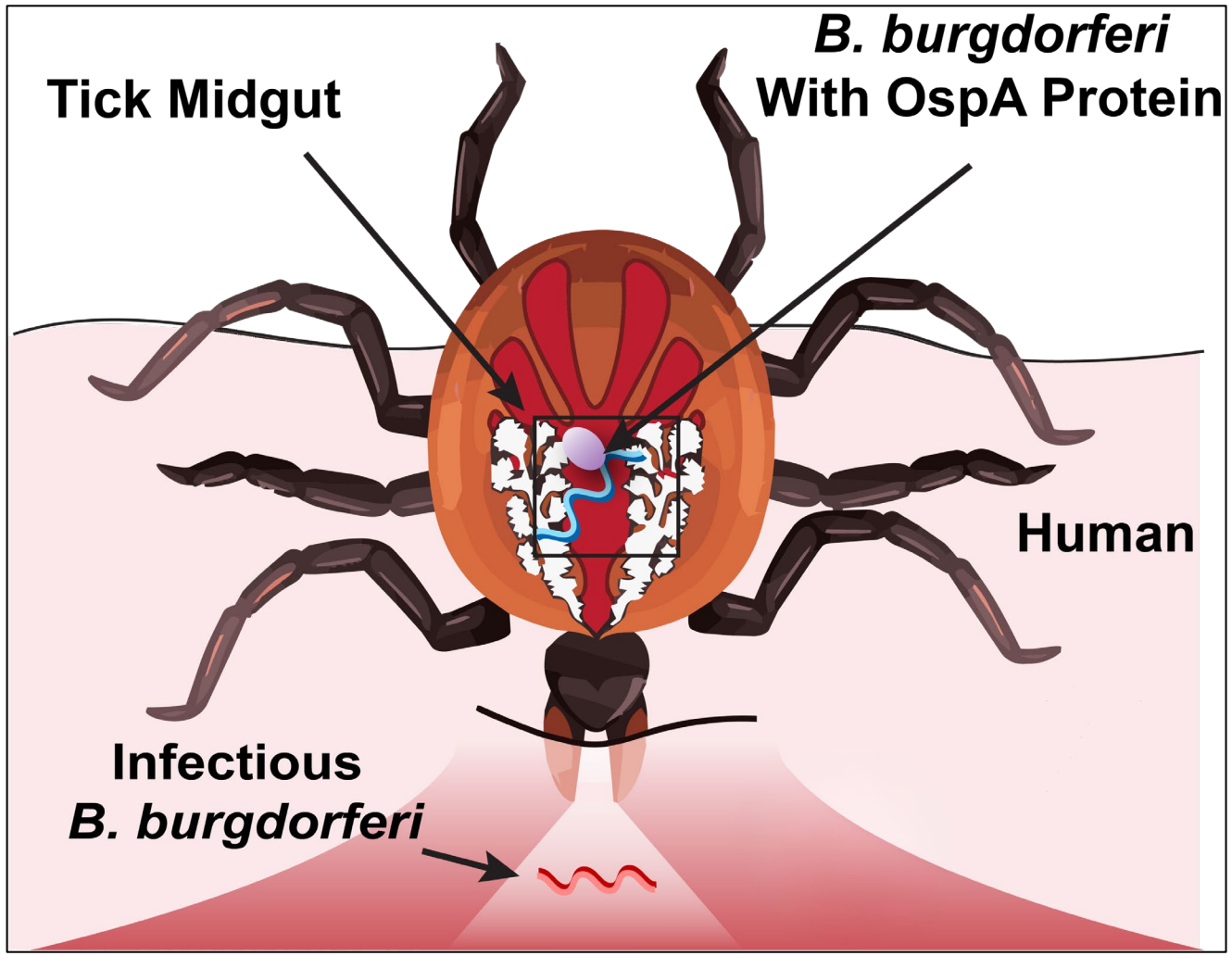
- **The only approved U.S. vaccine was directed to *B. burgdorferi* OspA**
  - SmithKline Beecham’s LYMErix vaccine had ~70-80% protection, but was withdrawn from the market[4]

1. Marques AR, et al. *Emerg Infect Dis.* 2021. 27(8):2017-2024.
2. Pritt BS, et al. *Lancet Infect Dis.* 2016. 6(5):556-564.
3. Lemieux JE, et al. *PLoS Pathog*. 2023.19(8):e1011243.
4. Nigrovic LE, et al. *Epidemiol* Infect. 2006. Aug 8;135(1):1-8.

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OspA Is an Outer Membrane Protein on *Borrelia* That Facilitates Bacterial Adherence to the Tick Midgut[1-3]



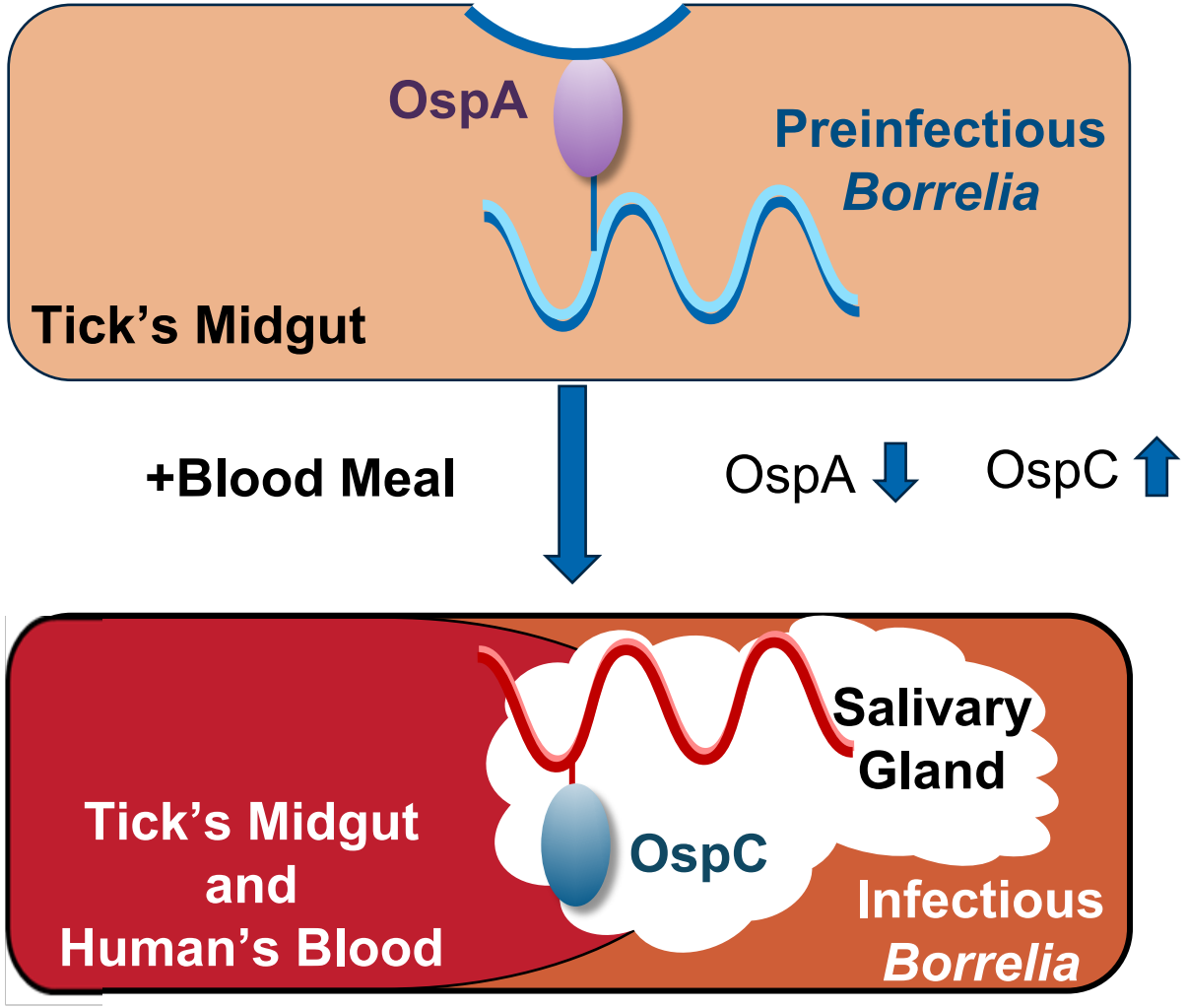
- People who contract Lyme disease rarely make antibodies to OspA because *Borrelia* at the pre-infectious stage stays in the midgut[1,2]
- The lack of an antibody response to OspA may explain why infection confers no protection and humans can be repeatedly infected[1,2]

1. de Silva AM, et al. *J Exp Med*. 1996;183(1):271-275.
2. Radolf JD, et al. *Nat Rev Microbiol*. 2012;10(2):87-99.

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Blood Induces Metamorphosis of *Borrelia* From the Preinfectious to Infectious Stage[1,2]



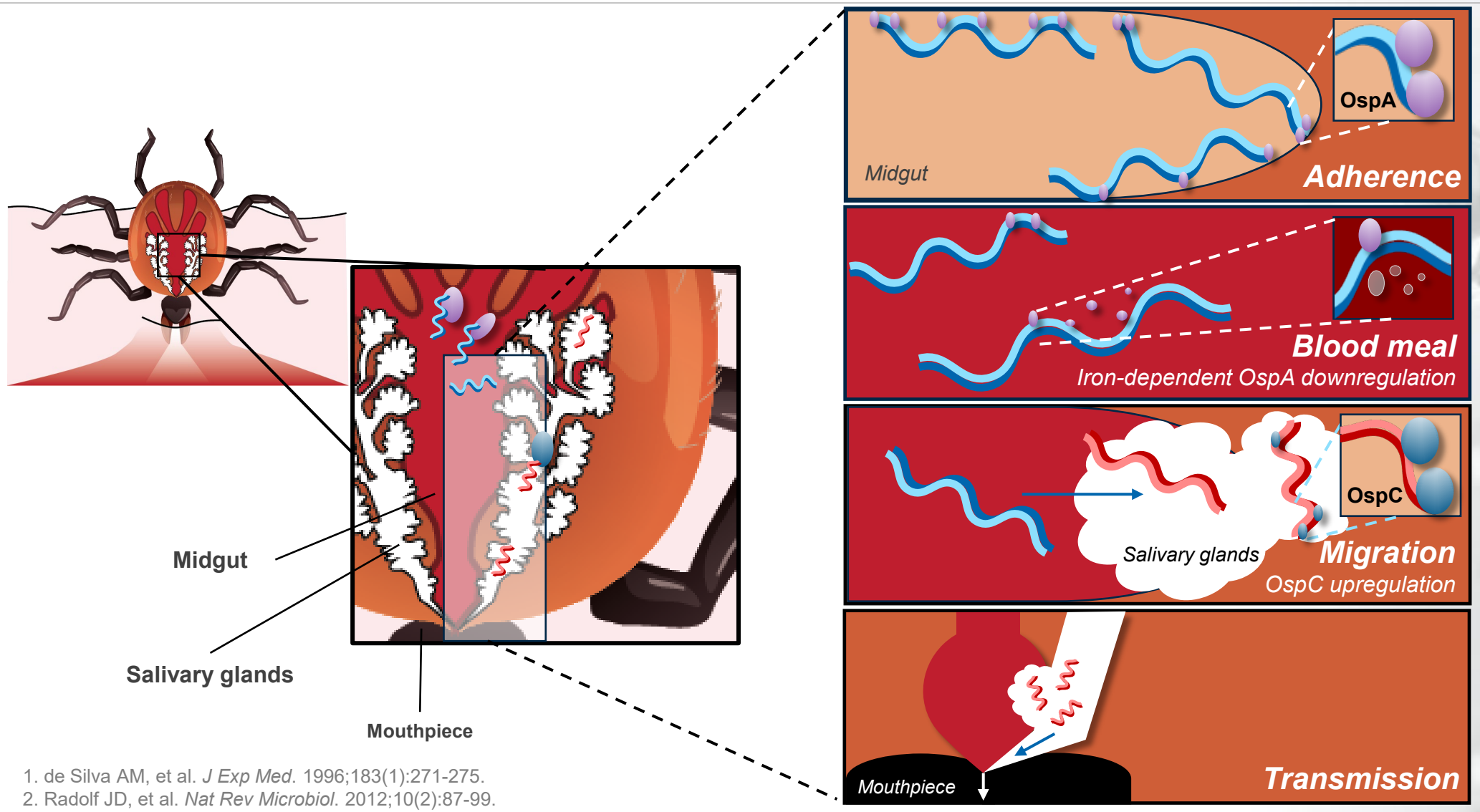
- The outer membrane protein OspA supports *B. burgdorferi* survival in the tick midgut via adherence[1-3]
- Once the tick bites a host, the iron in a blood meal downregulates OspA, and bacteria migrate from the midgut to the salivary glands for transmission[1-3]
- While OspA is essential for transmission, it is only expressed within infected ticks, and levels seen in the human host are insufficient for seroconversion (antibody production)[4]

1. de Silva AM, et al. *J Exp Med*. 1996;183(1):271-275.
2. Radolf JD, et al. *Nat Rev Microbiol*. 2012;10(2):87-99.
3. Anderson C, et al. *Pathogens*. 2021;10(3):281.
4. Woodman ME, et al. *FEMS Immunol Med Microbiol*. 2008;54(2):277-282.

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OspA Facilitates Bacterial Adherence to the Tick Midgut, and Downregulation Promotes Bacterial Migration to Salivary Glands for Transmission[1-3]



1. de Silva AM, et al. *J Exp Med*. 1996;183(1):271-275.
2. Radolf JD, et al. *Nat Rev Microbiol*. 2012;10(2):87-99.
3. Anderson C, et al. *Pathogens*. 2021;10(3):281.

Osp=outer surface lipoprotein

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OspA is a Target for Antibodies to Block Transmission

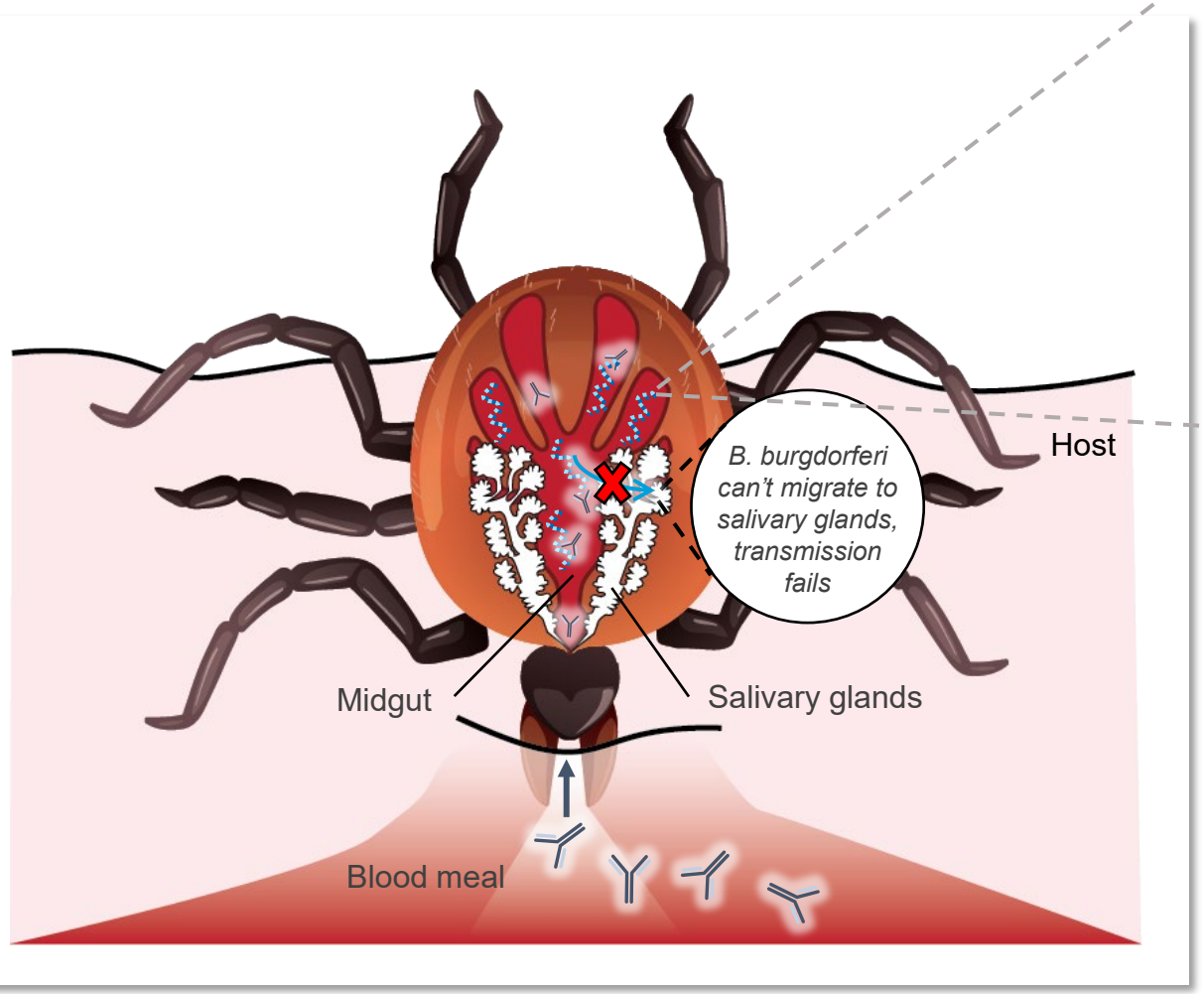
- Anti-OspA antibodies, or immunization with recombinant OspA protein (rOspA), block transmission[1-3]
- Feeding on OspA vaccinated mice or monkeys also eliminates *B. burgdorferi*[4,5]
- Anti-OspA antibodies' ability to agglutinate *B. burgdorferi* suggests a *second* bactericidal mechanism of action[6-8]
- Other mechanisms may be operative since titer of anti-OspA antibody required to eliminate *B. burgdorferi* from ticks is 100 times higher than the titer required to block transmission[9]
- Even low concentrations of anti-OspA monoclonal antibody blocked transmission despite the presence of live spirochetes in the tick[10]

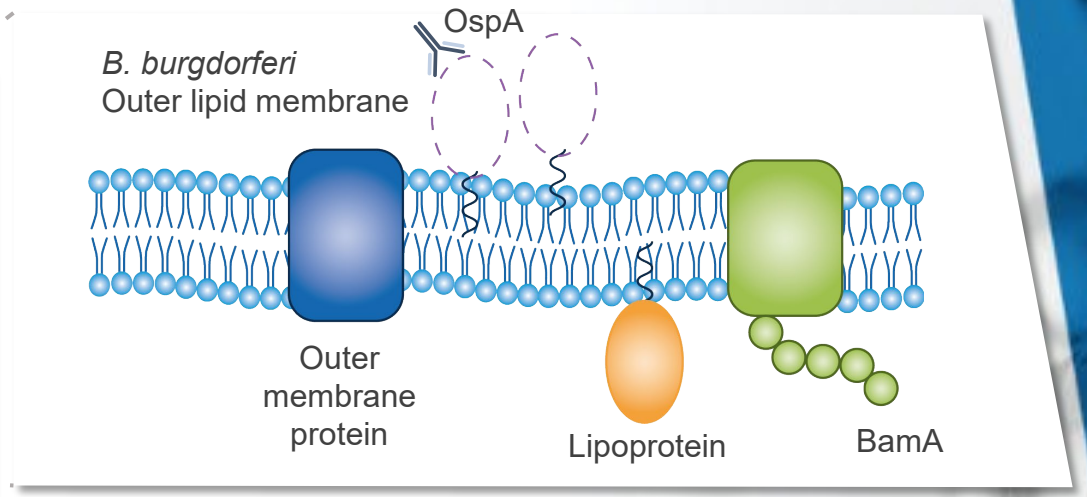
1. Schaible UE, et al. *Proc Natl Acad Sci USA.* 1990;87(10):3768–3772.
2. Schaible UE, et al. *Eur J Immunol.* 1991; 21(10):2397–2405.
3. Fikrig E, et al. *Science.* 1990;250(4980):553–556.
4. Fikrig E, et al. *Proc Natl Acad Sci USA.* 1992;89(12):5418–5421.
5. Philipp MT, et al. *Vaccine.* 1997;15(17-18):1872–1887.
6. de Silva AM, et al. *J Exp Med.* 1996;183(1):271–275.
7. Barbour AG, et al. *Yale J Biol Med.* 1984;57(4):581–586.
8. Sadziene A, et al. *J Infect Dis.* 1993;167(1):165–172.
9. de Silva AM, et al. *Infect Immun.* 1999;67(1):30-35.
10. Gipson CL, et al. *Infect Immun.* 2005;73(3):1644–1647

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Circulating Anti-OspA Monoclonal Antibody (TNX-4800) Ingested by Tick Blocks *B. burgdorferi* Transmission From Tick to Human[1]





- TNX-4800 is a human monoclonal antibody against OspA[1]
- An Fc region mutation in TNX-4800 extends its half-life: such that a two-dose regimen is expected to provide protection during the months of high infection risk
- If a tick bites a human immunized with TNX-4800, anti-OspA antibodies enter the tick midgut and bind to OspA on *B. burgdorferi* spirochetes[2,3]
- After TNX-4800:OspA binding, bacteria are killed or fail to migrate from the midgut to salivary glands, preventing transmission to the human host[2]

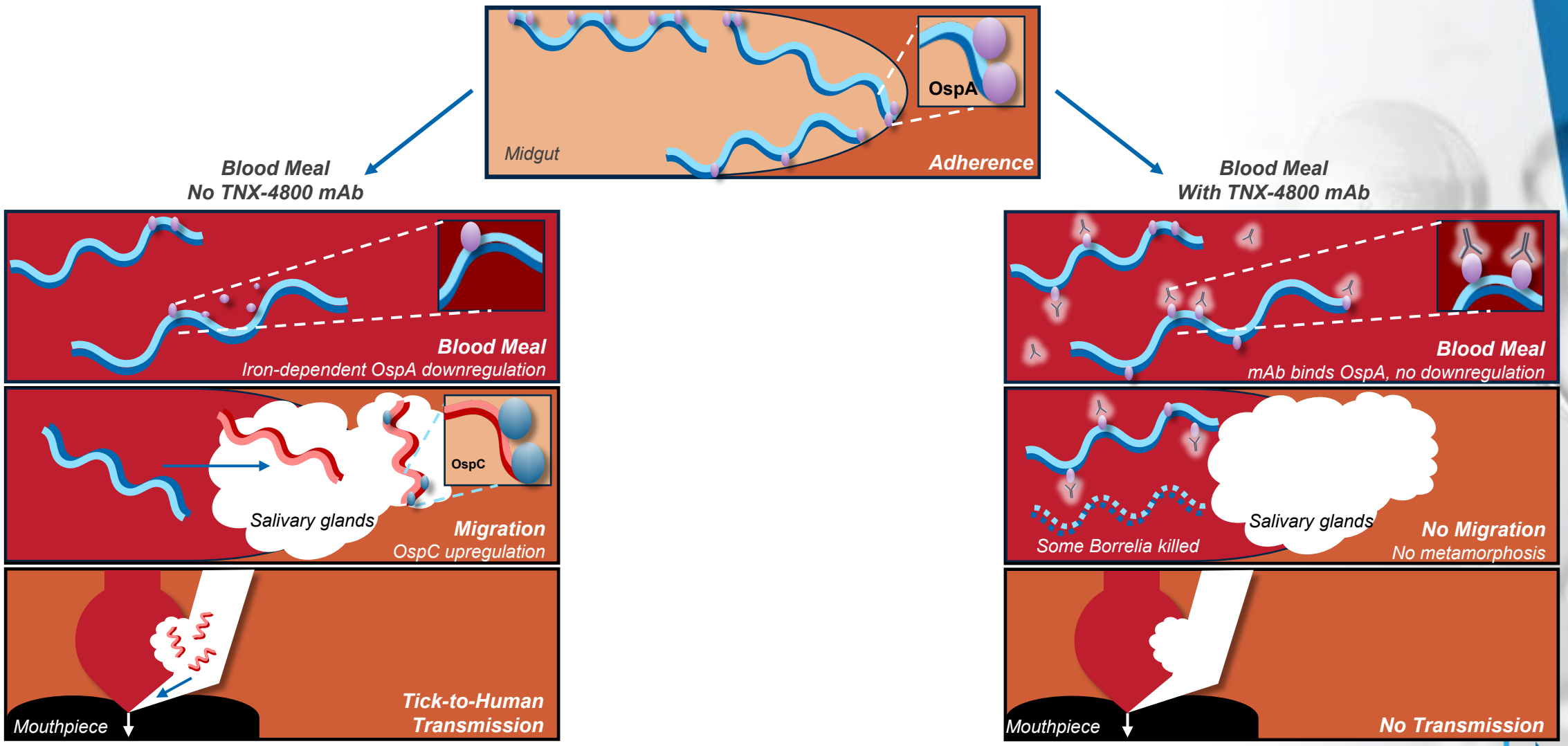
1. Schiller ZA, et al. *J Clin Invest*. 2021;131(11):e144843.
2. de Silva AM, et al. *J Exp Med*. 1996;183(1):271-275.
3. Radolf JD, et al. *Nat Rev Microbiol*. 2012;10(2):87-99.

Bam=β-barrel assembly machinery; Fc=fragment crystallizable; Osp=outer surface lipoprotein

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Anti-OspA mAb TNX-4800 Blocks Differentiation of *Borrelia* From the Pre-infectious to Infectious Stage, Migration to Salivary Glands, and Transmission



Woodman ME, et al. *FEMS Immunol Med Microbiol*. 2008;54(2):277-282.

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Introducing TNX-4800

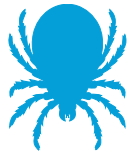
TNX-4800[1,2] is a human anti-OspA monoclonal antibody with engineered Fc domain for extended half-life, licensed from UMass Chan Medical School in 2025

Expected Mechanism of Action



Two-dose Regimen

Two SC doses (Day 1 and after ~12 weeks (Day 85)) expected to provide ≥6 months* protection



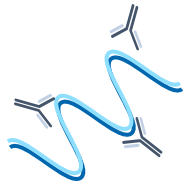
Tick Attaches

Infected tick feeds on an individual who received TNX-4800



Antibody Ingested

TNX-4800 enters tick midgut via blood meal



OspA Binding

Antibody binds OspA on *Borrelia*



Transmission Blocked

Bacteria killed or trapped in midgut—cannot reach human tissue

TNX-4800 supplies anti-OspA antibodies directly, without requiring the recipient to generate vaccine-induced antibodies. Clinical efficacy has not yet been established.

1. TNX-4800 is an investigational biologic and is not approved for any indication.
2. TNX-4800 is protected by Issued US Patent US 10,457,721, which is licensed from UMass Chan with expiry in January 2036 (with PTA), excluding any possible patent term extension.

*Primary efficacy endpoint through 6 months
Key secondary efficacy endpoints through weeks 12 and 38

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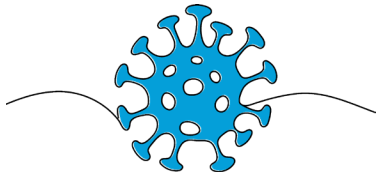
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Antibodies Can Be Created Endogenously or Received From Exogenous Sources

Active

Natural

Pathogen Exposure



Infection with a pathogen stimulates the immune system to create antibodies

Engineered

Vaccines



Injection of weakened pathogens or pathogen components stimulates the immune system to create antibodies

Passive

Natural

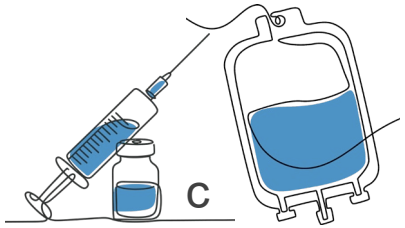
Maternal Antibodies



Breast milk contains maternal antibodies that support underdeveloped infant immune systems

Engineered

Monoclonal Antibodies



Monoclonal antibodies may be infused or delivered subcutaneously including in patients who require additional immune support

Active immunity necessitates the creation of endogenous antibodies, while passive immunity entails the transfer of external antibodies

U.S. Centers for Disease Control and Prevention. July 30, 2024. Accessed July 15, 2025. https://www.cdc.gov/vaccines/basics/immunity-types.html.

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Clinical and Market Acceptance of Monoclonal Antibody Preventive Treatments

Monoclonal antibody prophylaxis includes FDA-approved RSV products ENFLONSIA™[1] and BEYFORTUS®[2], and COVID-19 product PEMGARDA™[3] under emergency use authorization



1. Enflonsia. Prescribing information. Merck Sharp & Dohme LLC; 2025.
2. Beyfortus. Prescribing information. Sanofi; 2024.
3. FDA. PEMGARDA (pemivibart) Emergency Use Authorization Fact Sheet for Healthcare Providers; 2025.

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Not All anti-OspA mAbs are Bactericidal

Name		OspA Epitope[1,2]				Bactericidal
Antibody	Vaccine	*N*-terminus	Central Domain		*C*-terminus	
				~aa 165–173		
184.1		+				-
TNX-4800			+			+
LA-2					+	+
	LYMErix	+	+	+	+	+
	PF-07307405	+	+	-	+	+

- **Monoclonal anti-OspA antibodies can be bactericidal**
  - In a series of mAbs, only those directed towards the *C*-terminal and central domains manifested bactericidal activity *in vitro*, and prevention of transmission *in vivo*[1]
  - For example, mAbs TNX-4800 (central domain)[2] and LA-2 (*C*-terminal) are bactericidal
- ***N*-terminal anti-OspA antibodies can be inactive**
  - 184.1 is an example of a non-bactericidal mAb that binds the *N*-terminal region

1. Embers ME, et al. *Vaccine*. 2026 75:128231. doi: 10.1016/j.vaccine.2026.128231.
2. Schiller ZA, et al. *J Clin Invest*. 2021;131(11):e144843.
3. LYMErix used OspA aa 20–273 from *B. burgdorferi* strain B31 produced in *E. coli.*
4. PF-07307405 (LB6V, formerly VLA15) excludes the putative arthritogenic/LFA-1 epitope (~aa 165–173).

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Comparison of TNX-4800 with PF-07307405, mRNA-1982, and mRNA-1975

	TNX-4800	PF-07307405	mRNA-1982	mRNA-1975
Sponsor	Tonix	Pfizer/Valneva	Moderna	Moderna
Status	Phase 2 ready	EMA review	Phase 2	Phase 2
Type	Monoclonal Antibody	Vaccine alum adjuvant	Vaccine mRNA	Vaccine mRNA
Immunity	Passive	Active	Active	Active
Target Market	U.S.	EU + U.S.	U.S.	U.S. + Europe
Borrelia targeted[1-4]	*B. burgdorferi* (U.S.)	*B. burgdorferi* (U.S.) *B. afzelii* (Europe) *B. garinii** (Europe) *B. bavariensis* (Europe)	*B. burgdorferi* (U.S.)	*Seven OspA serotypes:* *B. burgdorferi* (ST1) *B. afzelii* (ST2) *B. garinii* (ST3, 5, 6, 7) B. bavariensis (ST4)

1. Marques AR, et al. *Emerg Infect Dis.* 2021. 27(8):2017-2024. doi: 10.3201/eid2708.204763.
2. Pritt BS, et al. *Lancet Infect Dis.* 2016. 6(5):556-564. doi: 10.1016/S1473-3099(15)00464-8.
3. Lemieux JE, et al. *PLoS Pathog*. 2023.19(8):e1011243. doi: 10.1371/journal.ppat.1011243.
4. Comstedt P, et al. *PLoS One*. 2014 9(11):e113294. doi: 10.1371/journal.pone.0113294.

*PF-07307405 includes three B. garinii OspA serotypes. Moderna: mRNA-1982 is monovalent; mRNA-1975 is heptavalent.

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Comparison of TNX-4800 with Alum-Adjuvanted Subunit Vaccines LYMErix (Withdrawn) and PF-07307405 (in Development) in Terms of OspA Targeting

	TNX-4800	LYMErix[1-4]	PF-07307405[1-4]
Sponsor	Tonix	SmithKline (GSK)	Pfizer/Valneva
Status	In Development	Withdrawn	In Development
Type	Monoclonal Antibody	Vaccine	Vaccine
Immunity	Passive	Active	Active
Target Market	U.S.	U.S.	EU + U.S.
Clinical Studies	U.S.	U.S.	EU + U.S.
Borrelia targeted	*B. burgdorferi* (U.S.)	*B. burgdorferi* (U.S.)	*B. burgdorferi* (U.S.) *B. afzelii* (Europe) *B. garinii** (Europe) *B. bavariensis* (Europe)

1. Marques AR, et al. *Emerg Infect Dis.* 2021. 27(8):2017-2024. doi: 10.3201/eid2708.204763.
2. Pritt BS, et al. *Lancet Infect Dis.* 2016. 6(5):556-564. doi: 10.1016/S1473-3099(15)00464-8.
3. Lemieux JE, et al. *PLoS Pathog.* 2023.19(8):e1011243. doi: 10.1371/journal.ppat.1011243.
4. Comstedt P, et al. PLoS One. 2014 9(11):e113294. doi: 10.1371/journal.pone.0113294.
*PF-07307405 includes three B. garinii OspA serotypes.

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TNX-4800, LYMErix, and PF-07307405: Dosing and Timing of Protection

	TNX-4800	LYMErix (Withdrawn)	PF-07307405[1]
Sponsor	Tonix	SmithKline (now GSK)	Pfizer/Valneva
1st dose	Day 1	Day 1	Day 1
2nd dose	~12 weeks (Day 85) from 1st dose	1 month	2 months
3rd dose	-	12 months	5-9 months
4th dose	-	-	12 months after dose 3
Protection duration	At least ~6 months*	Seasonal	Seasonal
Protection onset	Target: within 2 days**	After 3rd shot	Assessed after dose 4[2]

- **TNX-4800 targets protection within 2 days****
- **Vaccine schedules require multiple doses over several months**
  - Protection depends on antibody levels; seasonal boosters may be needed
  - Complex immunization schedule may have contributed to poor LYMErix uptake

1. Comstedt P, et al. *PLoS One.* 2014 9(11):e113294.10.1371/journal.pone.0113294.
2. VALOR efficacy assessed after dose 4; onset was not established. Pfizer press release, March 23, 2026.

*Primary efficacy endpoint through 6 months
Key secondary efficacy endpoints through weeks 12 and 38.
**Projected from human PK and animal models; clinical efficacy unproven

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TNX-4800 and PF-07307405: Administration and Intended Protection

Criteria	TNX-4800 (mAb)[1,2]	PF-07307405[4,5]
Treatment mode	Pre-exposure two-dose mAb regimen: one 450 mg SC dose or placebo at Day 1, and one 450 mg SC dose or placebo 12 weeks later at Day 85	Pre-exposure 4-dose vaccination regimen
Protection timing / evidence	Target: within 2 days after SC dosing; clinical efficacy not yet established	Efficacy assessed from 28 days after dose 4 in season 2[3]
Target population	Adults ≥18 years at risk who live, work, or travel to endemic areas in the U.S.	People aged ≥5 years at risk of Lyme disease (VALOR population)
Activity	Designed against *B. burgdorferi*	Targets six OspA serotypes prevalent in North America and Europe
Dosing regimen	Two-dose regimen expected to provide at least 6 months protection*	Multiple doses needed to obtain initial protection with seasonal durability[6]
Dosing route	SC	IM
Safety evidence	Phase 1 showed no significant clinical or laboratory safety signals; larger studies are needed Binds outside the putative arthritogenic epitope	Well tolerated in Phase 3 VALOR, with no safety concerns identified at analysis[3]

1. Wang Y, et al. *J Infect Dis.* 2016. 214(2):205-11.
2. Schiller ZA, et al. *J Clin Invest*. 2021;131(11):e144843.
3. Pfizer press release, March 23, 2026: 73.2% efficacy; first analysis missed its statistical criterion.
4. Proposed attributes; not yet finalized or validated
5. https://valneva.com/research-development/lyme-disease.
6. VALOR: months 0, 2, 5–9; booster one year after dose 3.
Pfizer, March 23, 2026.

*Primary efficacy endpoint through 6 months
Key secondary efficacy endpoints through weeks 12 and 38.

IM=intramuscular; mAb=monoclonal antibody; Osp=outer surface protein

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Comparison of TNX-4800 and PF-07307405 for Lyme Disease Prevention

- **TNX-4800 is a long-acting human mAb (in development) against *B. burgdorferi* OspA**
  - Bactericidal activity against *B. burgdorferi* B31
    - Strong bactericidal activity of TNX-4800 with EC_{50} = 0.345 to 0.469 µg/mL *in vitro*[1]
  - Planned testing targets B. *burgdorferi* sensu stricto (OspA serotype 1)
  - Safety studies, field testing, and marketing approval, if any, planned for U.S. only

- **Pfizer/Valneva's PF-07307405 (in development) is a vaccine that elicits antibodies against 6 different *Borrelia* OspAs**[2]
  - Vaccine that elicits polyclonal antibodies to six OspA-derived peptide antigens
  - Field tests in EU and the U.S.
  - Five OspA serotypes address species prevalent in Europe:
    - *B. afzelii* (one serotype), *B. garinii* (3 serotypes), *B. bavariensis* (one serotype)
  - One OspA serotype targets B. *burgdorferi* sensu stricto, prevalent in North America and also found in Europe

1. Schiller ZA, et al. *J Clin Invest*. 2021;131(11):e144843.(TNX-4800 has EC_{50} = 3.71 ± 2.81 nM).
2. Comstedt P, et al. *PLoS One.* 2014 9(11):e113294. doi: 10.1371/journal.pone.0113294.

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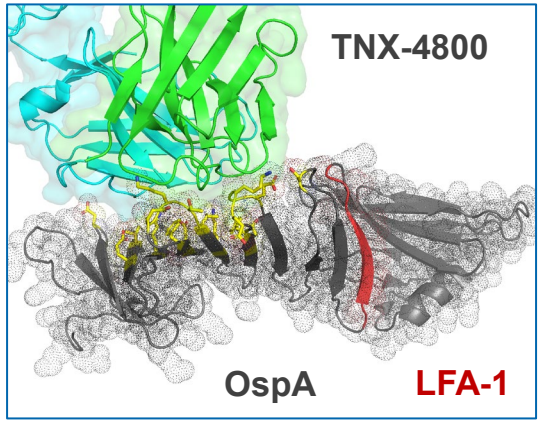
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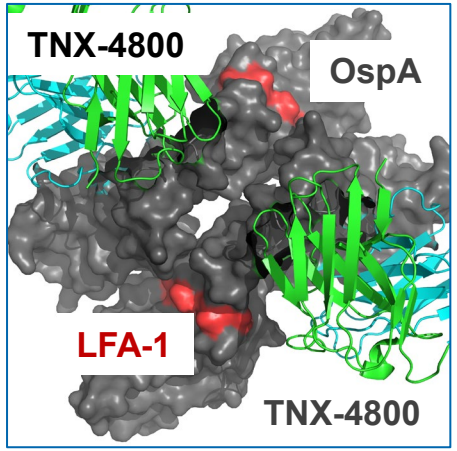
TNX-4800 Binds Outside the Putative Arthritogenic OspA Epitope

- An epitope in the OspA protein mimics human leukocyte function–associated antigen 1 (hLFA-1 or LFA-1)[1]
- A proposed link to autoimmune arthritis raised historical concerns but did not establish vaccine causation[1,2]
- LYMErix™ was withdrawn from the market in part over unsubstantiated claims of this concern[2]
- TNX-4800 binds the 71–141 region, outside this putative epitope; this does not establish an absence of clinical risk[3]
- A safety advantage in previously infected individuals or those with *HLA-DRB1*0401* has not been established clinically

OspA Protein







1. Steere AC, et al. *Arthritis Rheum*. 2003;48(2):534-540.
2. Nigrovic LE, Thompson KM. *Epidemiol Infect*. 2007 135(1):1-8.
3. Schiller ZA, et al. *J Clin Invest*. 2021;131(11):e144843.

Osp=outer surface lipoprotein

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TNX-4800 Target Product Profile (TPP)[1]

Variable	Target
Primary Indication	Pre-exposure prophylactic against Lyme disease
Clinical Pharmacology	Blood levels sufficient to provide protection within 2 days and maintained efficacy for ≥6 months* Consistent with bacterial-targeted, fully human mAbs
Nonclinical Toxicology	Consistent with bacterial-targeted, fully human mAbs
Patient Population	Adults ≥18 years of age initially, then ≥6 months old Persons at risk who are living in, working in, or traveling to endemic areas in the U.S.
Limitations of Use in Specific Populations	None
Duration of protection	Two-dose regimen (Day 1 and ~12 weeks (Day 85) from the first dose) Expected to provide at least six months protection
Delivery Mode	SC injection; each 450 mg SC dose will be divided into 2 injections of 1.5 mL volume with 225 mg each
Efficacy	Protection against the transmission of Lyme disease from an infected tick ≥80% efficacy[2]
Storage Requirements	2°C to 8°C
Drug Interactions	None
Target Jurisdictions	United States
Safety Profile **Risks/Side Effects** **Warnings and Precautions** **Adverse Reactions**	Predominantly mild and moderate side effects consistent with other infectious disease mAbs
Contraindications	None currently

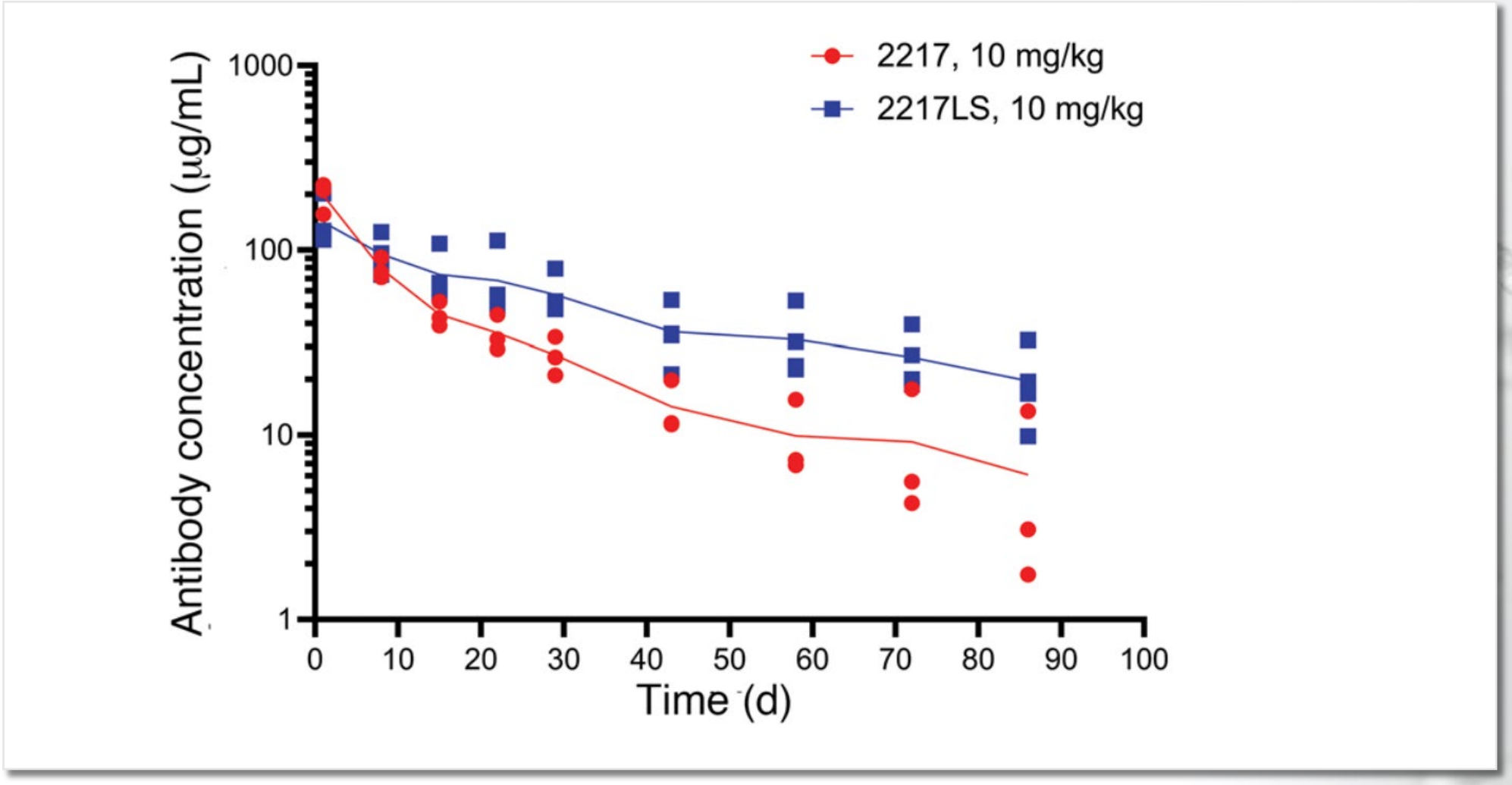
1. Subject to change and FDA approval.
mAb=monoclonal antibody; mg=milligrams; SC=subcutaneous

2. Primary efficacy endpoint through 6 months
Key secondary efficacy endpoint through weeks 12 and 38.

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Engineered Fc Mutations Extend Half-Life of TNX-4800 (2217LS) in Nonhuman Primates Relative to Parent mAb 2217[1]



[1]Schiller ZA, et al. *J Clin Invest*. 2021;131(11):e144843.
N=4 for each group and each dot represents one monkey. Half-lives are reported in days and hours as mean ± SD (line).
Fc=fragment crystallizable.

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Analysis of Efficacy Relevant Threshold #1 – *In vitro* Bactericidal Activity

- **TNX-4800 showed EC_{50} = 0.345 - 0.469 µg/mL *in vitro*[1]**
  - Efficacy relevant threshold ~ 10 X EC_{50}[2]

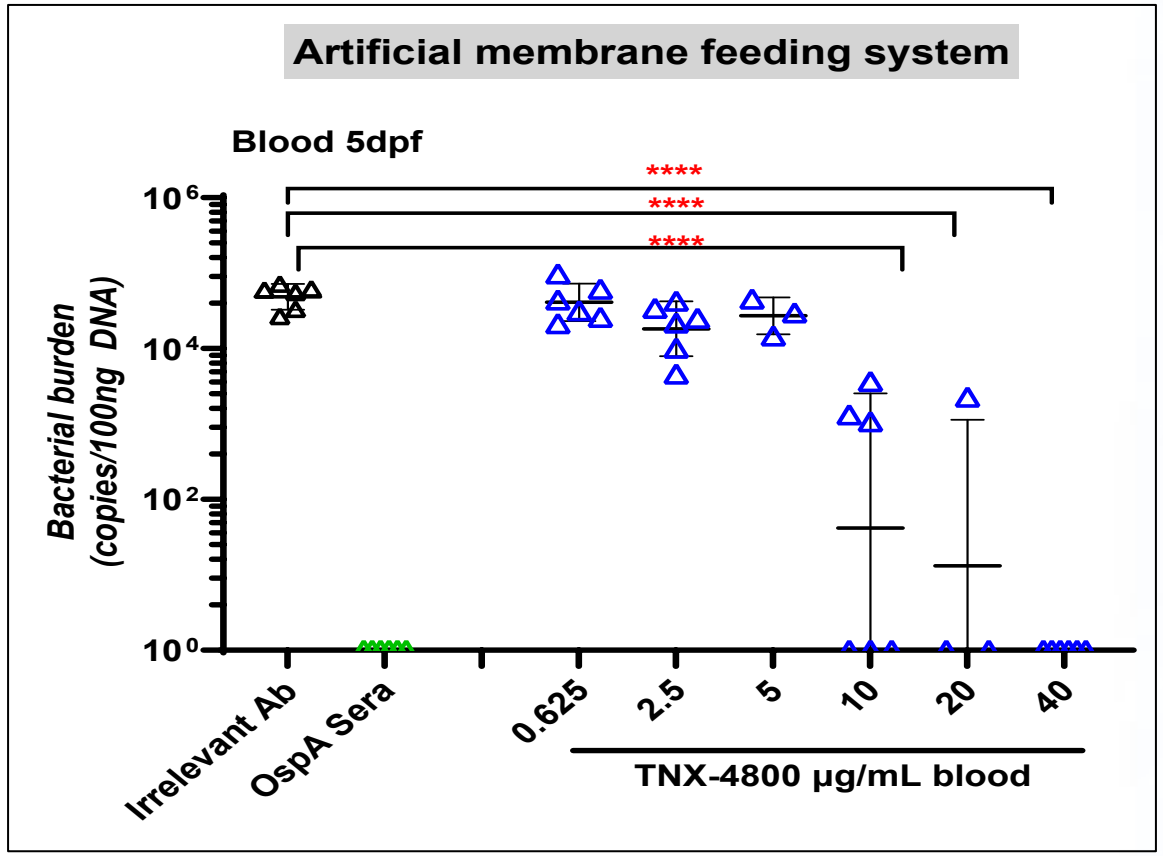
- **Efficacy relevant threshold based on Borreliacidal activity:**
  - Efficacy relevant threshold ~5 µg/mL

1. Wang Y, et al. *J Infect Dis.* 2016. 214(2):205-11.
2. Rogers RR et al , *Antimicrobial Agents and Chemotherapy*, Oct. 2004, p. 3670–3676.

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Analysis of Efficacy Relevant Threshold #2: Artificial Membrane Tick Feeding Method

TNX-4800 blocks tick-to-blood transmission of *B. burgdorferi* B31



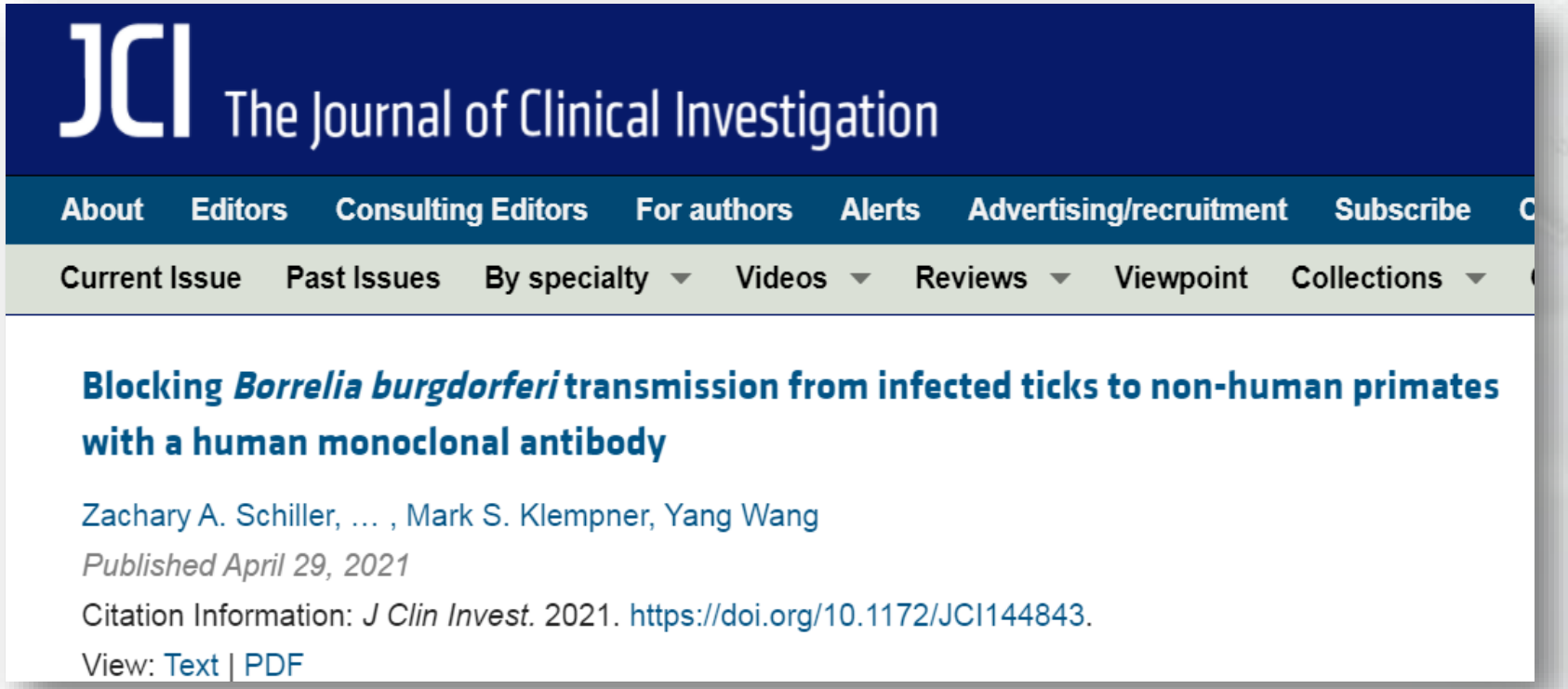
Data on file. N=5, Asterisk * = statistically significant

Methods described in: Kröber T, Guerin PM. *Trends Parasitol.* 2007 23(9):445-9. Klempner M. Presentation at 4th Annual Ticks and Tickborne Diseases Symposium. April 2026.

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Analysis of Efficacy Relevant Threshold #3 – *in vivo* Primate Challenge Model



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

Zachary A. Schiller, … , Mark S. Klempner, Yang Wang

Published April 29, 2021

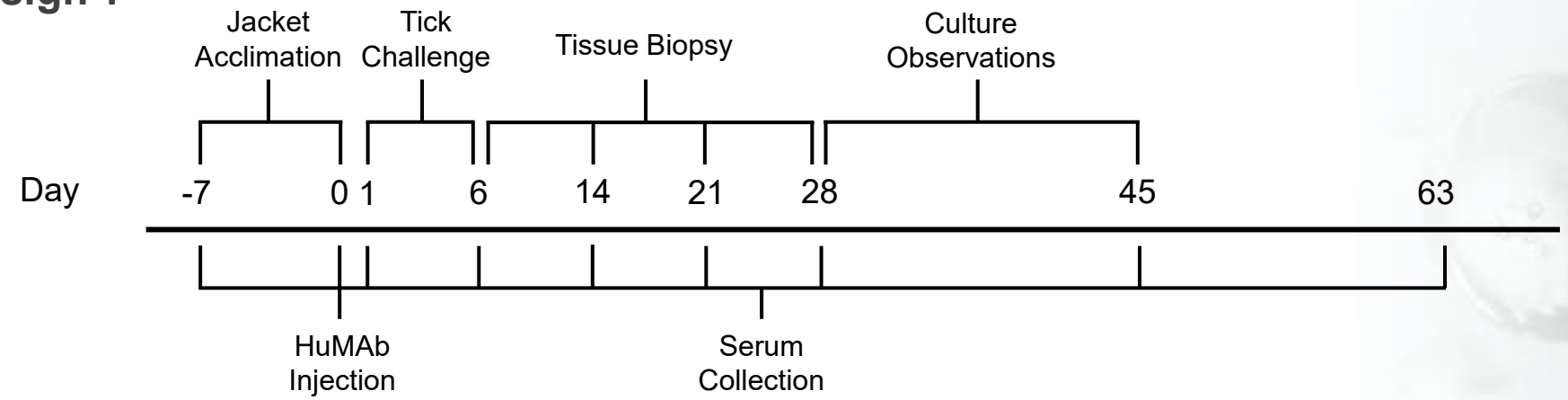
Citation Information: *J Clin Invest.* 2021. https://doi.org/10.1172/JCI144843.

View: Text | PDF

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Nonhuman Primate Challenge Model: Protocol and Protection by Dosage Level

Study Design[1]:



- 4 dosing groups, 1 irrelevant IgG control
- 4 to 6 animals per group
- Seroconversion for IgG antibodies against *B. burgdorferi* was measured as an indicator of efficacy

Results:

Group	Group 1	Group 2	Group 3	Group 4	Irrelevant IgG
Dose (mg/kg)	3	10	30	90	10
Protection (%)	100	83	100	100	0
P value	<0.001	<0.001	<0.001	<0.001	N/A

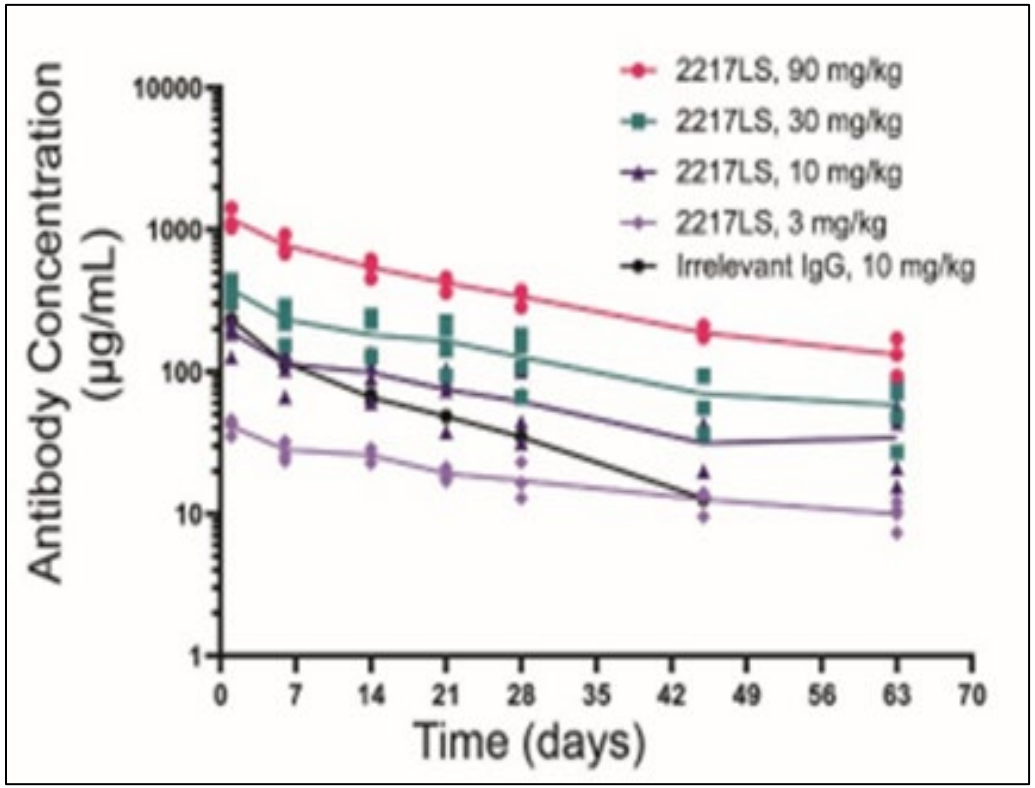
1. Schiller ZA, et al. *J Clin Invest*. 2021;131(11):e144843.
HuMAb=human monoclonal antibody; IgG=immunoglobulin G

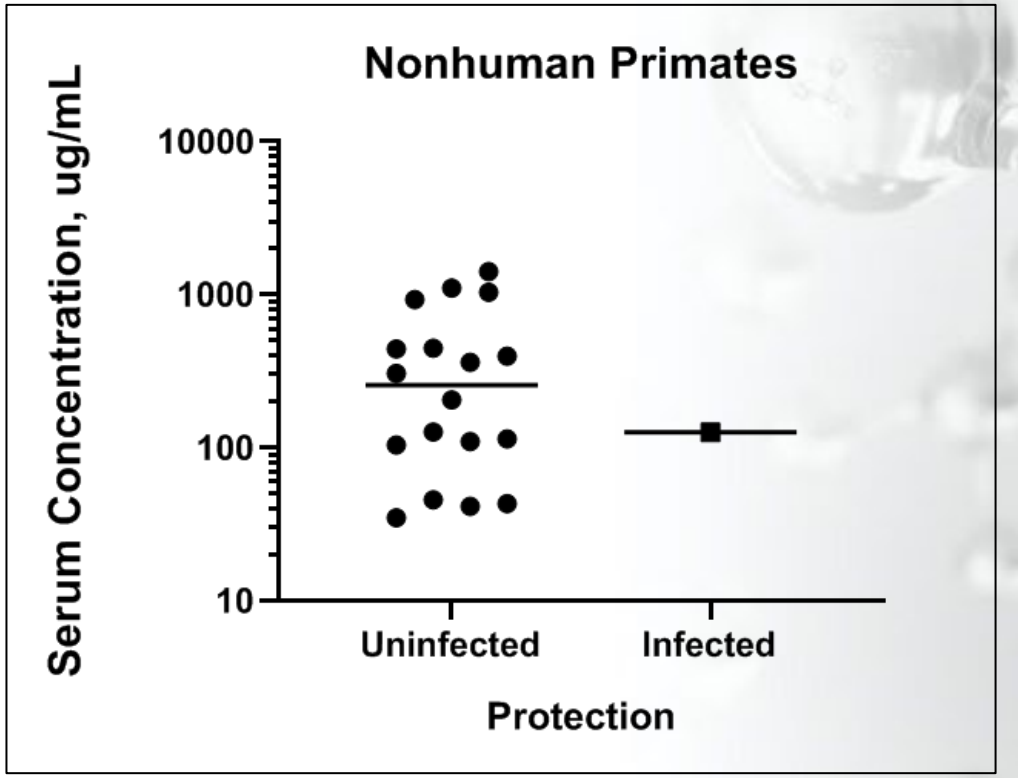
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TNX-4800 Efficacy in Primate Challenge Model

- Infected ticks were placed on each non-human primate administered TNX-4800 (N=20) for 5 days[1]
- Trough serum level ≥10 µg/mL was associated with mean protection of 91.3% in the primate model





1. Schiller ZA, et al. *J Clin Invest*. 2021;131(11):e144843.

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Analysis of Efficacy Relevant Threshold by Three Methods

- ***In vitro* bactericidal activity**
  - TNX-4800 EC_{50} = 0.345- 0.469 µg/mL *in vitro*[1]
  - Efficacy relevant threshold ~ 10X EC_{50}[2]
  - Serum level ~5 µg/mL
- ***In vitro* tick feeding**
  - TNX-4800 showed blocking transmission[3] ≥ 10 µg/ml
- ***In vivo* efficacy in primate challenge model**
  - TNX-4800 serum levels ≥10µg/mL were 91.3% protective[1,3]

1. Wang Y, et al. *J Infect Dis.* 2016. 214(2):205-11.
2. Rogers RR et al , *Antimicrobial Agents and Chemotherapy*, Oct. 2004, p. 3670–3676.
3. Schiller ZA, et al. *J Clin Invest*. 2021;131(11):e144843.

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TNX-4800: Nonclinical Safety Data

- **cGLP Tissue Cross Reactivity study in rat and human tissues**
  - No significant cross-reactivity
- **Non-GLP pharmacokinetic and tick challenge studies in monkeys**
  - Did not reveal a safety signal
- **cGLP 5-week multiple dose study with 4-week recovery in rats and a cGLP single dose local tolerance study in rats**
  - Observed abnormalities were mild to moderate and all findings were judged non-adverse (hematologic and ALT, AST ALP and APTT increases (notably without bilirubin changes), injection site inflammation, liver and spleen organ weight increases, liver histopathology, primarily in males. All findings were reversible)
- **Phase 1 exposures were lower than exposures at the rat NOAEL**
  - Starting dose (0.5 mg/kg): 37- to 166-fold lower
  - Highest dose (10mg/kg): 1.5- to 6.7-fold lower

cGLP = current Good Laboratory Practice, ALT = alanine transaminase, AST = aspartate aminotransferase, AP = alkaline phosphatase, APTT = activated partial thromboplastin time, NOAEL = No-observed-adverse-effect level

Once weekly administration of TNX-4800 (intravenous or subcutaneous) for 4 weeks followed by a 35-day recovery period in male and female Sprague Dawley rats was tolerated at doses of up to 500 mg/kg/week intravenous or 300 mg/kg/week SC with no adverse findings. Therefore, under the conditions of this study, 500 mg/kg/week intravenous or 300 mg/kg/week SC was considered to be the NOAEL.

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TNX-4800 Phase 1 Study Overview

Primary Objective:

- Evaluate safety and tolerability of a SC injection of TNX-4800 (2217LS) when administered to healthy participants

Secondary Objective:

- Evaluate pharmacokinetics of a SC dose of TNX-4800 (2217LS) when administered to healthy participants

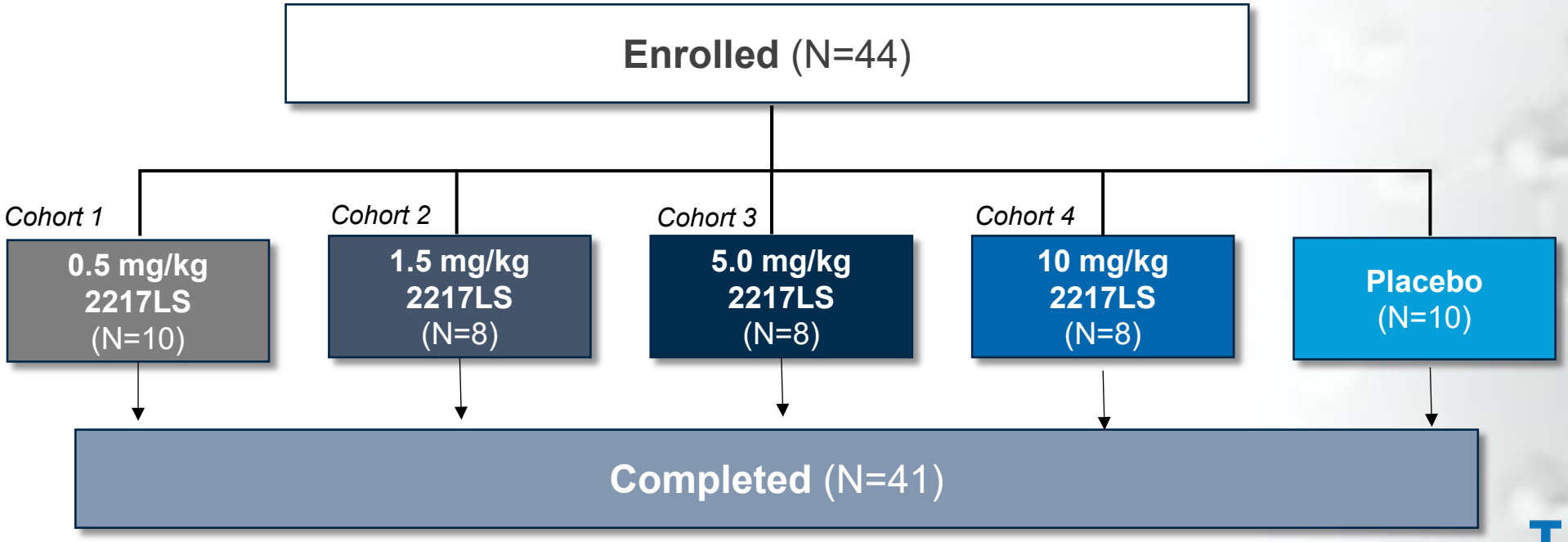
Study Population:

- Healthy male and female participants, age 19 to 65 years, inclusive

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Human Phase 1 Study: Safety, Tolerability and Immunogenicity: Design

- First-in-human, randomized, double-blind, sequential dose-escalation study (N=44)
- Healthy male and female participants aged 19 to 65 years, serum negative for anti–*B. burgdorferi* antibodies, by an FDA-approved modified 2-tier ELISA test, were recruited
- Safety was assessed via clinical and lab evaluations
- Serum TNX-4800 concentrations were measured by ELISA, with pharmacokinetic analysis
- Antidrug antibodies were detected using an electrochemiluminescence immunoassay



Sullivan-Bólyai JZ, et al. Manuscript in progress. 2025.

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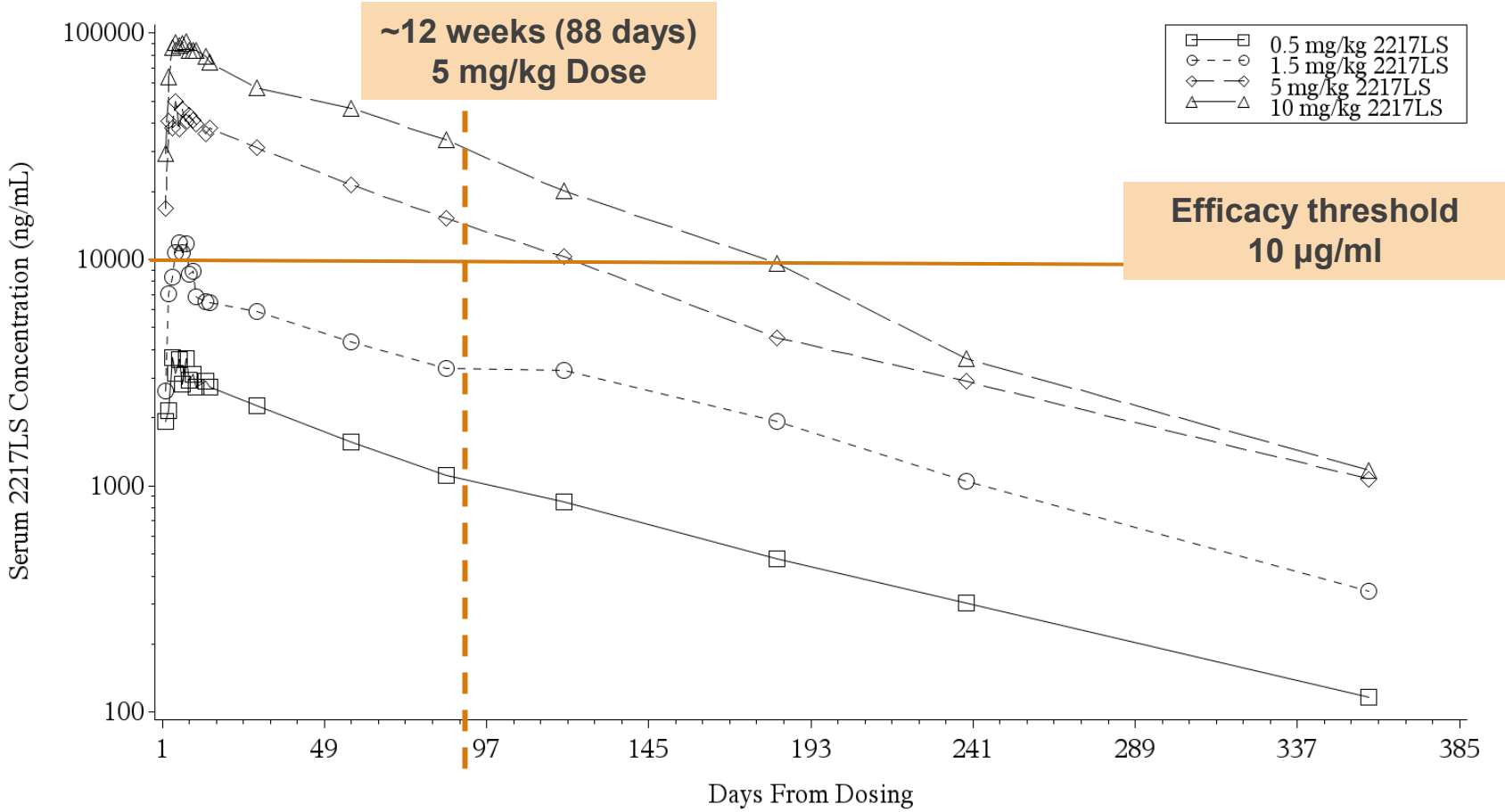
TNX-4800 Phase 1 Study Results[1]

- No significant clinical or laboratory safety signals
- The mean exposure, based on AUC-inf and C_{max} for Cohort 4 (10mg/kg), was less than 17% of the highest exposures in the rat toxicology study
- Serum TNX-4800 (2217LS) was measurable at the earliest sampling time of 2 days indicating rapid absorption
- Across cohorts, median T_{max} ranged from 4.0 to 6.0 days, followed by prolonged elimination
- At 5 mg/kg dose T_{max} observed at 4.5 days and half-life $T_{½}$ 63 days
- Cohort 3 (5mg/kg) serum concentrations:
  - TNX-4800 serum level ≥15 µg/ml achieved for 88 days (*in vivo* efficacy relevant threshold and > ~ *in vitro bactericidal* relevant threshold)

1. Klempner M. Presentation at the 4th Annual Ticks and Tickborne Diseases Symposium. April 2026.

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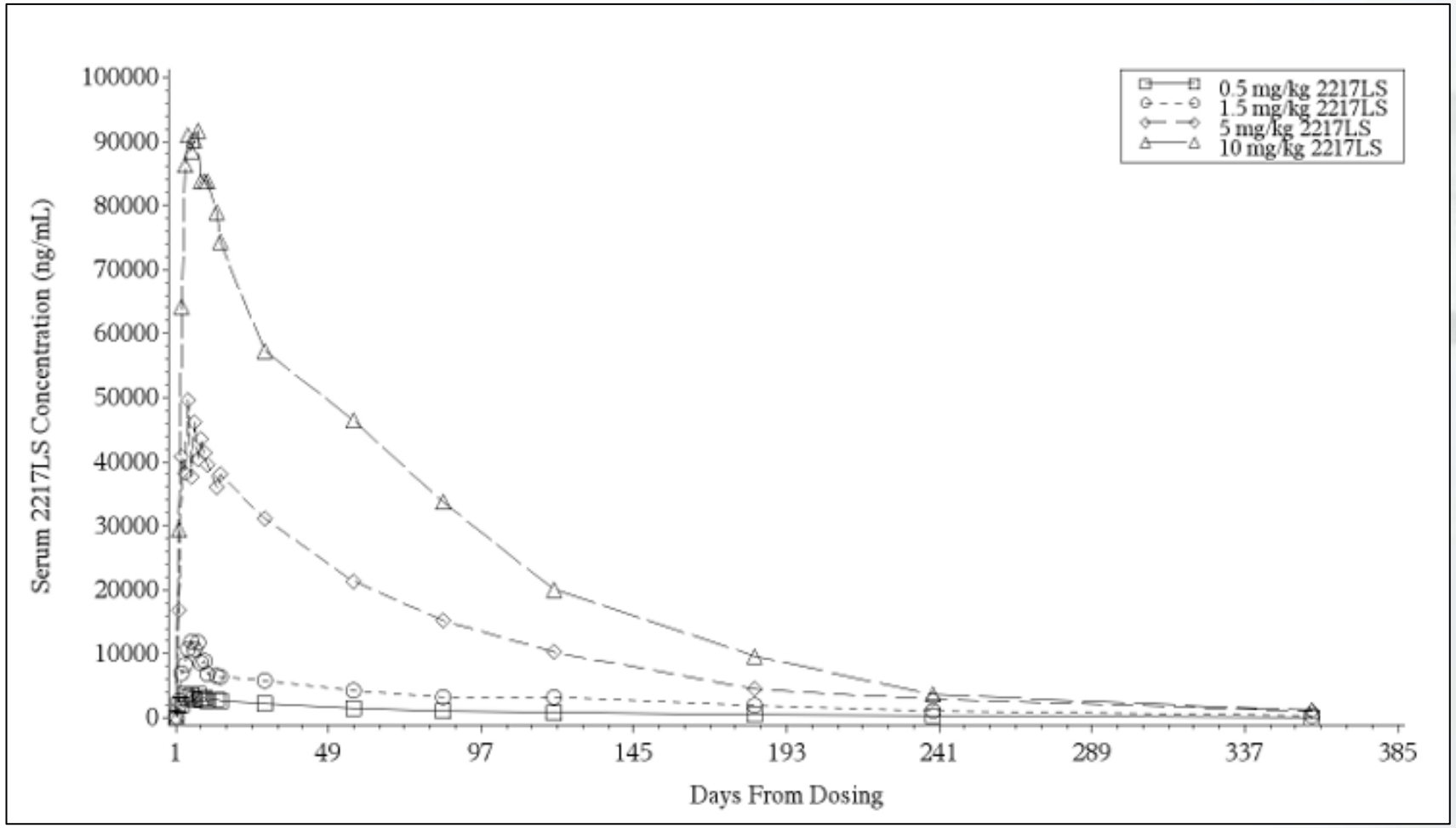
Observed Phase 1 Pharmacokinetics and Efficacy Threshold



Each point represents a mean for the cohort at the specified timepoint and dose.

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TNX-4800 Phase 1: Serum Concentrations at Sampling Time Points in Each Cohort



Each point represents a mean for the cohort at the specified timepoint and dose.
The profiles for 1.5 mg/kg, 5 mg/kg, and 10 mg/kg TNX-4800 (2217LS) are shifted to the right for ease of reading.

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TNX-4800 Phase 1 Pharmacokinetics Parameters

Pharmacokinetic Parameters	Cohort 1 TNX-4800 : 0.5 mg/kg (n=10)	Cohort 2 TNX-4800 : 1.5 mg/kg (n=8)	Cohort 3 TNX-4800 : 5 mg/kg (n=8)	Cohort 4 TNX-4800 : 10 mg/kg (n=8)
AUC0-t (µg*hr/mL)	6271 (26.0)	20610 (23.7)	79760 (36.5)	165500 (26.0)
AUC0-inf (µg*hr/mL)	6812 (25.3)	21490 (23.5)	82070 (37.2)	168100 (25.9)
AUC%ext (%)	7.83 ± 4.87	4.10 ± 1.63	2.81 ± 1.39	1.49 ± 0.49
Cmax (µg/mL)	3.39 (31.4)	10.88 (41.3)	45.65 (22.0)	84.56 (37.5)
Tmax (hr)	96.078 (72.0, 335.9)	144.02 (95.9, 215.9)	108.32 (71.9, 216.1)	108.05 (48.0, 167.8)
Kel (1/day)	0.0120 ± 0.0061	0.0102 ± 0.0014	0.0140 ± 0.0089	0.0114 ± 0.0017
t½ (days)	67.3 ± 22.2	69.1 ± 10.1	63.2± 27.3	62.1± 10.2
CL/F (mL/day/kg)	1.814 ± 0.483	1.716 ± 0.418	1.554 ± 0.622	1.469 ± 0.373
Vd/F (mL/kg)	171.2 ± 61.3	170.1 ± 47.3	123.7 ± 29.8	133.0 ± 44.4

Cohort 1,2 and 3 : A single subcutaneous injection, Cohort 4: Two subcutaneous injection
AUCs and Cmax are presented as geometric mean (geometric CV%).
Tmax values are presented as median (min, max).
Other parameters are presented as arithmetic mean ± SD.
Source: Tables 14.2.1.5 through 14.2.1.8
Program: /CA29655/sas_prg/pksas/adam_intext_pkparam.sas 13FEB2023 9:20

Each point represents a mean for the cohort at the specified timepoint and dose.

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Phase 1 Clinical Study Summary Results

- TNX-4800 studied in randomized, double-blind, sequential dose-escalation study (NCT04863287) to evaluate its safety, tolerability, pharmacokinetics and immunogenicity
- 44 healthy adult participants randomized and 41 completed study; participants received a single subcutaneous (SC) administration of placebo or TNX-4800 at 0.5, 1.5, 5, or 10 mg/kg
- Peak serum concentration (C_{max}) increased by ~25-fold for a 20-times increase in dose
- Serum TNX-4800 measurable at earliest sampling time of 2 days, indicating rapid systemic absorption
- TNX-4800 levels remained quantifiable for >200 days in 80% of participants at lowest dose and for up to 350 days in majority of participants at higher doses (i.e., ≥ 1.5 mg/kg)
- Mean half-life ranged from 62–69 days across TNX-4800 groups; serum concentrations quantifiable for up to 12 months in most participants
- At the highest dose of TNX-4800 tested in rats with 1.5 to 6.72-fold higher exposure compared to 10 mg/kg cohort, no adverse toxicity was observed, thus the highest dose tested was considered No Observed Adverse Effect Level (NOAEL)
- Anti-drug antibodies (ADA) detected in <10% of treated participants
- Most adverse events were mild or moderate[1]
- TNX-4800 was generally well tolerated in this Phase 1 study

1. One serious adverse event deemed unrelated to study drug.

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Planned Phase 2 TRAIL Field Study

TNX-4800 is intended to be studied in an adaptive randomized, double-blind, placebo-controlled field study

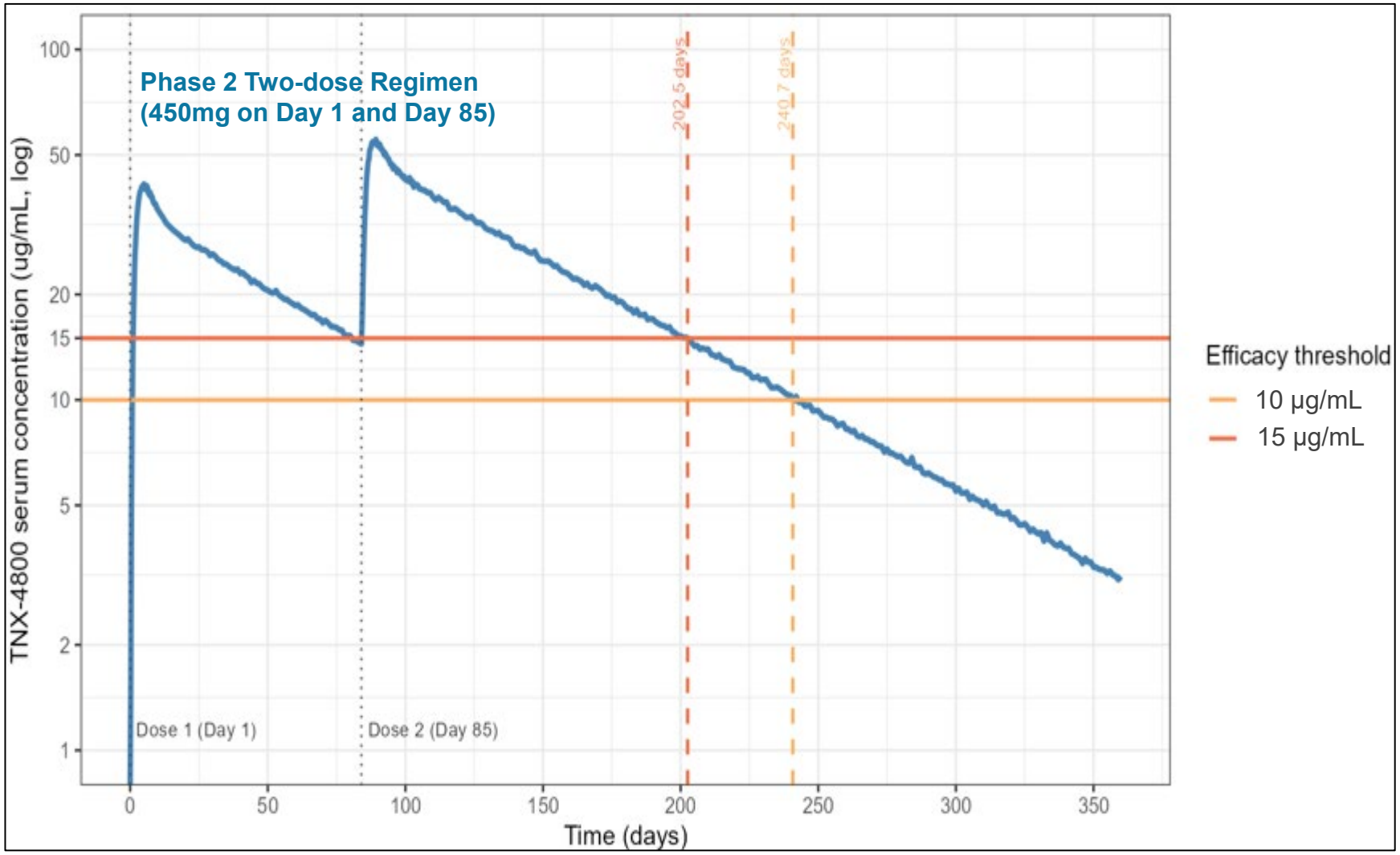
- **Primary Efficacy Endpoint:** Incidence of a first confirmed case of Lyme disease, caused by *B. burgdorferi* within the period of two days post administration up through six months following the first administration[1]
- **Primary Efficacy Objective:** Evaluate the efficacy of TNX-4800 in preventing the first occurrence of confirmed Lyme disease during the primary efficacy surveillance period from Day 2 after the first administration through six months following the first administration
- **Primary Safety Objective:** Evaluate safety and tolerability over 52 weeks in a lead-in cohort of at least 200 TNX-4800-exposed participants (n=500, randomized 1:1)
- **Inclusion:** Adult participants ≥18 years of age from Lyme-endemic areas in the U.S. who engage in activities that increase their risk of deer tick bites
- **Dosing:** Two total doses; one 450 mg SC dose or placebo at Day 1, and one 450 mg SC dose or placebo 12 weeks later at Day 85
- **Administration:** Each 450 mg SC dose comprises two 1.5 mL injections of 225 mg each, or matching placebo
- Pending FDA agreement on final protocol, the Company is planning an adaptive Phase 2 field study to evaluate the safety, efficacy, and tolerability of TNX-4800 in preventing Lyme disease in adult participants from Lyme-endemic areas
- The Phase 2 study is expected to enroll in the 2027 and 2028 seasons, with the majority of participants enrolled in 2028 (balance of efficacy cohort). If the attack rate is lower than expected, the study could continue enrolling in 2029
- **Rationale:** Efficacy relevant threshold based on Phase 1 pharmacokinetic results and nonclinical protection models against *B. burgdorferi* transmission

1. Key secondary efficacy endpoints through weeks 12 and 38.

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Simulation Median Profile of Two 450 mg Doses and Efficacy Threshold of TNX-4800



Target attainment is 10 µg/mL. The higher bound is 15 µg/mL.

Internal simulation based on Phase 1 data. Tonix. 2026.

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Addressing the Significant Public Health Challenge of Lyme Disease in the U.S.

- ✓ Phase 1 study complete, showing favorable safety, tolerability, immunogenicity, and pharmacokinetics
- ✓ Phase 2 adaptive field study planning and manufacturing of investigational product underway for 1Q 2027

TNX-4800 Upcoming Milestones



Manufacturing Investigational Product for Human Studies Currently on Track for 1Q 2027

Plan to Initiate Adaptive Phase 2 Field Study, Pending FDA Agreement on Final Protocol

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THANK YOU



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