Investor Day 2024

October 10th, 2024

valneva

Today's Agenda

Welcome & Introduction	**Joshua Drumm, Ph.D.** *VP Global Investor Relations*
Company Strategy & Value Drivers	**Thomas Lingelbach** *Chief Executive Officer*
Lyme Disease Vaccine Program	**Thomas Lingelbach** *Chief Executive Officer*
Commercial Portfolio & IXCHIQ® Launch	**Dipal Patel** *Chief Commercial Officer*
Q&A Break	**Speaker Panel**

Today's Agenda

Chikungunya Vaccine Program	**Susanne Eder-Lingelbach** *VP Clinical Development*
***Shigella* Vaccine Program & Opportunity**	**Juan Carlos Jaramillo, M.D.** *Chief Medical Officer*
Second-Generation Zika Vaccine	**Susanne Eder-Lingelbach** *VP Clinical Development*
Pipeline Strategy / Preclinical Priorities	**Thomas Lingelbach** *Chief Executive Officer*
Financial Outlook	**Peter Bühler** *Chief Financial Officer*
Final Q&A	**Speaker Panel**

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This presentation presents information about investigational vaccine candidates that have not been approved for use and have not been determined by any regulatory authority to be safe or effective.

Management uses and presents IFRS results, as well as the non-IFRS measure of Adjusted EBITDA to evaluate and communicate its performance. While non-IFRS measures should not be construed as alternatives to IFRS measures, management believes non-IFRS measures are useful to further understand Valneva's current performance, performance trends, and financial condition. Adjusted EBITDA is a supplemental measure of performance used by investors and financial analysts. Management believes this measure provides additional analytical tools.

Company Strategy & Value Drivers

Thomas Lingelbach
Chief Executive Officer

valneva

A Leading Specialty Vaccine Company

Focused on vaccines that make a difference

We **develop, manufacture, & commercialize** prophylactic vaccines for infectious diseases addressing unmet medical needs

- **Proven Expertise:** Three in-house vaccine approvals; three proprietary commercialized travel vaccines
- **Focus on Innovation:** Advancing a pipeline of first-, only- or best-in-class vaccine candidates; Experience across multiple vaccine platforms
- **Key Value Driver – De-risked Blockbuster Lead Program:** Phase 3 Lyme disease vaccine candidate partnered with Pfizer
- **Growing Commercial Revenues:** Targeting €160 - €180 million of vaccine sales in 2024 to support continued R&D investments; Revenues expected to ~double by 2026/7 with launch of IXCHIQ®
- **Targeting profitability in 2027:** Based on continued commercial growth plus Lyme vaccine commercial entry

Valneva's Augmented Commercial and R&D Portfolio

Further extending a unique, differentiated portfolio

	Program	Vaccine Design	Pre-Clinical	Phase 1	Phase 2	Phase 3	Commercial
Commercial Products	**IXIARO®**	Only U.S./ EU approved vaccine against Japanese encephalitis					
	DUKORAL®	Established Cholera (ETEC[1]) vaccine approved in >30 countries					
	IXCHIQ®	World's first and only approved chikungunya vaccine (U.S., Europe, Canada); Reviews ongoing in UK and Brazil					
Clinical Programs	**VLA15:** Lyme disease	Most clinically advanced Lyme vaccine program worldwide					
	VLA1553: Chikungunya	Phase 3 adolescent study (Brazil) and Phase 2 pediatric study support potential label expansion					
	S4V: Shigellosis	Phase 2 CHIM[2] and pediatric studies to begin H2 2024					
	VLA1601: Zika	Potential for first/best-in-class					
Key Pre-Clinical Activities	**VLA2112:** EBV						
	Various Enteric diseases						

1 ETEC indication in some markets only; 2 Controlled human infection model

Our Strategy to become a Globally Recognized Vaccine Company

Contribute to a world where no one dies or suffers from a vaccine preventable disease

Drive Commercial Growth

- Unlock IXCHIQ® value by building awareness and market
- Capitalize on the bundle effect within travel business
- Expand global reach; reach more LMICs via partnerships
- Expect cash-flow positivity from 2025

Capture R&D Upside

- Leverage proven R&D engine and strategic partnerships
- Continue to focus on vaccines that can make a difference: (first-, only-, best-in-class)
- Execute efficiently to generate meaningful clinical catalysts

Maximize integrated biotech model

- Build continual value from R&D and commercial execution
- Support timely Lyme approval(s)
- Achieve sustained profitability with potential VLA15 commercial revenues from partner Pfizer*

*Subject to successful development, licensure and launch of Lyme disease vaccine candidate partnered with Pfizer

Track Record of Strong Execution

Key Recent Accomplishments

Regulatory

- U.S., European and Canadian approvals for IXCHIQ®
- Submitted for label extension (12yrs +) and inclusion of data on antibody persistence to enhance access to IXCHIQ®

Clinical

- Completed primary vaccination series and first booster in pivotal Phase 3 Lyme disease trial (VALOR)
- Completed adolescent Phase 3 study and initiated Pediatric Phase 2 study for IXCHIQ®; Reported 24-month antibody persistence
- Initiated Phase 1 trial of second-generation Zika vaccine candidate

Commercial

- Exceeded pre-pandemic sales revenue levels (2023); continued growth expected
- Recorded first IXCHIQ® sales in the U.S. in 2024

Strategic

- Augmented clinical pipeline with Phase 2 *Shigella* vaccine candidate
- Initiated transfer of production to new state-of-the-art manufacturing facility in Scotland

Financial

- Successfully completed ~€60 million private placement
- Extended cash runway with update of debt financing agreement
- Received and successfully sold PRV for $103 million
- Provided mid-term financial outlook
- Completed agreed-upon payments to Pfizer for VALOR trial
- Secured additional $41.3 million in grant funding from CEPI

World’s leading Lyme Disease Vaccine Candidate

Thomas Lingelbach
Chief Executive Officer

valneva

Lyme Disease Represents A Major Medical Need And Market Opportunity

No vaccine is currently available to prevent Lyme disease in humans

Population Living in Endemic Regions[1,2]

U.S.
87 million

Europe
202 million

Annual Burden of Disease

U.S.[1]

~476K cases

Europe[2]

>129K cases

Severe Manifestations[3]

10-30%
cases develop

→ Lyme carditis
Lyme neuroborreliosis
Lyme arthritis

Persistent Symptoms[4,5]

5-10%

cases continue to have persistent symptoms following treatment

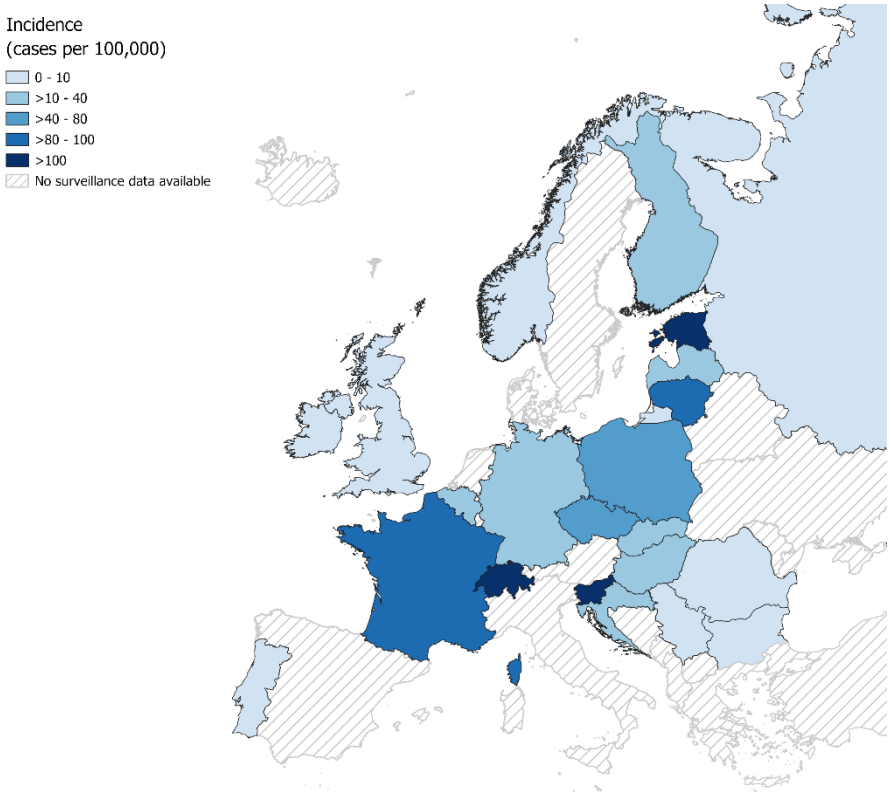
Commercial opportunity for Valneva

- **>$1 billion estimated global market[6]**
- **Valneva eligible for $143 million in milestone payments upon commercialization**
- **Tiered sales royalties 14-22%**
- **$100M in cumulative sales milestones**

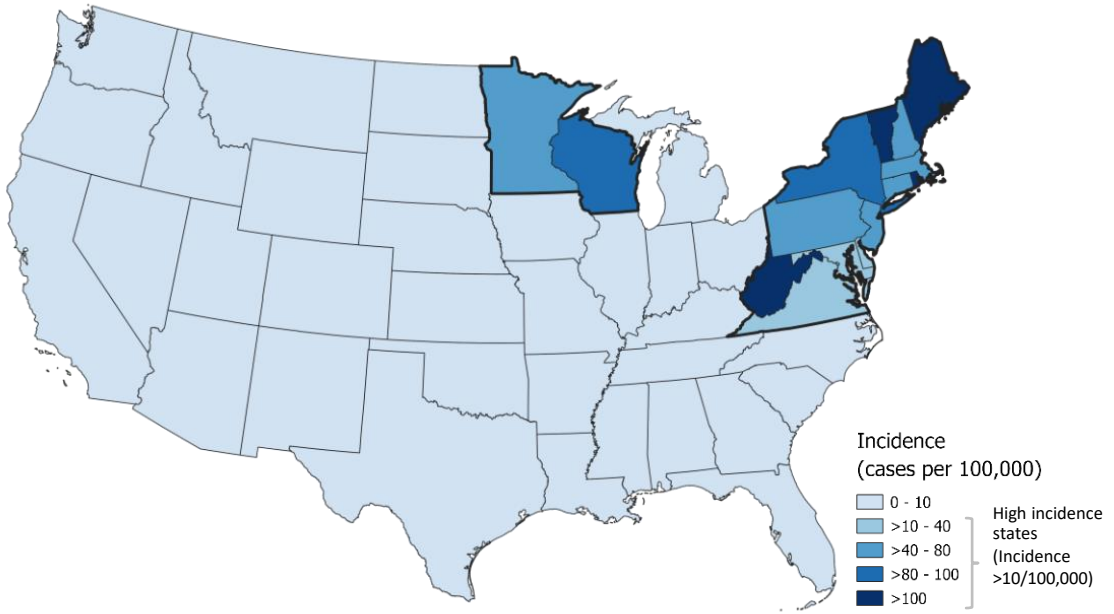
1 Kugeler et al. Emerging Infectious Disease, 2021 (doi.org/10.3201/eid2702.202731); **2** Burn at al. Vector Borne and Zoonotic Disease, 2023 (DOI: 10.1089/vbz.2022.0071); **3** Schwartz et al. Morbidity and Mortality Weekly Report Nov. 10, 2017; **4** Ursinus: https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(21)00119-8/fulltext; **5** Aucott, J.N., et al., Risk of post-treatment Lyme disease in patients with ideally-treated early Lyme disease: A prospective cohort study. Int J Infect Dis, 2022. 116: p. 230-237.; **6** Lyme Disease research and analysis conducted by an independent market research firm

Incidence of Lyme disease in Europe and the United States

Average national incidence of Lyme borreliosis in the most recent three-year period in Europe



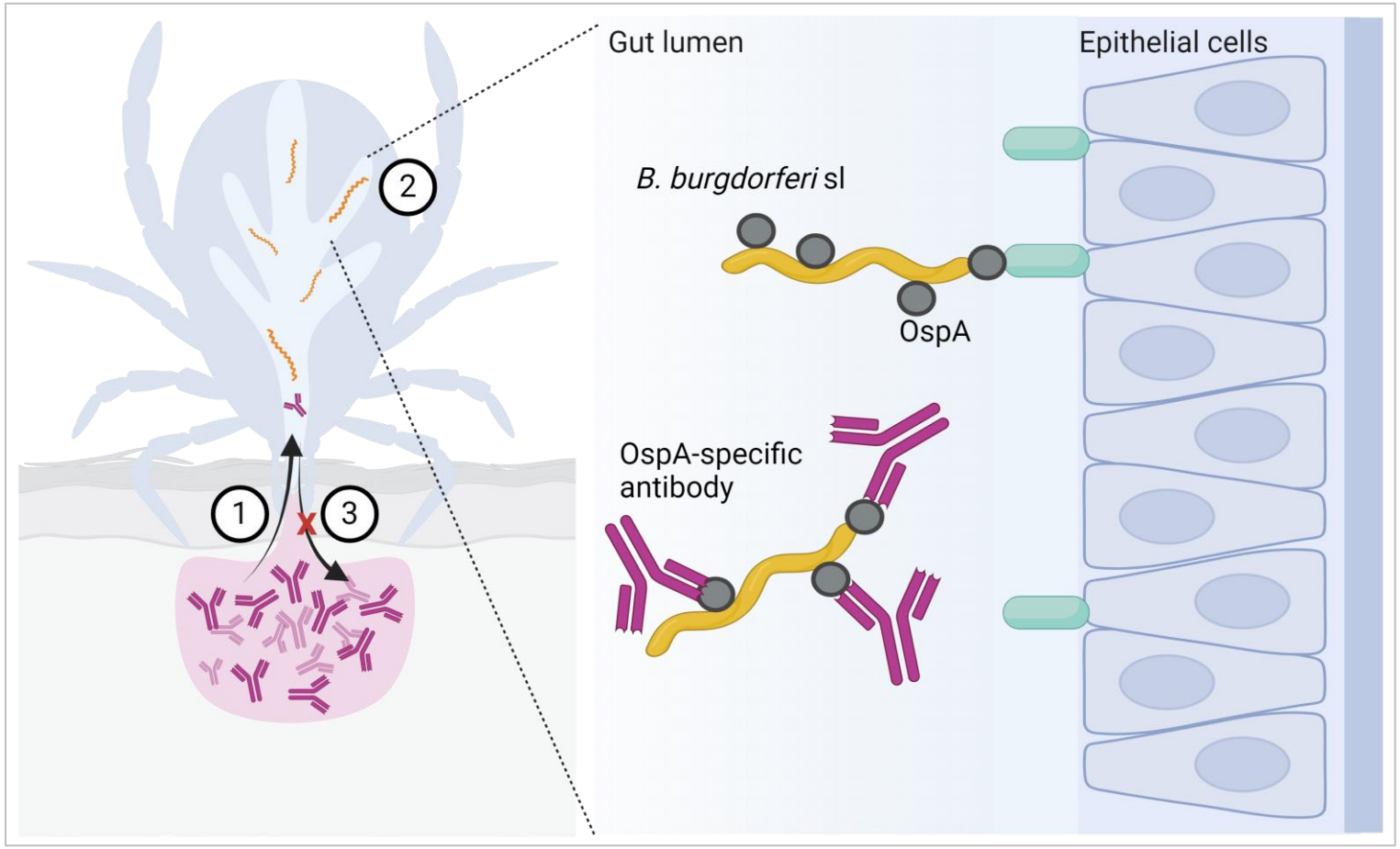
Incidence of surveillance-reported Lyme disease, by state, United States, 2022



Europe: adapted from Burn et al. Incidence of Lyme Borreliosis in Europe from National Surveillance Systems (2005-2020). Vector Borne Zoonotic Dis. 2023 Apr;23(4):156-171. doi: 10.1089/vbz.2022.0071; Most recent three-year period of available data varies between countries. United States: *Surveillance data is adapted from the U.S. Centers for Disease Control and Prevention's (CDC) annual Lyme disease data and reflects CDC's updated Lyme disease case definitions: http://dx.doi.org/10.15585/mmwr.mm7306a1

Mechanism of OspA vaccines

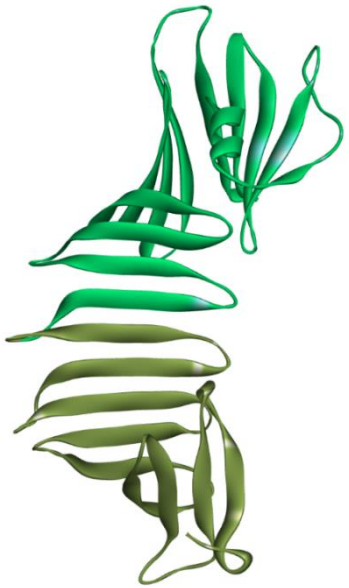
1. Tick ingests antibodies from the host blood upon feeding
2. In the tick gut, OspA antibodies bind to *B. burgdorferi*'s OspA
3. OspA-bound antibodies inhibit the dissemination of bacteria in the tick, blocking transmission to the host



Wormser GP et al. Diagn Microbiol Infect Dis. 2022;102(1):115572. Nayak A et al. Infect Immun. 2020;88(4):e00917-19. Federizon J et al. Bioconjug Chem. 2019; 30(5):1259-1272. Kurokawa C et al. Nat Rev Microbiol . 2020;18:587-600
Outer Surface Protein, OSP

Prior monovalent serotype 1 vaccines (North America) validated the vaccine mechanism in humans

GSK Lymerix (ST1)
OspA



N-terminal lipidation

Lymerix (GSK) Phase 3 efficacy study[1]
(schedule: 0-1-12 months)

	Placebo (N = 5467)	Lymerix (N = 5469)	Vaccine Efficacy (95% CI)
Year 1 cases	43	22	49% (15-69)
Year 2 cases	66	16	76% (58-86)

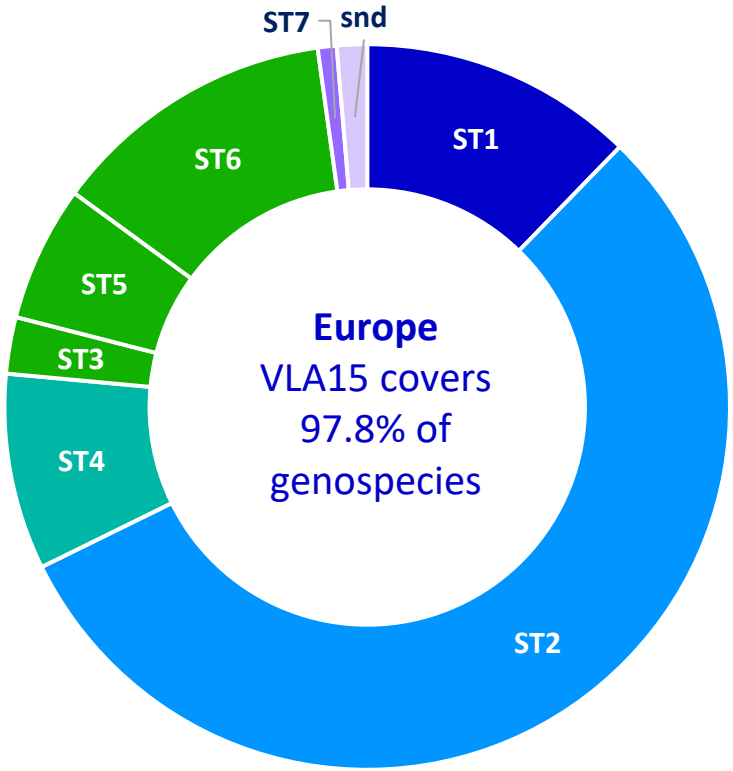
Imulyme (Sanofi) Phase 3 efficacy study[2]
(schedule: 0-1-12 months)

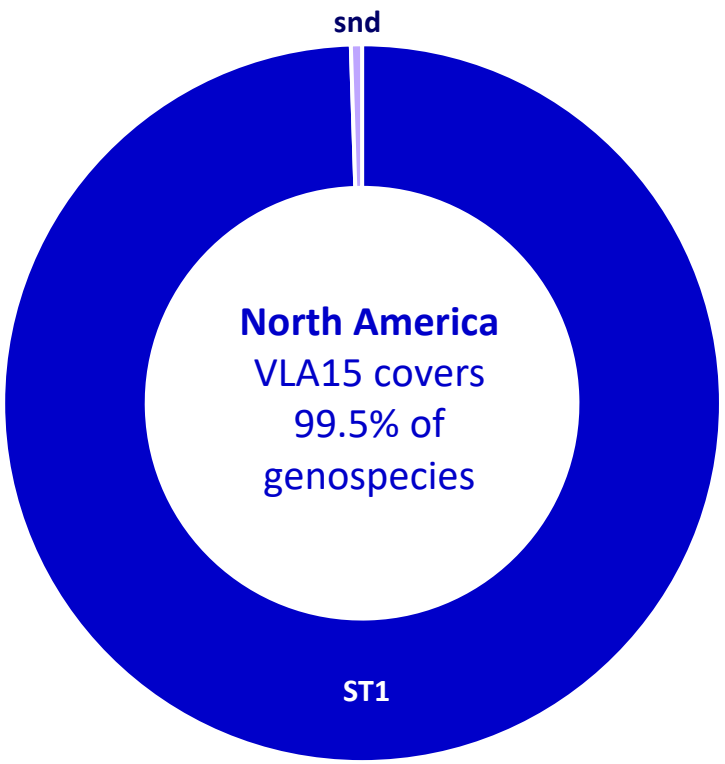
	Placebo (N = 5149)	Imulyme (N = 5156)	Vaccine Efficacy (95% CI)
Year 1 cases	37	12	68% (36-85)
Year 2 cases	26	2	92% (69-97)[a]

1. 1998. NEJM. 339(4):209; **2**. 1998. NEJM. 339(4):216; a) cohort that received 2 prime + booster (N= 3770 placebo/3745 vaccine)

VLA15 designed to cover >97% of *Borrelia* in North America and Europe

Serotypes 1-6 included in VLA15





Included in VLA15

- ST1 *B. burgdorferi ss*
- ST2 *B. afzelii*
- ST4 *B. bavariensis*
- ST3, 5, 6 *B. garinii*

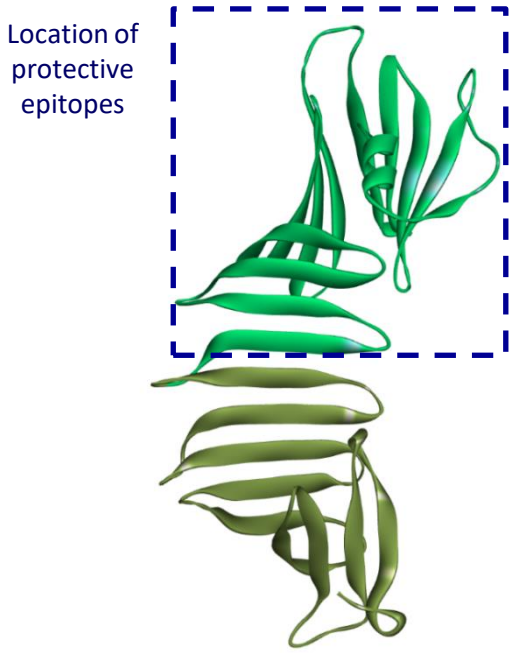
Not included in VLA15

- ST7 *B. garinii*
- snd, *B. spielmanii, B. mayonii*

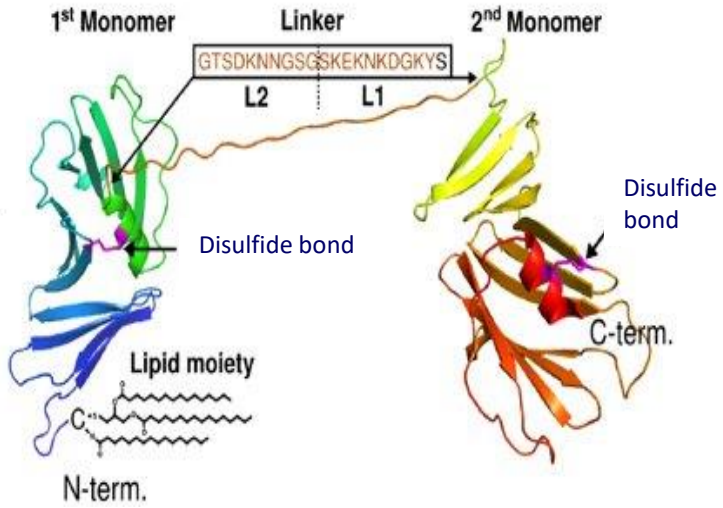
Data on Asia not available
Data sources: US: Centers for Disease Control and Prevention. EU: Data from German National Reference Center for Borrelia at the Bavarian Health and Food Safety Authority (Germany) and Baxter.
snd: serotype not determined

VLA15 hexavalent vaccine based on the C-terminal fragment of OspA ST1-ST6 linked in pairs, forming 3 fusion proteins

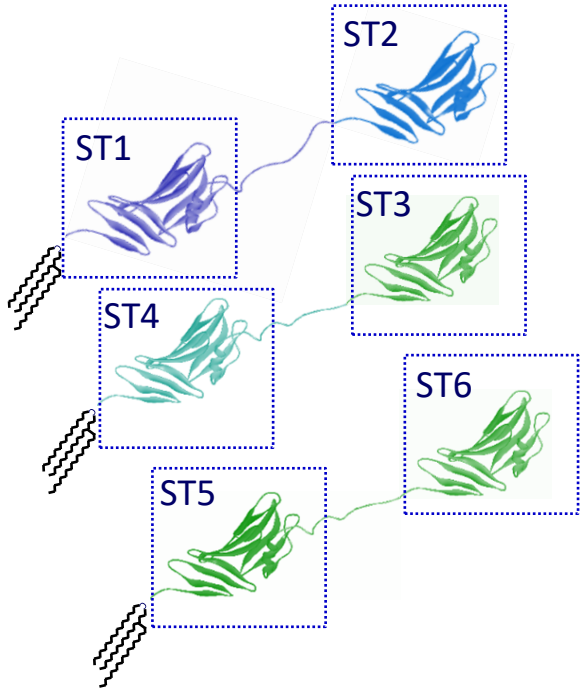
Lymerix/Imulyme full length ST1



VLA15 fusion protein



VLA15*



1, Golde et al. 1997 Inf. Imm. 65:882-9. 2, Comstedt et al. 2014, PLoS One 9:e113294; Comstedt et al. 2015, Vaccine 33:5982-8. 3, Lathrop et al. 2002, Vaccine 20:1603-8. 4, Steere et al. 2011, CID 52 (Suppl 3) S259,
* 1:1:1, formulated with $Al(OH)_3$

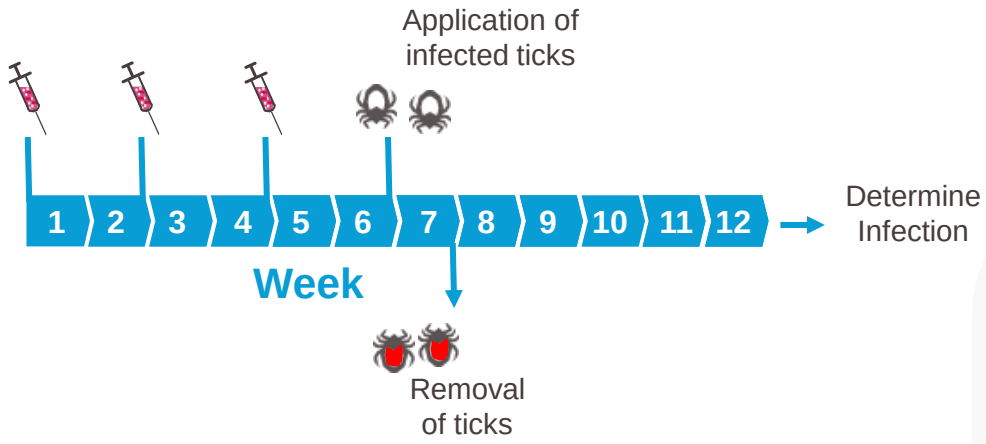
VLA15 Protects Against Infection in Tick Challenge Mouse Model

Proof-of-concept

Active Immunization

VLA15 was as efficacious as native full-length OspA

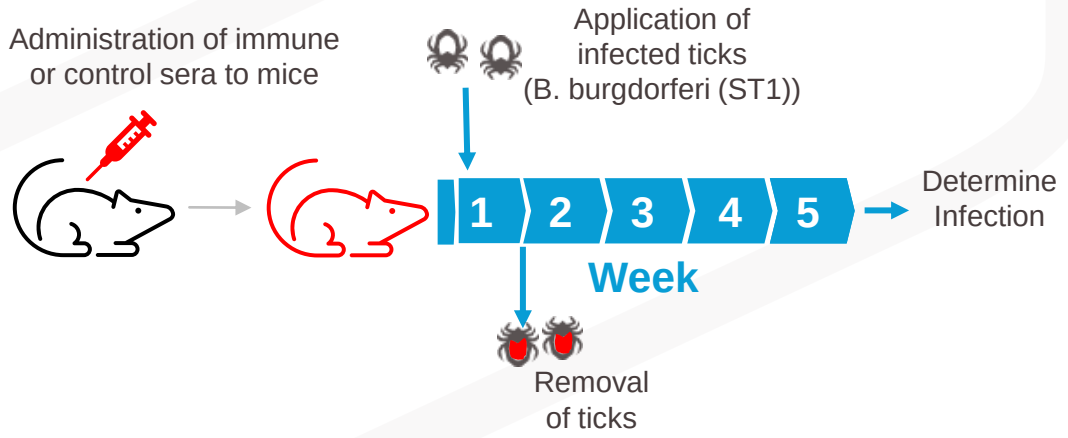
Immunization		Infection (infected/total)		
Immunogen	Dose	*B. burgdorferi* Pra1 (ST1)	*B. afzelii* IS1 (ST2)	*B. bavariensis* Marx1 (ST4)
Lip-OspA	1 µg	2/17**	0/17***	0/11***
VLA15	3 µg	0/18***	0/16***	0/11***
Placebo	-	9/13	13/13	12/15



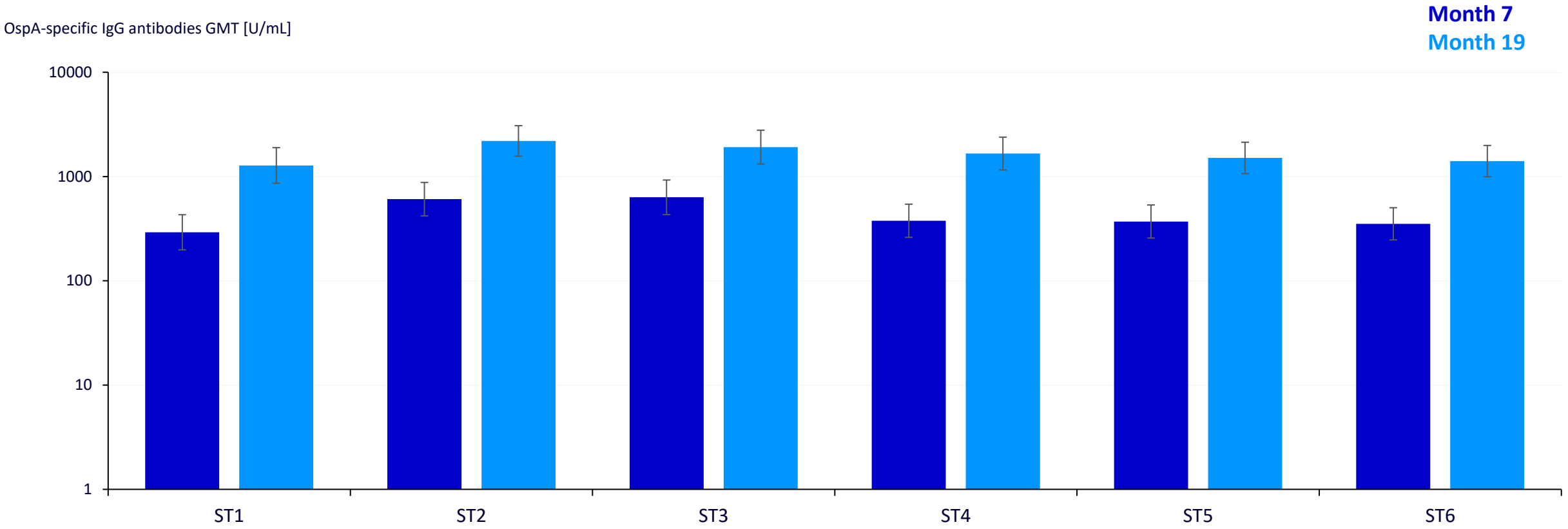
Passive Transfer

High dilutions of VLA15 human sera were protective

Human serum for passive transfer	GMT post transfer (U/mL)	Infection infected/total	P value
Neat VLA15-202 serum pool	1196	0/9	0.0090
1:2 diluted VLA15 pool	559	0/10	0.0031
1:4 diluted VLA15 pool	256	1/8	0.0498
1:8 diluted VLA15 pool	131	1/9	0.0498
Non-immune serum	negative	6/9	n/a

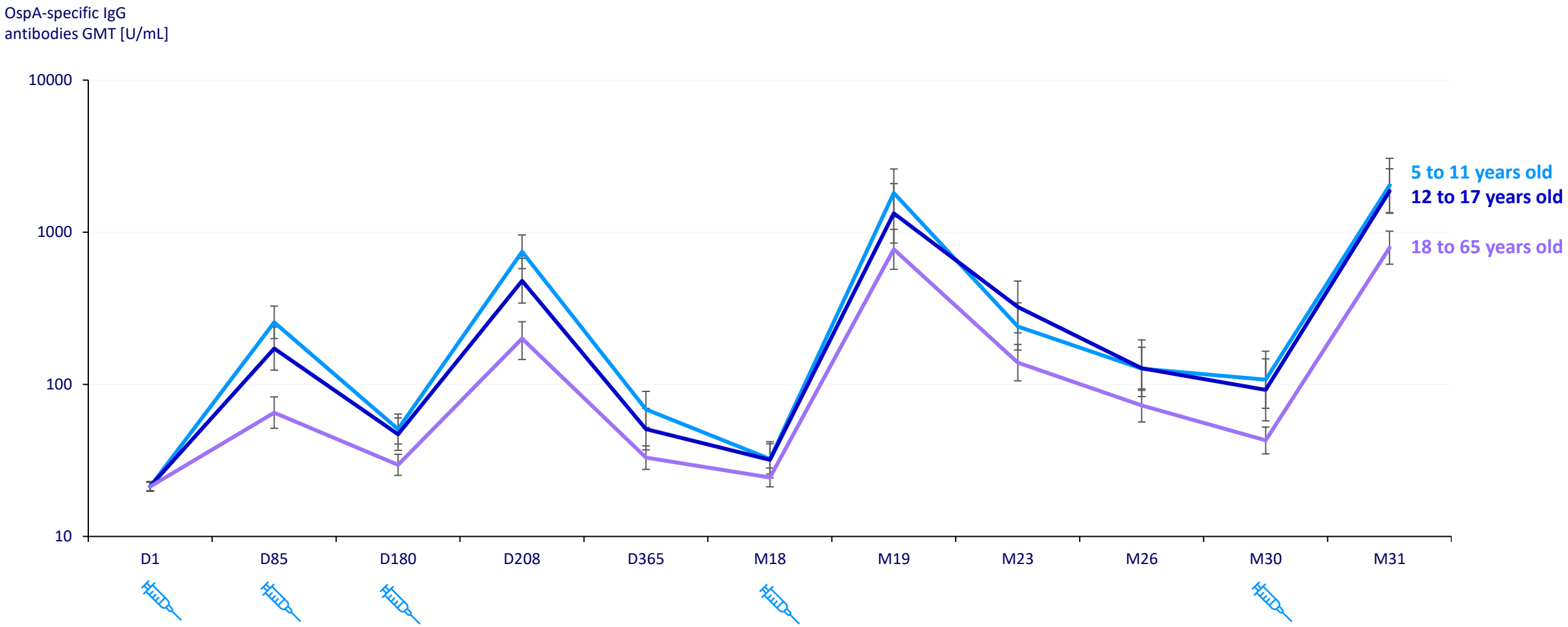


VLA15-202: Increased GMTs against all six serotypes for adults immunized with a 4th dose of VLA15



VLA15-202:BSP Final Analysis Version 2 Table 14.7.3.1.4-9: ELISA: GMTs for OspA ST1-6-specific IgG by Visit (Booster PP Population) and Figure 14.7.3.46: Bar Chart: ELISA OspA- Specific IgG Antibodies (GMT) by Serotype Over Time for Group 180 µg w/ B (Booster PP Population)

VLA15-221: A 5th dose of VLA15 significantly increases OspA-specific ST1 IgG GMT titers in all age groups

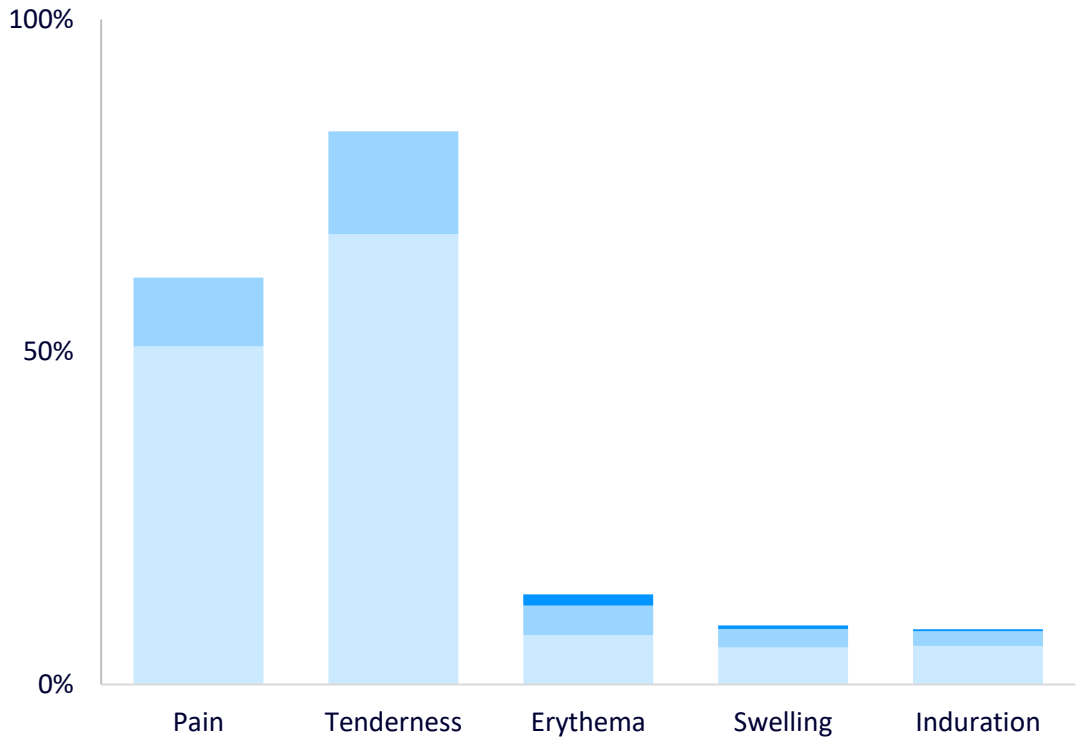


VLA15-221: Analysis 4 Table 14.4.3.2.4: ELISA: GMTs for OspA ST1 Specific IgG Antibodies by Visit (Full Analysis Set)

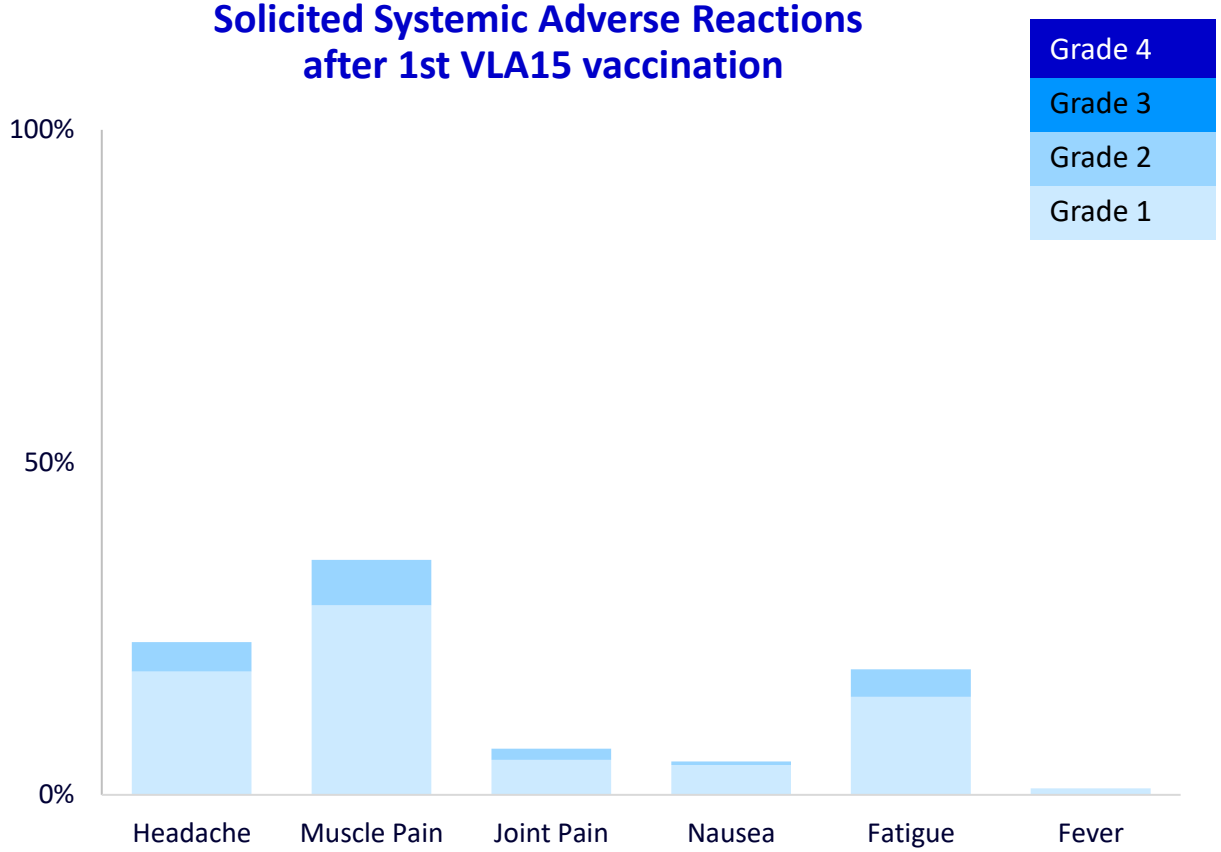
VLA15-221:VLA15 candidate was well tolerated

Most adverse reactions were mild or moderate with similar frequencies after any VLA15 vaccination

Solicited Local (Injection Site) Adverse Reactions after 1st VLA15 vaccination



Solicited Systemic Adverse Reactions after 1st VLA15 vaccination



VLA15-221 Analysis 1, Version 2: Table 14.1.4.23.1: Solicited Local Adverse Events by Symptom and Vaccination Period Classified by Maximum Severity (Safety Analysis Set); Table 14.1.4.24.1: Solicited Systemic Adverse Events by Symptom and Vaccination Period Classified by Maximum Severity (Safety Analysis Set); Rates after subsequent vaccinations were in similar range.

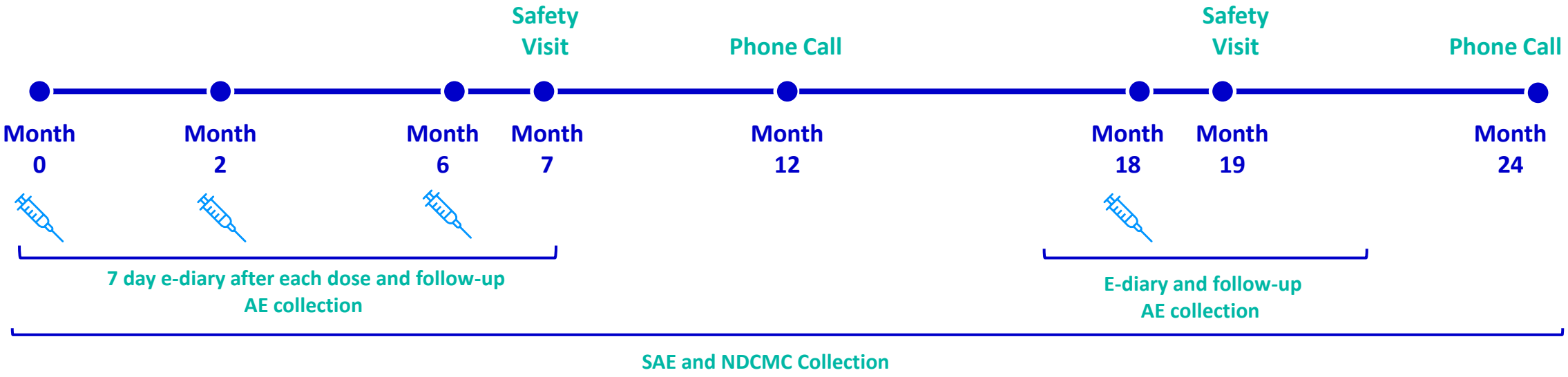
Phase 3 pediatric safety study design

Evaluate safety in pediatric population

Age Group
5-17 years
(N=3550)

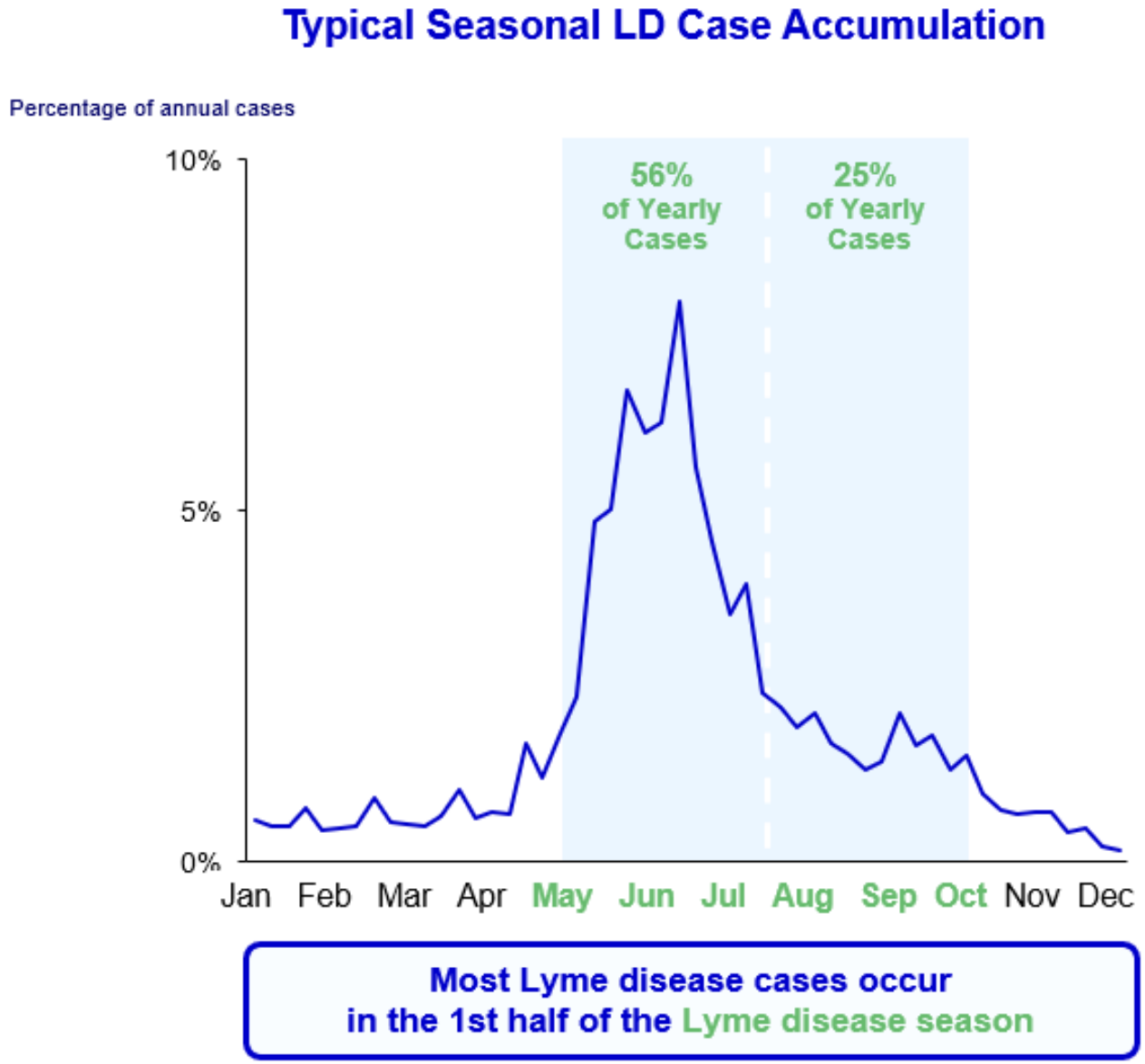
Schedule
Month 0-2-6-18

Dose
VLA15 180 µg w/ Alum
Randomized 3:1 VLA15: Placebo



AE: adverse event; SAE: severe adverse event; NDCMC: newly diagnosed chronic medical condition

Phase 3 study vaccination schedule designed to provide maximal immunogenicity through the LD season



C4601003: Phase 3, multicenter, placebo-controlled, randomized, observer-blinded trial to evaluate the efficacy, safety, tolerability, immunogenicity, and lot consistency of VLA15 in healthy participants ≥5 years of age

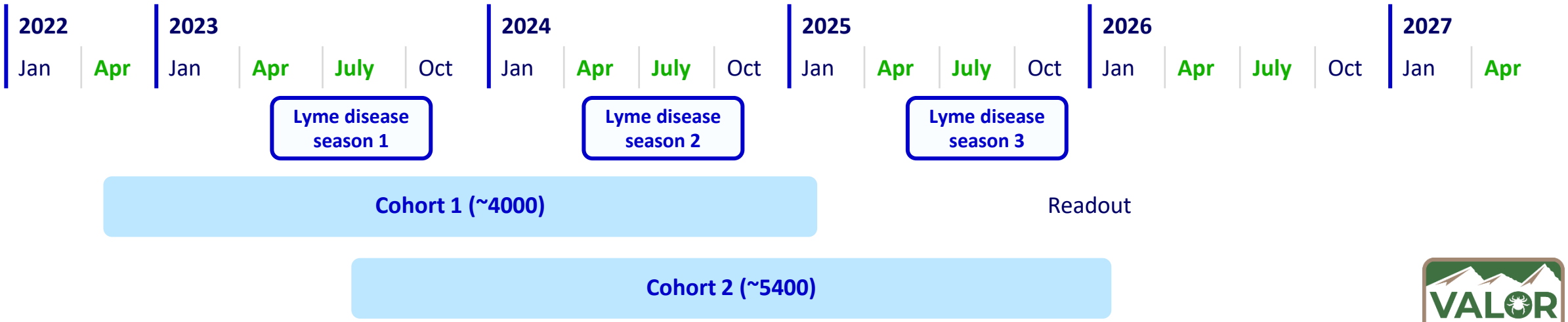
Primary efficacy endpoint post dose 4 (season 2)

Age
5+ years
(N=~9400)

Schedule
Month 0, 2, 5-9,
1 year booster

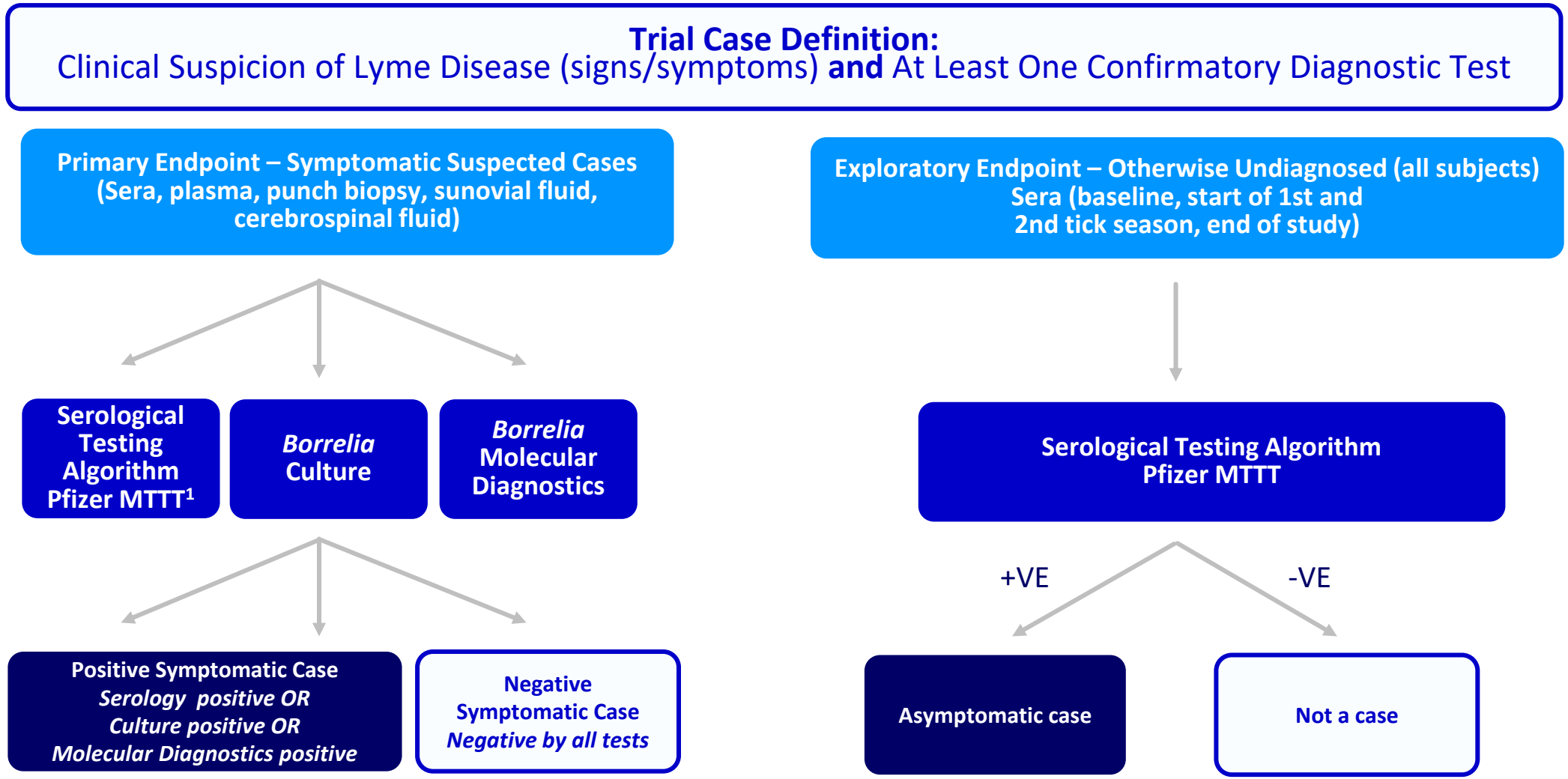
Dose
VLA15 180 µg w/ Alum
Randomized 1:1 VLA15: Placebo

Sites
86 sites in high incidence areas in Canada, United States, Germany, Poland, Finland, Sweden, Netherlands



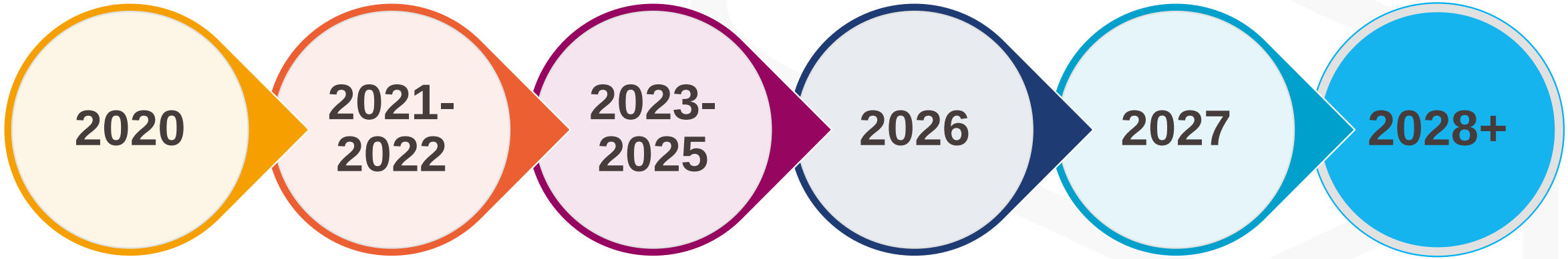
NCT05477524
https://www.valorlymestudy.com/

Lyme vaccine Phase 3 diagnostic algorithms



1. Modified 2-tier testing

Valneva and Pfizer's Collaboration to Co-Develop and Commercialize Lyme Disease Vaccine VLA15



2020

Established co-development and exclusive commercialization license with Pfizer

$130 million upfront

2021-2022

Positive Phase 2 results

Accelerated pediatric development with Phase 2 study 221;
$10 million milestone

Initiated Phase 3 VALOR study;
$25 million milestone

$95 million equity investment by Pfizer

2023-2025

VALOR study execution (ongoing)

Primary vaccination completed

Completed contribution to Phase 3 costs (April 2024)

2026

U.S./European regulatory filings, pending positive data

FDA Fast Track

2027

1st potential approvals and commercialization

$143 million in milestone payments

2028+

Global commercialization

14-22% sales royalties

$100 million in cumulative sales milestones

Valneva Commercial Business

Dipal Patel
Chief Commercial Officer

valneva

Valneva has a Growing Presence in Travel Medicine

Driven by portfolio of differentiated products[1]

IXIARO®
Japanese encephalitis vaccine (inactivated, adsorbed)

Only Japanese encephalitis vaccine approved in U.S. and Europe

Vaccine requirement for U.S. military deployed to parts of Asia

IXCHIQ®
(CHIKUNGUNYA VACCINE, LIVE)

First and only approved **single-shot** chikungunya vaccine

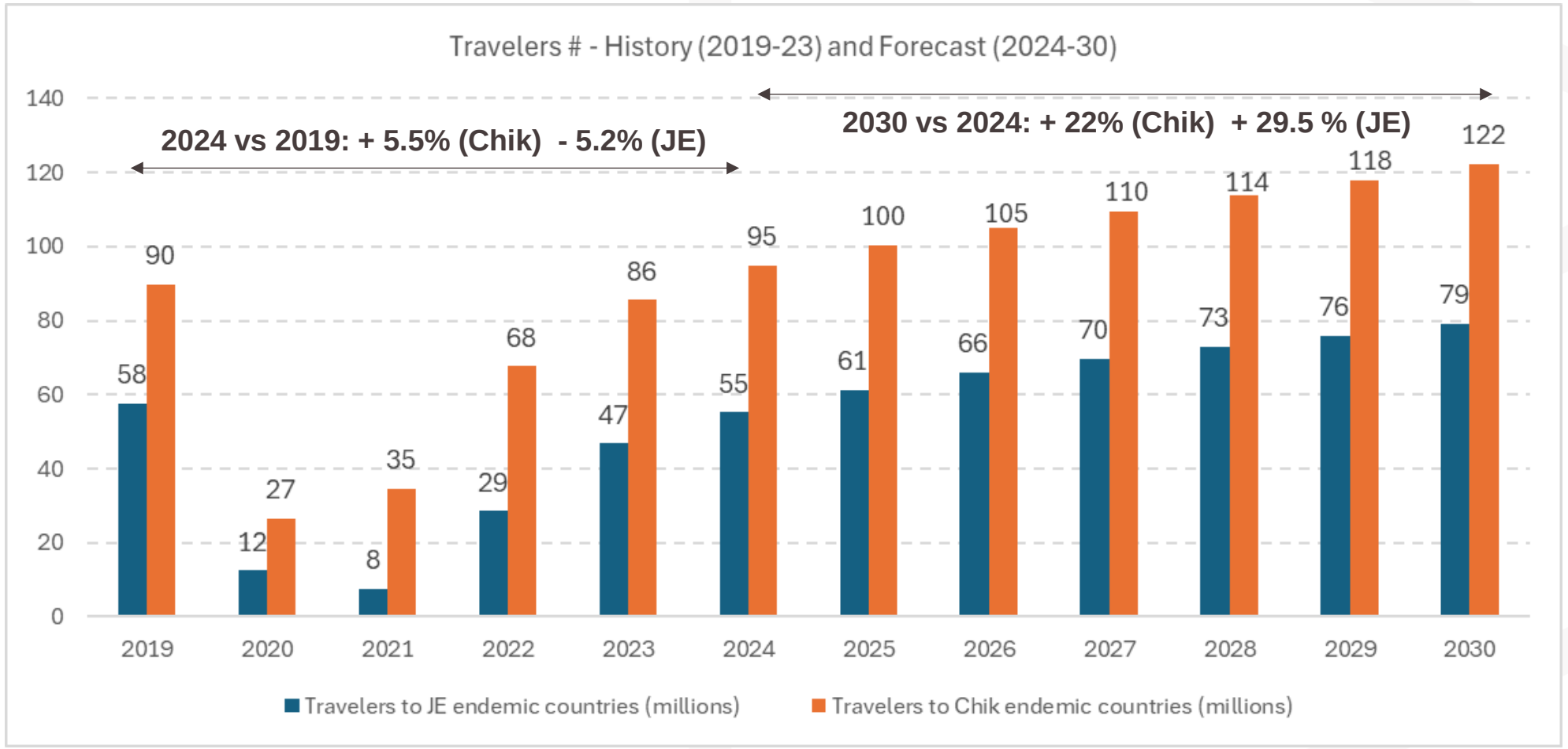
DUKORAL®
Oral inactivated cholera vaccine

Only Cholera and ETEC[2] vaccine approved

1 Please refer to Product / Prescribing Information (PI) / approved in your respective country for complete information about this vaccine; **2 Enterotoxigenic *E. Coli*** (ETEC) indication in some markets only

Traveler from U.S. and EU: History and Forecast

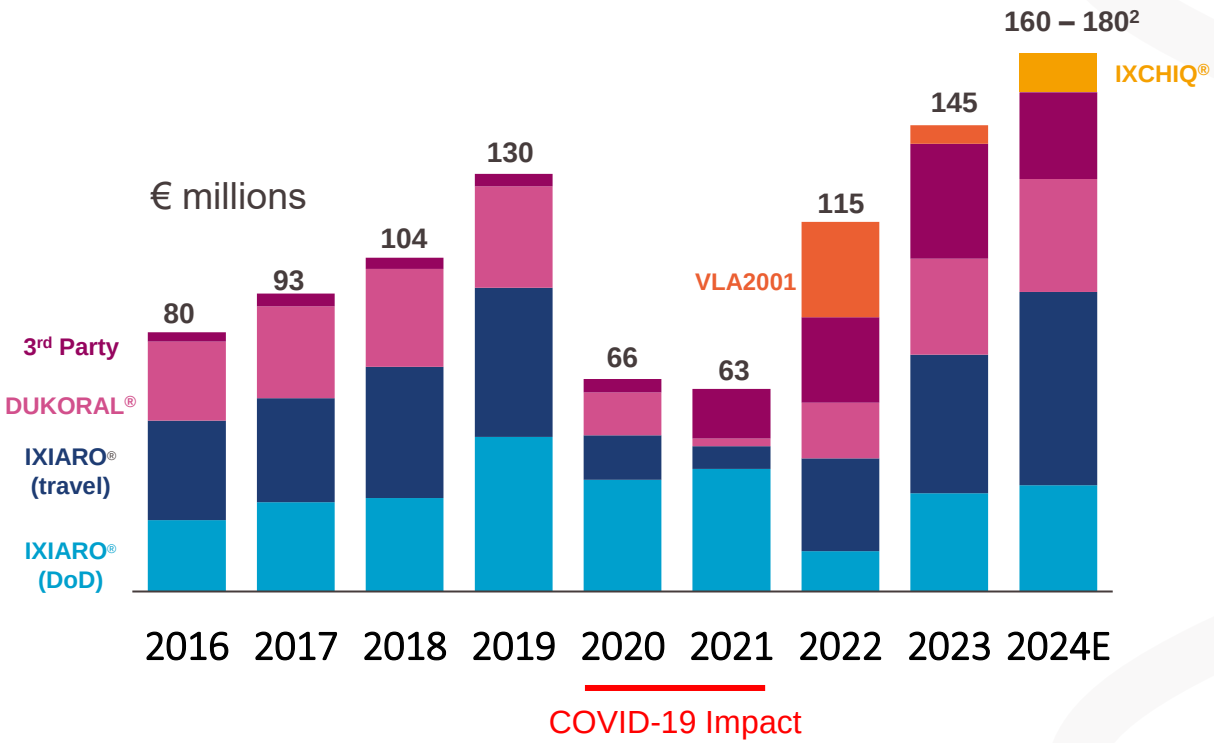
Recovering from pre-COVID-19; strong growth anticipated



Data source: IATA data – last update August 2024

Strong Travel Revenue Recovery and Growth Post-Pandemic

Surpassed Pre-Pandemic Levels by 12% in 2023[1]; continued growth in H1 2024[2]



Targeting ~2X Growth by 2026/7

- Continued travel sales growth for IXIARO® and DUKORAL®
- Double-digit CAGR for IXIARO® for at least the next three years
- Global IXCHIQ® launch acceleration and label expansions
- Key Growth Drivers
  - Targeted execution
  - Channel expansion
  - Enhanced access via IRA

1 Valneva Reports Full Year 2023 Revenue and Cash, Provides First 2024 Guidance; 2 Valneva Reports Half Year 2024 Financial Results and Provides Corporate Updates

IXCHIQ® Builds on Key Differentiators to Drive Growth

IXCHIQ®
(CHIKUNGUNYA VACCINE, LIVE)

The 1st and only vaccine against chikungunya providing a strong and persistent immune response with only one dose

- 98.9% seroresponse rate at Day 29 - Sustained seroresponse rate at 97% after two years (EU label)
- Only chikungunya vaccine to show strong immunogenicity in adults 18-64 yrs and 65+ (U.S., EU, CA labels)
- Generally well tolerated among the >3,600 adults and 754 adolescents evaluated for safety
- Convenient single dose

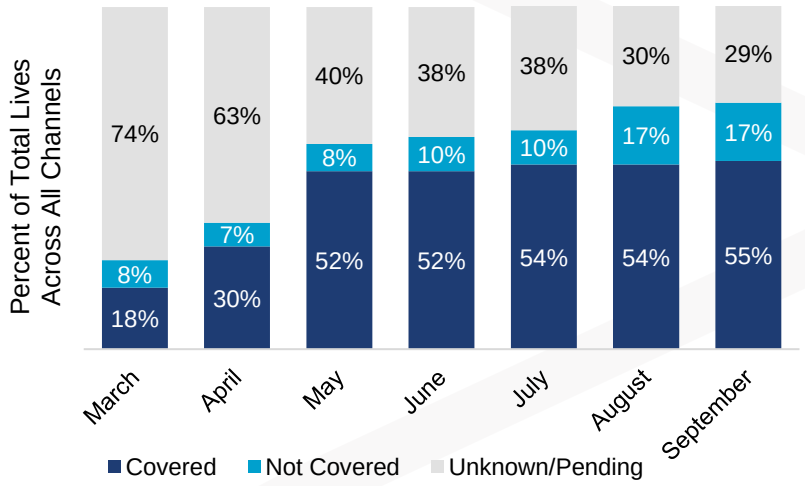
Promising Lead Metrics in IXCHIQ® Launch

Focus on building HCP confidence and establishing IXCHIQ® as a differentiated brand

What Gives Us Confidence in the Launch

- Stronger uptake, driven by greater awareness
- Accounts and order volumes increasing month-over-month; new contracts with customers
- Distributors and customers re-ordering
- Growth in retail channel and public health
- DHA-IHD[1] adopted CDC[2] recommendations; published CHIKV and vaccines guidance

Insurance coverage continues to grow



Successful Efforts Driving Awareness and Intent to Utilize IXCHIQ®

82%
likely or very likely to implement IXCHIQ® into their practice

Recent HCP Survey

1 Defense Health Agency – Immunization Healthcare Division; **2.** U.S. Centers for Disease Control and Prevention; 3.Covered Lives defined as individuals with access to IXCHIQ through an explicit coverage policy; based on MMIT coverage Data as of September 10, 2024

Accessing the Global Market for Chikungunya Vaccines

Current Focus
U.S./ACIP Priority
Certain Travelers[1]

Expand Population
Travelers
- Additional launches (CA/EU)
- Label expansion
- Improved surveillance
- Efficacy data to drive confidence

Improve Access
Endemic / LMIC
LATAM and Asia via partnerships

Expand Use
Military
Protocol and policy effort with DoD

1 Individuals aged 65+ at risk traveling to an area where there's been chikungunya transmission within the last 5 years; 18–64-year-olds traveling to these regions for >6 months cumulatively; adult travelers to areas where there is a current chikungunya outbreak

Upcoming and Future Opportunities to Capture Greater Penetration

Upcoming and Future Opportunities

- MMWR[1] publication to drive further retail growth in U.S.
- European and Canadian launches
- Additional ACIP[2] and European recommendations
- Travel software protocol updates
- Significant label updates in the next 12 months expected to further differentiate IXCHIQ®
- LMIC[3] approval(s); additional partnership(s)
- Continued discussions with U.S. Department of Defense

1. Morbidity and Mortality Weekly Report; 2. CDC Advisory Committee on Immunization Practices; 3 Low and middle income countries

Q&A Break

Investor Day 2024

October 10th, 2024

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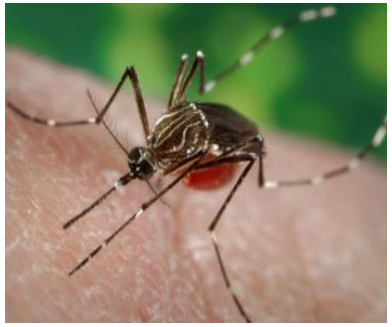
The World's First and Only Chikungunya Vaccine

Susanne Eder-Lingelbach
VP, Clinical Development

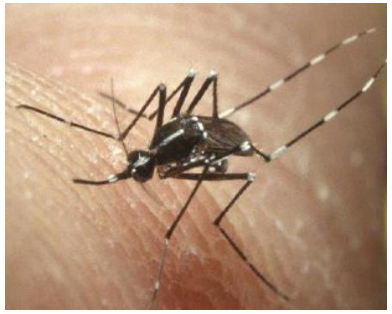
valneva

Chikungunya: A Major Public Health Threat

Mosquito-transmitted outbreak disease with potentially debilitating consequences



Aedes aegypti



Aedes albopictus

Often causes **large, explosive outbreaks**

Affecting **up to 75%** of the local population[1]

Substantial quality-of-life and **health-economic impact**

Nearly half (43%) of those infected develop **chronic symptoms**[2]

~460,000 cases and 170 deaths associated with chikungunya disease worldwide in 2024[3];

Most cases reported in **Brazil, Paraguay, Argentina and Bolivia**

Four-fold increase in India from 2023[3]

Identified in >110 countries across five continents

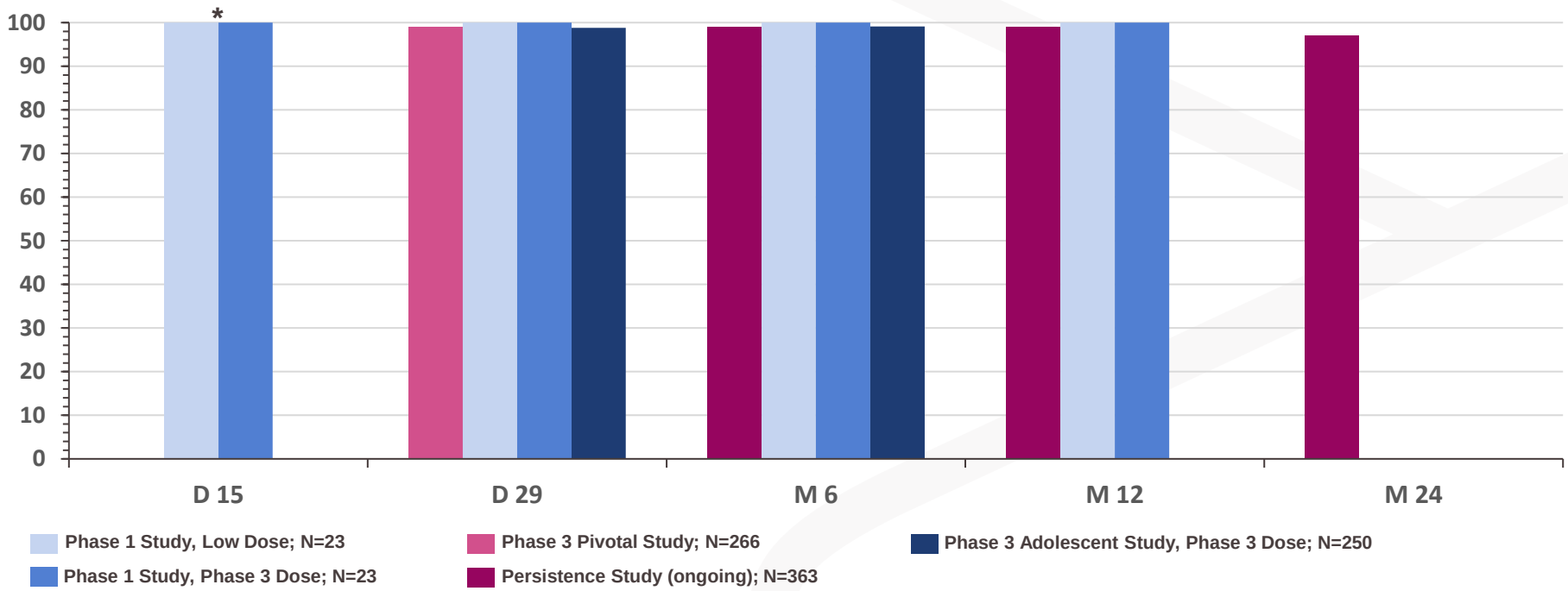
75% of world population lives in areas at-risk of chikungunya

1. Staples et al. CDC Yellow Book 2020, Chapter 4; 2. Bettis et al, PLOS Neglected Tropical Diseases 16(1): e0010069. 2. Rama K, et al. PLoS Negl Trop Dis. 2024;18(6):e0012254; 3. As of September 30th; https://bluedot.global/vaccines-on-the-table-as-chikungunya-outbreak-intensifies-in-india/

IXCHIQ® / VLA1553 - Strong and Sustained Response Regardless Of Age

Immunological profile

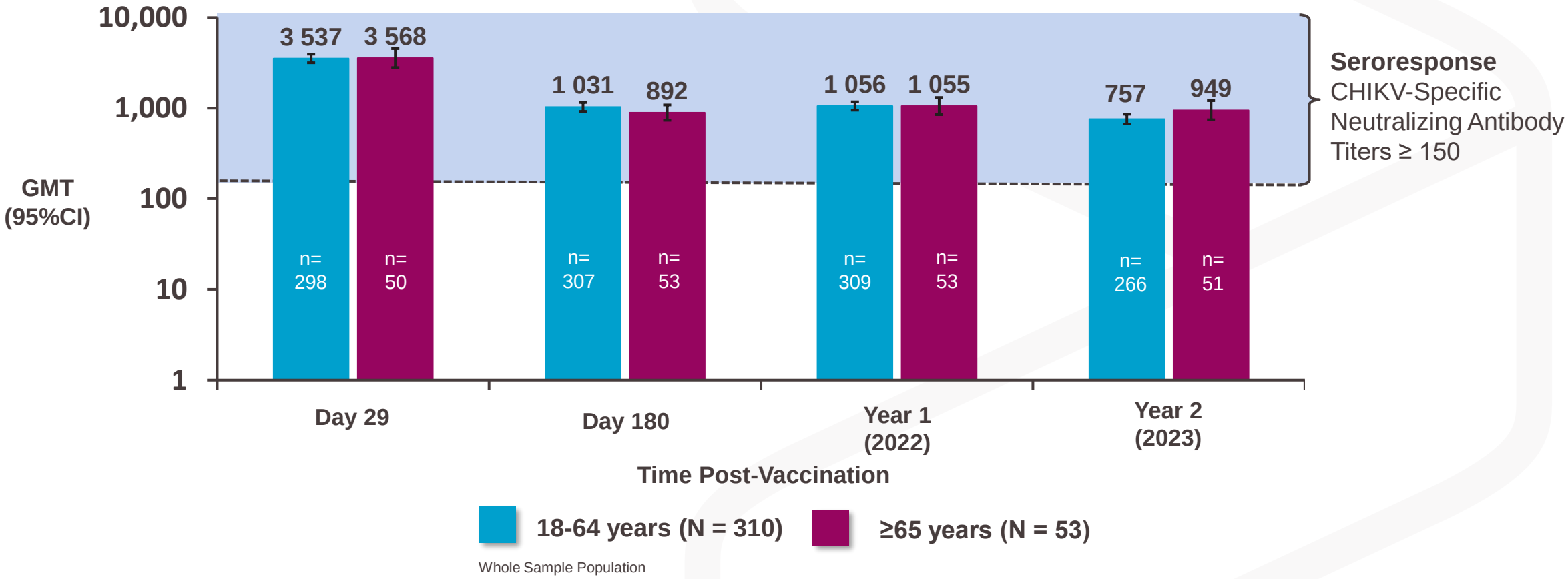
Seroresponse sustained at highest levels up to 24 Months



***** Wressnigg et al, Lancet ID: https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30238-3/fulltext; Re-testing of Phase 1 sera (vaccinated with liquid formulation of VLA1553) using the final assay/threshold used for the pivotal endpoint; data presented at CISTM18, May 2023

Two-year Antibody Persistence Further Supports Target Product Profile

Seroresponse in adults aged ≥ 18 years (VLA1553-303)



Whole Sample Population

IXCHIQ®: Focused on Expanding Access, Label Extension, Product Profile

Robust clinical program supported by new $43.1 million CEPI grant[1]

Post-Marketing Effectiveness[2] (Phase 4)

To confirm effectiveness following licensure based on an immunological surrogate of protection and to optimize description of the safety profile

- Observational effectiveness study in Brazil
- Pragmatic randomized controlled effectiveness and safety study[3]: adults (and adolescents - tbc) in endemic countries
- Prospective safety cohort study and pregnancy surveillance in Brazil

Label Extension

To expand access to the vaccine for all age groups

- Phase 3: Randomized, controlled study in adolescents aged 12 - <18 years; reported positive data up to Month 6 — **Completed**
- Phase 2: Randomized, dose response study in healthy children aged 1 to <12 years — **Fully Enrolled**

Product Profile

To confirm the long-term durability of the immune response and further differentiate the vaccine

- Phase 3: Ongoing antibody persistence and long-term safety study in adults; reported positive 24-month results to date

1. https://valneva.com/press-release/cepi-expands-partnership-with-valneva-with-a-41-3-million-grant-to-support-broader-access-to-the-worlds-first-chikungunya-vaccine/; **2.** https://www.fda.gov/media/173759/download;
3. https://www.fda.gov/media/172166/download

IXCHIQ® is approved under the accelerated licensure pathway[1]

Phase 4 aims to verify the clinical benefit in two[2] key post-marketing effectiveness studies

VLA1553-402	VLA1553-404
Observational effectiveness study in population in endemic areas of Brazil	**Pragmatic randomized controlled effectiveness and safety study in adults (and adolescents – tbc) in endemic countries (n ~ 20.000)**
▪ To estimate the effectiveness of IXCHIQ® (VLA1553) in the prevention of symptomatic laboratory-confirmed CHIKV cases after a single vaccination ▪ Test-negative case control study (RT-PCR case confirmation), target: ~450 cases / 890 controls ▪ Municipality selection based on CHIKV transmission epidemiological criteria, operational & logistical aspects ▪ Pilot vaccination program targeting 15-20% vaccination coverage – Prospective Safety Cohort Study (n ~ 5000) – Pregnancy Surveillance – Serosurvey (CHIKV pre-exposure assessment)	▪ To assess effectiveness of IXCHIQ® (VLA1553) in the prevention of symptomatic laboratory-confirmed CHIKV cases after a single vaccination compared to control participants during the same trial period ▪ 1:1 randomization ▪ Safety evaluation (n ≥10.000) including severe chikungunya-like adverse reactions and prolonged arthralgia ▪ Statutory requirement[3] for well-controlled clinical investigation, trial introduced to address potential biases associated with an observational design
2025/6 – 2028 (incl. pilot vaccination program)	**2025/6 - 2029**

1. https://www.fda.gov/vaccines-blood-biologics/ixchiq; **2.** https://www.fda.gov/media/173759/download; **3.** https://www.fda.gov/media/172166/download

IXCHIQ® targeted to be made available for all age-groups[1]

Staggered pediatric development program until 2030/1 (incl. below 1yr of age)

VLA1553-321

Randomized, controlled, double-blinded pivotal study in adolescents aged 12 years to <18 years in Brazil

- To evaluate safety and immunogenicity of VLA1553 in adolescents aged 12 years to <18 years (n=754; 2:1)
- Including individuals positive for chikungunya at baseline
- Primary Endpoint: seroresponse rate for baseline negative participants 28 days post-vaccination
- Secondary Endpoints including safety and immunogenicity up to Month 12

6m follow-up completed > submission for label extension

VLA1553-221

Randomized, controlled, double-blinded study in children aged 1 year to <12 years in Dom. Rep. and Honduras

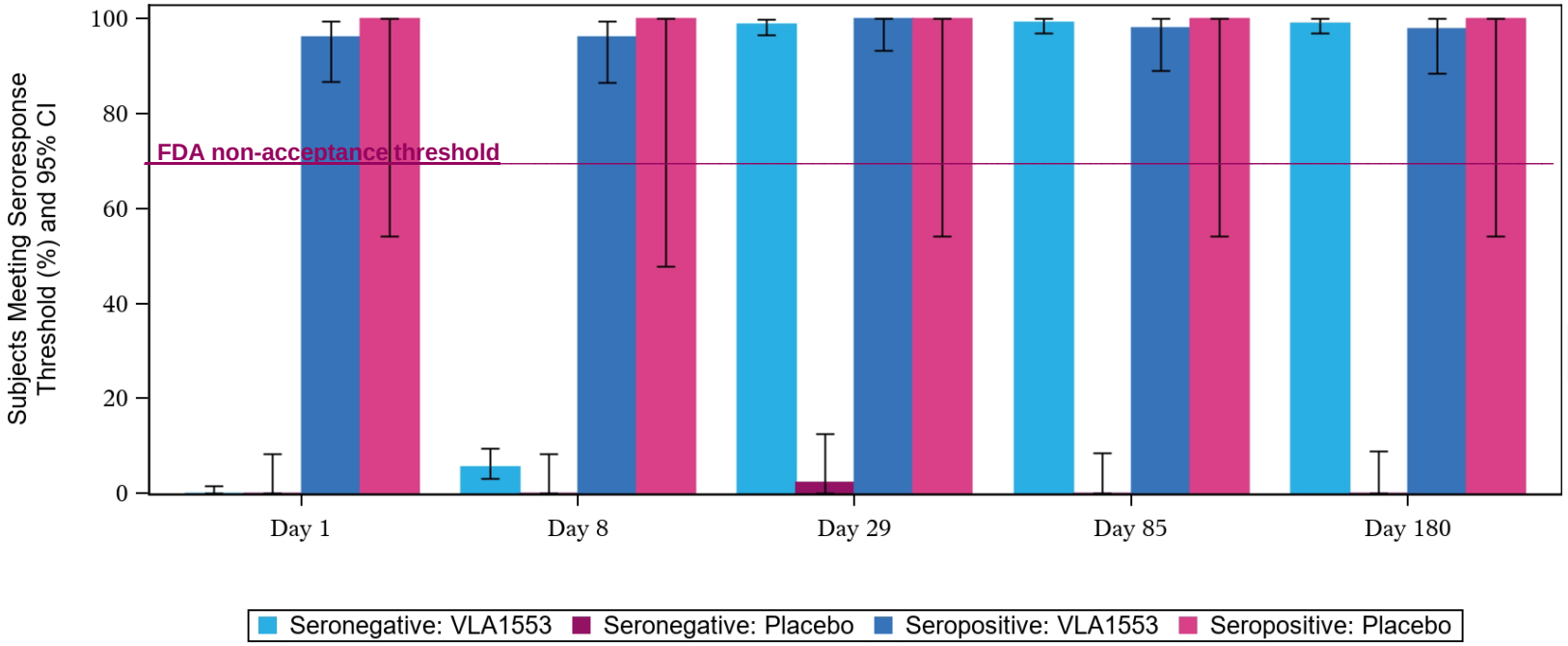
- To evaluate full and half adult dose for safety and immunogenicity in children (n~ 300; 2:2:1; active comparator = Nimenrix)
- Including individuals seropositive for chikungunya at baseline
- Primary Endpoint: Frequency and severity of solicited injection site and systemic reactions within 14 days post-vaccination
- Secondary Endpoints including safety and immunogenicity up to Month 12

Expected results 2025 – thereafter transition into Phase 3 (1 to <12yrs)

1. https://www.fda.gov/vaccines-blood-biologics/ixchiq; **2.** https://www.fda.gov/media/173759/download; **3.** https://www.fda.gov/media/172166/download

Strong and Sustained Seroresponse Rates in Adolescents

VLA1553 response is similar to baseline seropositive individuals



Seronegative: VLA1553	0/250	14/245	248/251	238/240	232/234
Seronegative: Placebo	0/42	0/42	1/42	0/41	0/39
Seropositive: VLA1553	50/52	49/51	52/52	48/49	45/46
Seropositive: Placebo	6/6	5/5	6/6	6/6	6/6

Seroresponse is defined as **$\mu PRNT_{50}$ ≥150** for all participants.
One sample of a participant in the placebo arm revealed a µPRNT result ≥150 only at Day 29, it was tested <20 at Day 85 and Day 180.

PP Population

Only CHIKV vaccine to achieve target immunogenicity with a single shot

Differentiated vaccine shows rapid, long-lasting immunity across all age groups tested[1,2,5]

Immunogenicity Data

- 99% Seroresponse[3] Rate (SRR) after single vaccination → maintained at 97% after 24 months[4,5]
- Similar SRR and antibody titers in age 65+ adults as younger adults[1,4]
- 100% SRR after 14 days and sustained to Month 12[2]
- Adolescent trial met primary endpoint[6]: highly immunogenic in baseline-negative individuals; 99% SRR

Safety Data

- Generally well tolerated by >3,600 adults and 754 adolescents
- Pivotal Safety (solicited systemic AEs):
  - ~50% of participants, most commonly headache, fatigue, myalgia
  - Majority mild or moderate; 2.0% reported as severe, most commonly fever
- Adolescent trial suggests favorable safety profile regardless of previous CHIKV infection[7]

1. Valneva Successfully Completes Pivotal Phase 3 Trial of Single-Shot Chikungunya Vaccine Candidate; 2. Re-testing of Phase 1 sera (vaccinated with liquid formulation of VLA1553) using the final assay/threshold used for the pivotal endpoint; data presented at CISTM18, May 2023; 3. CHIKV neutralizing antibody titer of ≥150 by $\mu PRNT_{50}$ (Micro Plaque Reduction Neutralization Test), agreed with regulators to be used as a surrogate endpoint in Phase 3; 4. Valneva Reports Positive 12-Month Antibody Persistence Data for Single-Shot Chikungunya Vaccine Candidate; 5. Valneva Reports Positive 24-Month Antibody Persistence Data for its Single-Shot Chikungunya Vaccine IXCHIQ®; 6. Valneva Reports Positive Pivotal Phase 3 Immunogenicity Data in Adolescents for its Single-Shot Chikungunya Vaccine Candidate; 7. Valneva Reports Positive Initial Phase 3 Safety Data in Adolescents for its Single-Shot Chikungunya Vaccine Candidate

World's Most Clinically Advanced Tetravalent *Shigella* Vaccine Candidate

Juan Carlos Jaramillo, M.D.
Chief Medical Officer

valneva

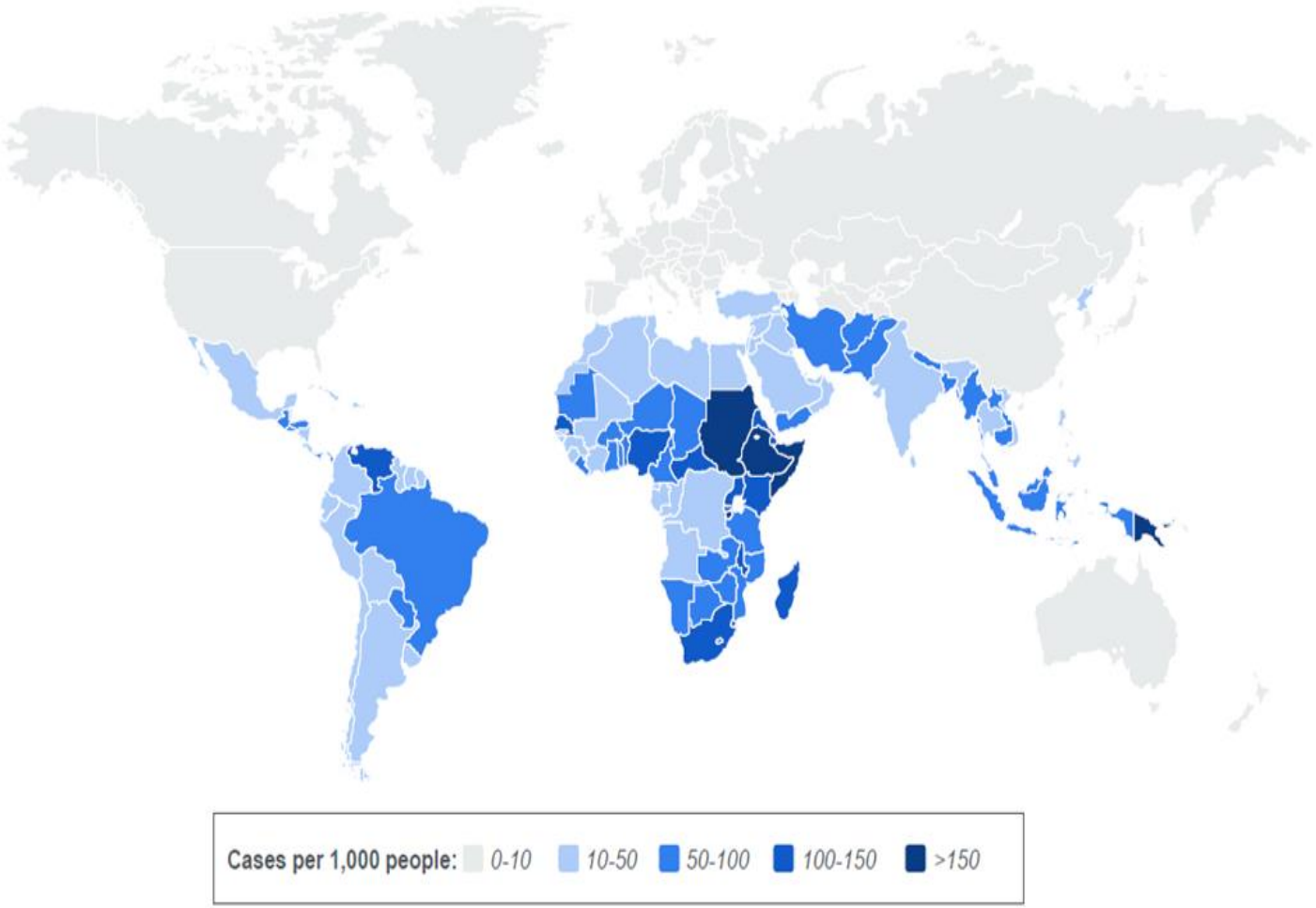
Shigellosis: Significant Unmet Medical Need[1]

No approved vaccine is currently available

- Caused by species of *Shigella* bacteria
- Second-leading cause of fatal diarrheal disease worldwide
- Estimated to cause up to 165 million cases and 600,000 deaths each year, particularly among children in LMICs[1,2]
- Highly contagious; person-to-person (directly or by contaminated materials), food- and water-borne transmissions are common
- Illness typically begins 1–2 days after exposure with symptoms lasting 5–7 days. Symptoms include diarrhea, fever and stomach cramps among others. Long term consequences can develop in children (linear growth faltering, stunting) and adults (arthritis).
- Considering the potential for herd immunity and protection from all-cause diarrhea, the development of a *Shigella* vaccine is an important goal for public health - priority for the World Health Organization (WHO)
- *Shigella* is an increasingly antimicrobial-resistant (AMR) enteric bacteria – a vaccine could indirectly help reduce the development of AMR

1. *Shigellosis* | CDC Yellow Book 2024; **2.** Low-and-middle-income countries;

Shigellosis: A Worldwide Public Health Threat



Global Incidence

- Strongly linked to economic development.
- Predominantly in the global South, especially eastern sub-Saharan Africa.
- Less common in the global North due to better infrastructure.

Lower-Income Countries

- High spread risk due to poor sanitation and limited healthcare access.
- Dense populations contribute to large case numbers (e.g., India, Indonesia, Nigeria, Ethiopia).

Higher-Income Countries

- Mostly small, sporadic outbreaks that are quickly contained.
- Often associated with international travel; local outbreaks are rare.

Source: CDC Yellow Book 2024: European Center for Disease Prevention and Control; Ekdahl et al. (2005); Badr et al. (2023); A. Khalil et al. (2018); L.E.K. IP and Research

Valneva Gains Exclusive Worldwide Rights to Tetravalent *Shigella* Vaccine

Strategic partnership with LimmaTech Biologics ("LMTB")

Vaccine candidate "S4V"

- World's most clinically advanced tetravalent Shigellosis vaccine candidate
- Tetravalent bioconjugate vaccine for prevention of disease caused by *Shigella* bacteria (O-antigens of *S. flexneri* 2a, 3a, 6 and *S. sonnei)*
- Developed following positive proof-of-concept clinical data with monovalent vaccine candidate, which demonstrated promising efficacy in challenge model
- LMTB reported positive Phase 1/2 clinical data on S4V, including robust immunogenicity against all strains; favorable safety and tolerability[1]

Key Aspects of Partnership

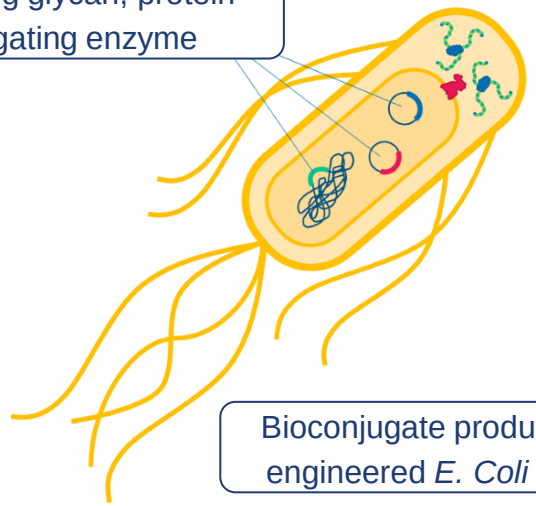
- €10 million upfront payment to LMTB
- Up to €40 million in future development, regulatory and sales-based milestones
- Low double-digit royalty on net sales (travel)
- Additional payments and single-digit royalties based on net sales (LMICs)
- Clinical collaboration through Phase 2
  - LMTB: Phase 2 CHIM[2] study (*S. Sonnei*) and pediatric immunogenicity study
  - Valneva: Phase 2 CHIM study (*S. flexneri* 2a)
- Valneva to lead all Phase 3, licensure, and commercial activities

1 https://lmtbio.com/wp-content/uploads/2024/02/20240221_LimmaTech_Shigella-Interim-Data-PR_Final.pdf; **2** Controlled Human Infection Model

Shigella Vaccine Candidate

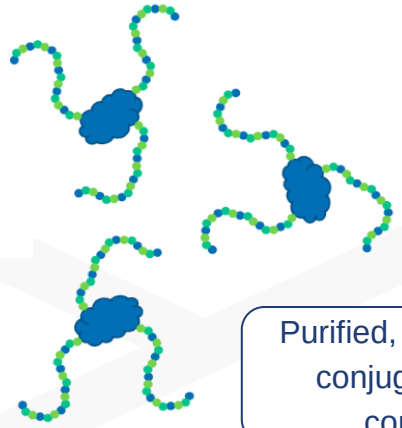
Bioconjugation technology

DNA encoding glycan, protein and conjugating enzyme



Bioconjugate produced in engineered *E. Coli* strain

Culturing and purification



Purified, homogeneous conjugate vaccine component

- O-antigen polysaccharides of the serotypes *S. flexneri* 2a, 3a, 6 and the *S. sonnei*
- These four predominant pathogenic serotypes cause around 75% of all infections globally

- O-antigen components are covalently linked to a recombinant detoxified version of *Pseudomonas aeruginosa* exoprotein A (EPA)
- Conjugation sites on EPA are pre-defined, so the bioconjugate molecule is easier to characterize and highly batch-to-batch consistent

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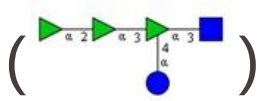
Optimized Multivalent Vaccine Candidate

Proof-of-concept studies with 4-valent bioconjugates ongoing; expected H2 2025

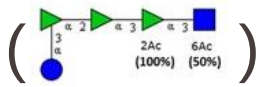
Past → Imminent

Repeating unit of the glycan structure

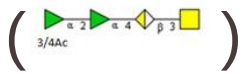
***S. flexneri* 2a**



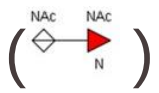
***S. flexneri* 3a**



***S. flexneri* 6**



S. sonnei



Monovalent

S. flexneri 2a
Phase 2b study*

- 37% vaccine efficacy against shigellosis
- 52% vaccine efficacy against more severe shigellosis
- >70% vaccine efficacy against more severe diarrhea (≥10 episodes/day)

Optimized Multivalent (4-valent)

- Increased O-Antigen level (Glycan:protein ratio)
- Increased Dose level (total protein)
- Increased number of conjugation sites

Human Challenge Study

Challenge with *S. sonnei*

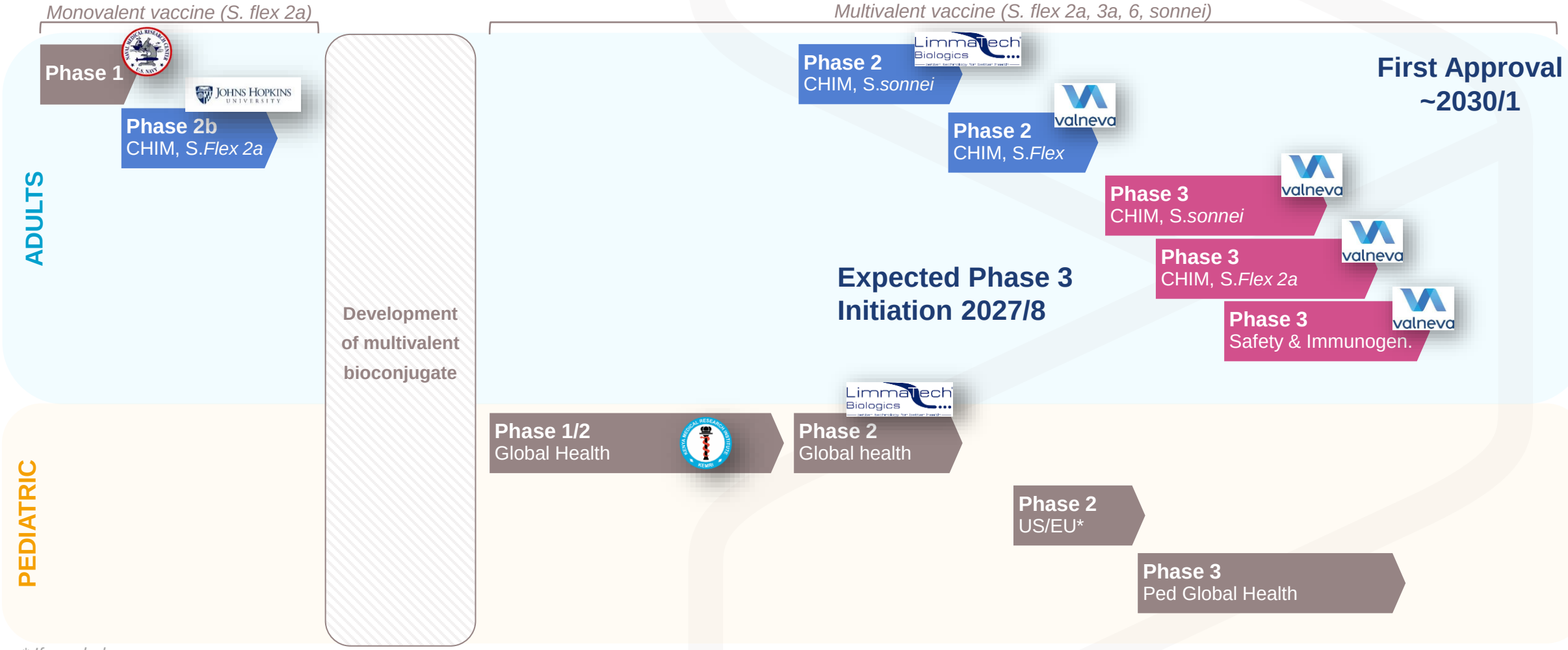
Immunogenicity for all 4 serotypes

Safety

https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(21)00103-1/fulltext; https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(21)00101-8/fulltext

Historical and Planned Clinical Studies

Multiple catalysts and decision points for envisaged development strategy



** If needed*

Anticipated Regulatory Strategy

Human challenge studies in adults combined with pediatric field efficacy studies

Adults (Initial Indication)

- Leverage existing CHIM models for *S. sonnei* and *S. flexneri* 2a
- Expand to non-CHIM serotypes provided similar immune responses can be established
- Establish safety database and lot-to-lot consistency in a dedicated study

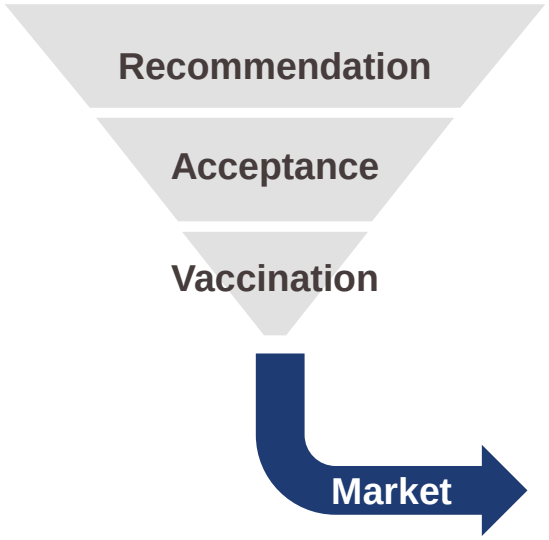
Children (Extension)

- Field efficacy studies will expand indication by providing data on
  - Pediatric population
  - Field efficacy data
  - Efficacy against any serotype of *Shigella*

Regulatory Strategy Aligned with *Lancet* Paper Authored by Key Stakeholders from FDA and EMA[1]

Commercial Assessment of Shigella vaccine

Shigella vaccine market estimated to peak at ~€500 million[1]



	Traveler (~23%)	Children in endemic countries (~76%)	Military (<1%)
Recommendation	20-50% (Med-high risk destinations)	30-100% (OOP-reimb.)	70-90% (Med-high risk destinations)
Acceptance	30% (OOP)	15-60% (OOP) 50-90% (reimb.)	90%
Vaccination	2-5%	9-11%[2] (OOP) 15-50%[2] (reimb.)	100%
Market	▪ Europe, North America, Japan, South Korea and Singapore with €80-85 million from the U.S. alone	▪ Non-Gavi endemic countries: public funding anticipated, driven by high disease burden notably in India, Brazil, Indonesia and Gavi supported countries. ▪ Gavi-supported countries, vaccines could cover over 10m children per year	▪ U.S. representing c.50% of the revenue

Source: Market Study: LEK 2024, 1 Appox. 7 years after launch; 2 Converted to vaccination rate by applying the yearly vaccination penetration every year over a cohort of 5 years

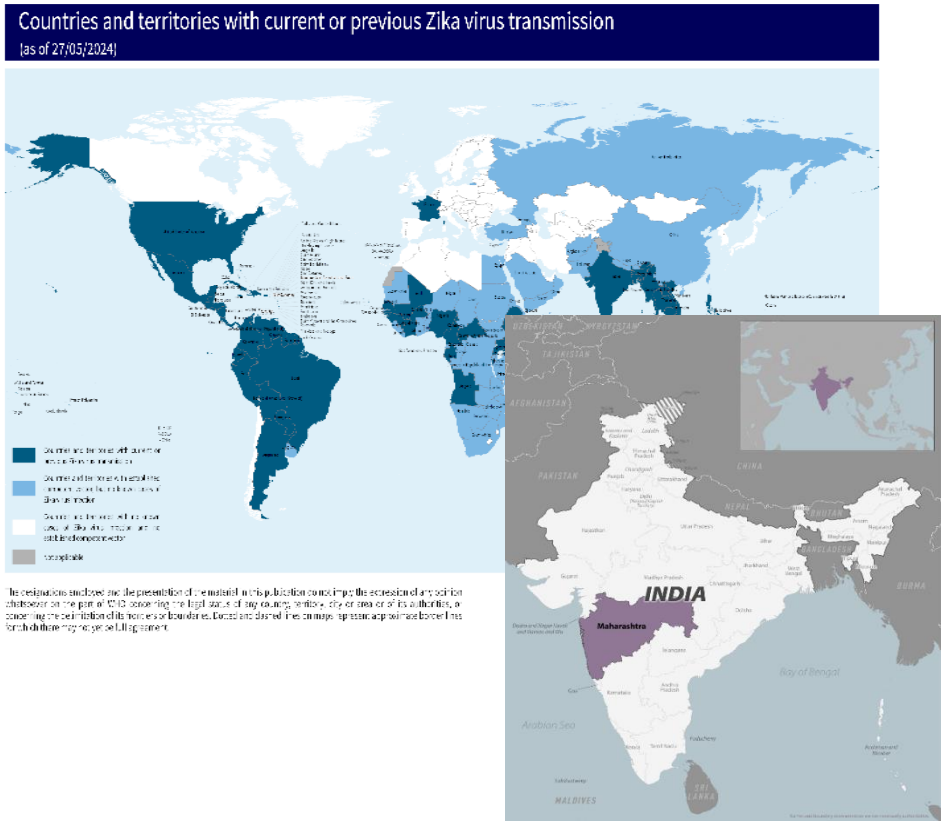
Second-Generation Zika Virus Vaccine Candidate

Susanne Eder-Lingelbach
VP, Clinical Development

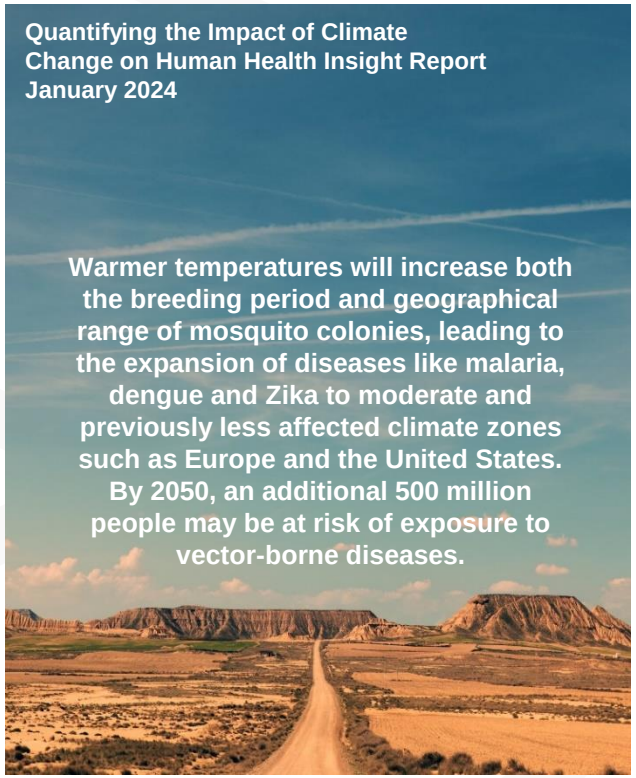
valneva

Current Zika Outbreaks and Travel Warnings / WHO / CDC / PAHO

Notable outbreaks in several countries, particularly in the Americas



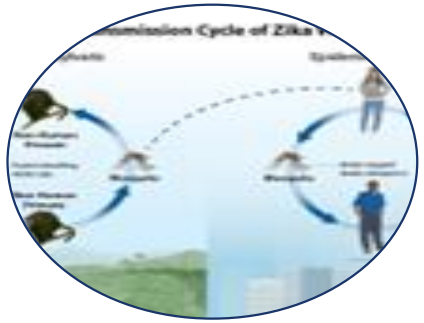
- **Cases in The Americas:**
  40,528 in 2024 (as of Sept. 29th)
  vs
  36,748 in 2023
- **Brazil remains** the most significantly impacted, followed by **Colombia, Bolivia, Peru, Costa Rica, and Puerto Rico.**



Sources: https://www3.weforum.org/docs/WEF_Quantifying_the_Impact_of_Climate_Change_on_Human_Health_2024.pdf; https://wwwnc.cdc.gov/travel/notices/level2/zika-maharashtra-india; https://www.who.int/publications/m/item/zika-epidemiology-update-may-2024; https://www.precisionvaccinations.com/zika-outbreaks

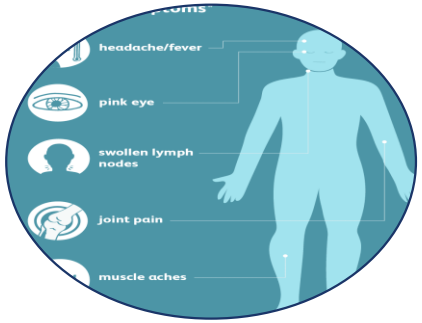
Zika Virus Infections: Short-Term and Long-Term Complications

Severity and nature of complications vary depending on age, health status, and pregnancy



Transmission and Impact:

- Primarily transmitted by Aedes mosquitoes
- Infectious urine
- Sexual transmission
- Vertical transmission
- Blood transfusion

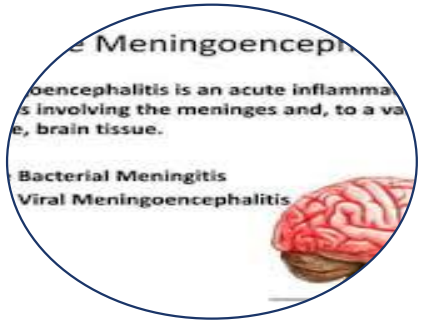


Short-Term Complications:

- Mild Symptoms:
  - Common include:
  - fever
  - rash
  - joint pain
  - conjunctivitis
  - headache
  - muscle pain

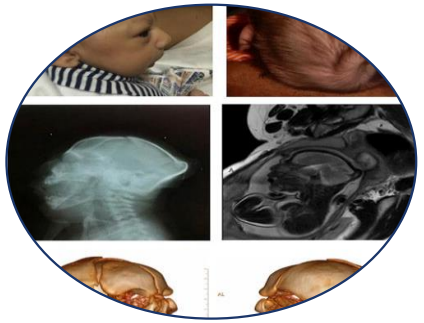
Guillain-Barré Syndrome (GBS):

- Rare neurological disorder
- Causing muscle weakness, paralysis, and potentially respiratory failure
- Recovery varies, some experience long-term effects



Meningoencephalitis and Myelitis:

- Brain or spinal cord inflammation
- Severe symptoms; seizures, paralysis, or altered mental status



Long-Term Complications in Children:

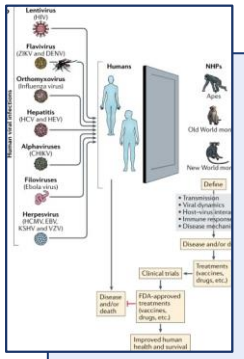
- **Congenital Zika Syndrome (CZS):** microcephaly, developmental delays or disabilities
- **Seizures**

Long-Term Complications in Adults:

- Chronic issues; prolonged weakness, pain, and balance problems
- Reproductive concerns
- Psychosocial impacts

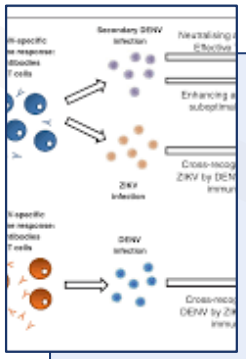
ZIKA Virus: Evidence of Waning Immunity

Robust immunity following infection may diminish over time; reports of repeat infections



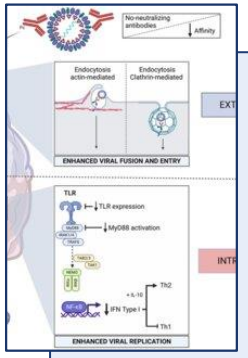
Non-Human Primate & Human Studies

- Antibody levels decline over months to years, possibly lowering protection (The Lancet ID, 2020).
- Raises concerns about reinfection, especially in Zika-endemic areas or future outbreaks.
- Reports of repeat Zika infections in endemic regions.



Cross-Immunity

- Prior dengue exposure may alter the immune response to Zika, affecting immunity strength and duration.



Waning Immunity Implications

- Public Health: Risk of new outbreaks in regions where Zika had previously subsided.
- Reproductive Health: Increased risk of congenital Zika syndrome, especially in women previously infected.

https://www.thelancet.com/journals/laneur/article/PIIS1474-4422(20)30232-5/fulltext / chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://pasteur.hal.science/pasteur-02875145/document

Re-Activation of Our Zika Program

Based on emerging epidemiology and learnings on the severity and nature of health impairments from ZIKV infection

1st-Gen. Vaccine Candidate VLA1601

- **Vero cell culture derived**
- **Purified, inactivated whole ZIKV**
  - Strain derived from Asian strain H/PF/2013
- **Adsorbed on aluminum hydroxide adjuvant**
- **Leveraged manufacturing platform for IXIARO®**

Key Conclusions from Phase 1

N=67 (18-49 yrs); two doses; two schedules :

- **Excellent safety profile**
- **Immunogenic – SCR of up to 85.7%**
- **Antibodies declined during six-month follow-up - SCRs remaining up to 40%**
- **Need for optimization of the immune response**

2nd-Generation Vaccine Candidate VLA1601 → Phase 1: VLA 1601-102

Creating a Second-Generation Zika Vaccine

Key consideration and vaccine improvements

Considerations

- Prior Phase 1 indicated the need for improving immunogenicity and antibody persistence
- Safe and effective vaccine development should be feasible as evidenced by other flavivirus vaccines (e.g. JE, Yellow fever)
- A balanced t-cell response (Th1/2) might improve longevity and cross-neutralization
- Large-scale production at low cost is needed to react to potential outbreaks

Improvements

- Keep inactivated whole virus technology
- Apply learnings from COVID vaccine development
  - VLA2001 achieved high NABs, good T-cell response and antibody persistence
- Applied changes:
  - BPL inactivation expected to generate high quality antibodies
  - Increased antigen content
  - Increased, potentially double adjuvantation (Alum + CpG 1018 or Alum + 3M-052-AF)

Current Phase 1 Study

VLA1601-102

Double-blind, randomized safety and immunogenicity trial in the U.S.

- To investigate safety and immunogenicity across different doses and formulations
- ~150 healthy flavivirus-naïve volunteers aged 18 to 49 years;
- Two-dose priming: Day 1 + 29 with follow-up after 1m (Day 57), 6m and 12m
- Primary Objectives: assessment of safety and tolerability up to 7 days after each vaccination and assess immunogenicity at Day 57 (1m after completion of priming)
- **Sentinel recruitment and vaccinations completed, start of randomized phase imminent**

2024 – 2025/6

Key consideration for data evaluation and progression

- Safety and tolerability profile
- Immunogenicity profile (neutralizing antibodies, t-cell response)
- Comparison to WHO convalescent serum single sample

Zika Vaccine Pivotal Development[1]

Considerations

- Vaccination should prevent infection and protect against severe complications
- May require post-licensure surveillance studies to generate clinical evidence and long-term safety data
- Potential for non-dilutive grant funding

Randomized Phase 3 Field Efficacy Trials

Symptomatic infections	Symptomatic & asymptomatic[2]
Confirmed by PCR	Potentially important if asymptomatic is associated with sequelae

Controlled Human Infection Model (CHIM)

Early indication of vaccine efficacy

Need to weigh risk with potential clinical benefit

Accelerated Approval Pathway

Establish surrogate of protection via passive transfer in animals

Additionally, apply for FDA Fast Track, Breakthrough Designation, Priority Review

1 https://www.nejm.org/doi/full/10.1056/NEJMp1607762#body-ref-r001 ; **2** 80% of infections are asymptomatic; Duffy, MR, Chen, T-H, Hancock, WT, et al. Zika virus outbreak on Yap Island, Federated States of Micronesia. N Engl J Med 2009;360:2536-2543

Pipeline Strategy & Pre-Clinical Priorities

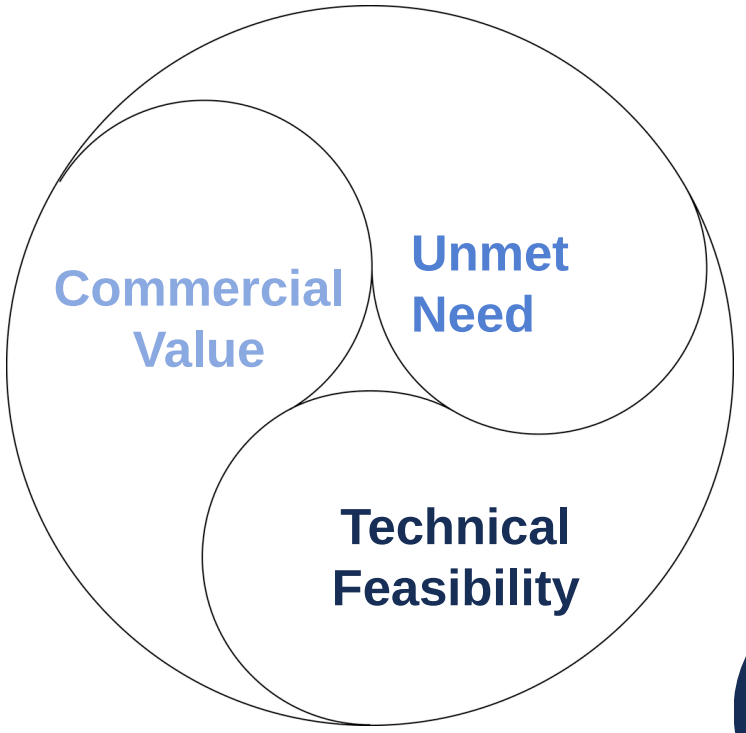
Thomas Lingelbach
Chief Executive Officer

valneva

Valneva's Guiding Principles in R&D

Balancing our expertise with unmet need and risk

Criteria for pipeline entry



Risk Profile

High risk-High gain

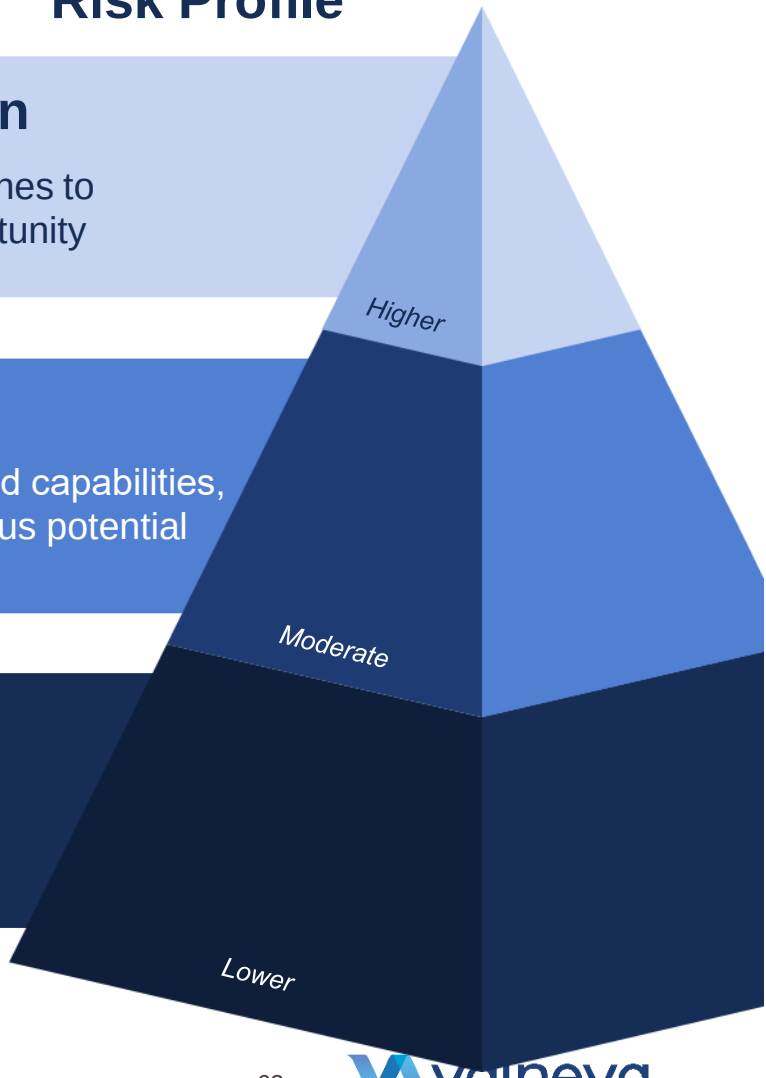
Innovative vaccine approaches to address huge market opportunity

Core specialty

Build upon Valneva's existing expertise and capabilities, consider potential for LCM incl. combos plus potential for accelerated approval pathways

Funding / Co-development

Leverage external funding/co-development opportunities to expand portfolio and capabilities



Our Current R&D Strategy at a Glance

Provide R&D upside to investors by investing in new vaccines that address unmet needs

1 **Lyme & Chik**

- Continue working closely with Pfizer to ensure timely execution, licensure and ACIP recommendation
- Execute on Chik territory, label extensions and PMC's

2 **Shigella**

- In-licensed Shigella candidate from Limmatech - deliver next Phase 3 program in an attractive, strategically fitting indication with attractive commercial prospects

3 **New Programs**

- Progress in-house or partnering pre-clinical programs to enter the clinic in 2027
- Progress ZIKA to EOP1 and decide whether to progress further or to replace with another asset – in-house or partnered in 2025

Prevention of Epstein-Barr Virus Infection is an Unmet Medical Need

Market potential: $600 million - $1.3 billion annual peak sales

Epstein-Barr Virus (EBV)

- Gammaherpesvirus, human herpesvirus 4
- Transmitted through saliva and other bodily fluids
- >95% of population infected by age 25
- Stays with the host for life

Infectious mononucleosis

- Estimated ~45 per 100,000 per year (90% caused by EBV)
- Symptomatic disease primarily in adolescents and young adults
- Acute complications in ~1%

Multiple sclerosis

- Global reported incidence 2.1 per 100,000 per year[1]
- Risk increases 32-fold after EBV infection[2]

Cancer

- Implicated in Burkitt's lymphoma, Hodgkin's lymphoma, post-transplant lymphoproliferative disease (PTLD), nasopharyngeal carcinoma, gastric carcinoma, and T & NK cell lymphomas

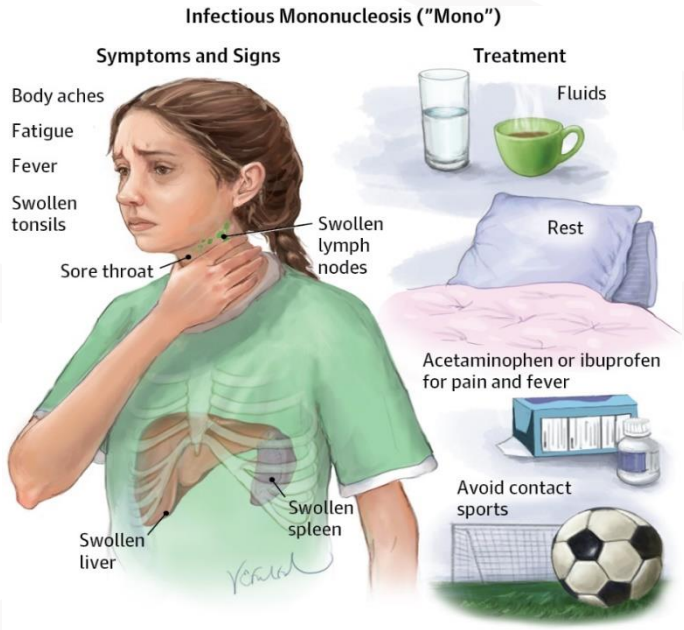


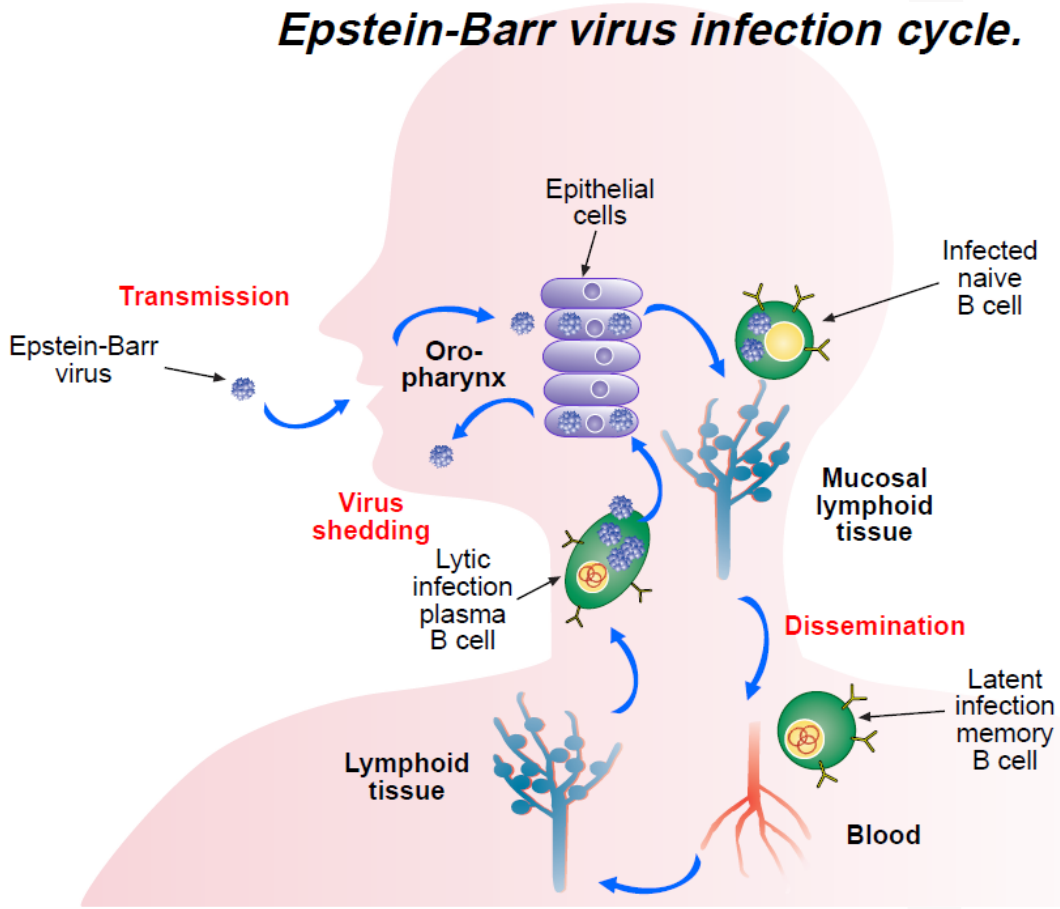
Figure from Thompson 2015. *JAMA*. 2015

High Hospitalization and Social Cost: Significant Morbidity and Negative Impact on Quality of Life

1 Walton et al 2020 *Mult. Scler.*, 2 Bjornevik et al 2022 *Science*

Potential Points of Intervention for Vaccine Development

Potential blocking of infection of epithelial cells and B cells



www.immunopaedia.org.za/immunology/archive/cytokine-storm/epstein-barr-virus-ebv/

Prevent infection and carcinomas by blocking infection of epithelial cells

- Viral glycoprotein gH/gL binds integrins to enable infection of epithelial cells[1]
- gH/gL-specific antibodies block EBV infection of epithelial cells (and B cells)[2,3]
- Other proteins may contribute to blocking entry of the virus into cell membrane gB fuses the viral envelope and target cell membrane for the virus to enter

Prevent infectious mononucleosis and B cell lymphomas by blocking infection of B cells

- Viral glycoprotein gp350 enables infection of B cells by binding to CD21[4]
- gH/gL/gp42 binds MHC-II to trigger infection of B cells[3]
- gB fuses the viral envelope and target cell membrane for the virus to enter

1 Chesnokova et al 2009 *Proc. Natl. Acad. Sci. USA;* 2 Bu et al 2019 *Immunity;* 3 Chen et al 2022 *Immunity;* 4 Nemerow et al 1987 *J. Virol.*

Prior Vaccine Candidate Reduced Incidence Of Mononucleosis But Not Infection

Informs design of second-generation vaccine candidates

- GSK developed a gp350 subunit protein vaccine adjuvanted with AS04 to Phase 2
- Vaccine recipients had a statistically significant 78% lower incidence of infectious mononucleosis than placebo recipients, although the number of cases was low[1]

Case, presentation category	ATP population		ITT population	
	Given placebo (n = 90)	Given gp350/AS04 vaccine (n = 86)	Given placebo (n = 91)	Given gp350/AS04 vaccine (n = 90)
Infectious mononucleosis	8	2	9	2[a]
Definite	8	2	8	2
Probable	0	0	1	0
Asymptomatic infection	9	11	9	11
Total	17	13	18	13

NOTE. Data are no. of subjects. AS04, aluminum hydroxide and 3-*O*-desacyl-4'-monophosphoryl lipid A; ATP, according to protocol; gp350, glycoprotein 350; ITT, intention to treat.

- Vaccine did not prevent EBV infection - gp350 antibodies only prevent infection of B cells, not epithelial cells!

Second generation vaccine candidates should include gp350 plus an EBV antigen which elicits antibodies that neutralize epithelial cell infection

1 Sokal et al 2007 *J. Infect. Dis.*

Enterotoxigenic *E. coli* (ETEC): Significant Unmet Medical Need and Opportunity

Market potential: $600 million - $1.3 billion annual peak sales

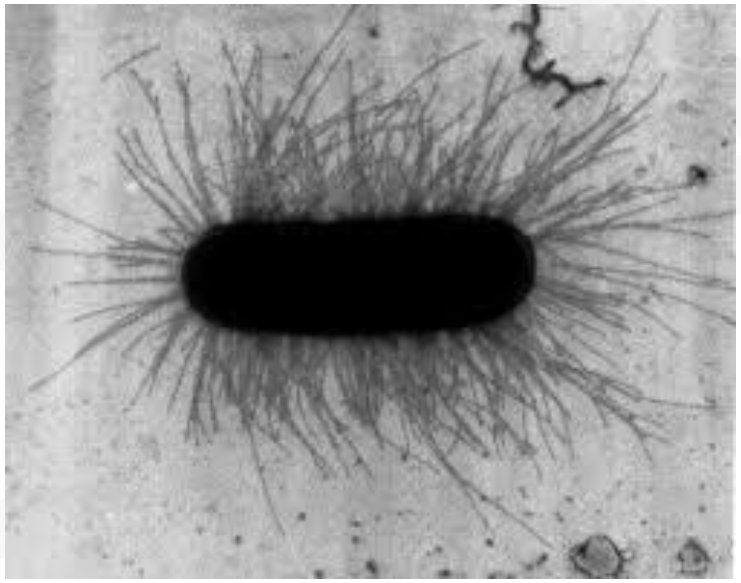
Causes ~30% of travelers' diarrhea

- Estimated 10 million cases/year (2011)
- Young children in LMIC at greatest risk for severe outcomes: 20-45k deaths/year
- Heaviest burden in Africa, Middle East, and Latin America
- Fecal-oral transmission, primarily from contaminated food and water

Causes profuse watery diarrhea and abdominal cramping

- Symptoms occur 1-3 days post-exposure and last 3-4 days

Gram-negative enteric bacteria



https://munsonlab.miami/etec/

No specific treatment or vaccine available

Antibiotics can reduce illness duration, however ETEC antibiotic resistance is increasing

Valneva's ETEC Program Prioritized in Pre-Clinical R&D

Targeting a Differentiated Approach Based on Validated Properties

ETEC – Vaccine Candidate

- ETEC adheres to intestinal epithelial cells using colonization factor antigens, and produces heat-labile toxin, heat-stable toxin, or both
- Combination of LT, ST, and colonization factors aiming to prevent moderate to severe diarrhea in travelers and pediatric population in LMIC
- Clinical development could be derisked by established human challenge models
- Life cycle management opportunities include potential combination with other enteric disease vaccine

Rationale to Support Differentiation

- ETEC infection induces immunity against re-infection with a homologous strain[1,2]
- Previous Phase 3 (post hoc analysis) demonstrated 61% protective efficacy against diarrhea caused by LT+ ETEC
- Dukoral®, which contains the LT-similar cholera toxin B, has shown >50% efficacy against ETEC and >60% efficacy against LT+ ETEC in clinical field studies[3-5]
- CTB-containing vaccine candidate showed 43% protective efficacy against diarrhea caused by an LT+ challenge strain[6] in a human challenge study
- Colonization factors for CfaE (part of CFA/I) and CssBA (part of CS6) in combo with LT - signs of clinical benefit in human challenge study and in *A. nancymaae* (New World NHP) diarrhea model, respectively[7-8]

1 Levine et al, 1979, Infect Immun.; 2 Harro et al 2011, Clin Vaccine Immunol.; 3 Clemens et al 1988 J Infect Dis.; 4 Peltola et al 1991, Lancet; 5 Scerpella et al 1995, J Travel Med.; 6 Talaat et al 2024, Microorganisms; 7 Gutiérrez et al 2024 Microorganisms; 8 Ramakrishnan et al 2021 Vaccine

Financial Highlights

Peter Bühler
Chief Financial Officer

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Successful ~€60 million Capital Raise Strengthens Financial Position

- Led by new U.S. healthcare specialist investor
- Strong support from new and existing shareholders
- Provides greater flexibility to invest in our future growth:
  - Chikungunya Phase 3 pediatric and Phase 4 trials
  - Phase 2 trials for *Shigella* and Zika vaccine candidates
  - Further commercialization of IXCHIQ®
  - Acceleration of pre-clinical R&D

Top Holders (% share capital[1])

Groupe CDC	8.68%
Pfizer Inc.	5.89%
Polar Capital	5.25%
Groupe Grimaud La Corbière	3.89%
Braidwell LP	3.33%

- Building on cash and cash equivalents of €131.4 million (June 30, 2024) and extended cash runway following update of debt financing agreement
- We believe we will have sufficient resources to finance our operational business[2] until potential milestone and commercial revenues from VLA15 enable Valneva to operate in a sustainably profitable way

1 As of September 30, 2024; **2** Excluding debt repayment

H1 2024 Financials: Product Sales of €68.3 million

Commercial business on track for continued, significant growth

€m (audited)	H1 2024	H1 2023	% Change
IXIARO®/JESPECT®	41.9	30.3	+38%
DUKORAL®	14.9	17.1	-13%
IXCHIQ®	1.0	--	--
Third party products	10.5	16.5	-37%
Total product sales	**68.3**	**64.0**	**+7%**
COVID-19	--	5.7	-100%
Total product sales including COVID-19	68.3	69.7	-2%

H1 2024 Financials: Income Statement

€m (unaudited)	H1 2024	H1 2023
Product sales	68.3	69.7
Other Revenues	2.5	4.1
Revenues	**70.8**	**73.7**
Cost of goods and services	(45.6)	(53.8)
Research and development expenses	(29.7)	(26.0)
Marketing and distribution expenses	(23.2)	(20.0)
General and administrative expenses	(22.8)	(22.9)
Gain from sales of Priority Review Voucher, net	90.8	--
Other income / (expense), net	6.4	14.0
Operating Profit / (loss)	**46.7**	**(35.0)**
Finance income / (expense) & income taxes, net	(12.7)	(0.1)
Profit / (Loss) for the period	**34.0**	**(35.0)**
Adjusted EBITDA[1]	**56.2**	**(28.3)**

1 H1 2024 Adjusted EBITDA was calculated by excluding €22.2 million (H1 2023: €6.7 million) of income tax expense, finance income/expense, foreign exchange gain/(loss), depreciation, amortization and impairment (excluding impairment loss of disposal) from the €34.0 million profit (H1 2023: €35.0 million loss) for the period as recorded in the consolidated income statement under IFRS.
Click here for important information about Non-IFRS measures such as Adjusted EBITDA and a reconciliation of Adjusted EBITDA to net loss, the most directly comparable IFRS measure.

Debt Financing Agreement with Deerfield and OrbiMed

Leading U.S. healthcare investors

Total Amount (December 31st, 2023)	**$200M €180M**	
Tranches	**$100M €90M**	**$100M €90M**
Year of Borrowing	**2020**	**2023**
Interest Rate	**9.95%**	
Repayments Begin	**Q1 2026**	**Q1 2027**
Maturity Date	**Q1 2027**	**Q4 2028**

- Terms per recent amendment (March 2024)

Valneva Remains Solidly Funded with Strong Near- and Mid-term Financial Outlook

Confirmed 2024 Guidance

- Product Sales: €160 - €180 million*
- Total Revenues: €170 - €190 million
- Other Income: €100 - €110 million
- R&D Expense: €60 - €75 million
- Significantly lower cash burn vs. 2023
  - Completed agreed-upon cost contribution to Phase 3 Lyme disease trial in Q2 2024
  - Commercial business expected to be cash-flow positive in 2024 (excluding IXCHIQ®)

Mid-Term Outlook

- Commercial business expected to be cash-flow positive (including IXCHIQ®) from 2025
  - Continued travel sales growth for IXIARO® and DUKORAL®
  - Double-digit CAGR for IXIARO® for at least the next 3 years
  - IXCHIQ® sales to exceed €100 million in year 3 of launch, even assuming competitive product entry
- Focused and strategic investments in R&D
  - Next Phase 3 program entry post Lyme data
- Gross margin improvement
  - Focus on proprietary sales
  - Cost-efficient manufacturing leveraging new facilities
- Further R&D funding support from CEPI: $41.3 million

* Assumes ~20-30% reduction in third party sales based on external supply constraints

Valneva's Near- and Mid-Term Value Drivers

VLA15 Success

- Potential for major value inflection with key study conclusions next year
- Sustained profitability upon potential approval, driven by substantial commercial milestones and royalties

Growing commercial revenues

- Near term: continued growth of IXIARO® and Dukoral®
- Further growth as IXCHIQ® gains global traction (driven by awareness, additional launches, label expansion)

Realizing future pipeline value

- *Shigella* clinical catalysts and de-risking steps in Phase 2
- Goal to enter Phase 3 post-Lyme
- Advances in Zika and select pre-clinical candidates

Q&A Break

Investor Day 2024

October 10th, 2024

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Key Upcoming Catalysts and News Flow

Chikungunya vaccine

- Upcoming potential approvals: Anvisa (Brazil), MHRA (UK)
- 36-month antibody persistence data expected in Q4 2024
- Initiate Phase 4 clinical program

Lyme disease vaccine candidate VLA15

- Key study conclusions by year end 2025
- Potential FDA/EMA submissions in 2026, subject to positive Phase 3 data

Additional newsflow

- New U.S. Department of Defense supply contract for IXIARO® expected in Q4 2024
- Initiate Phase 2 S4V *Shigella* vaccine studies in H2 2024 (CHIM and pediatric)
- Report Phase 1 data for second-generation Zika vaccine in H1 2025

Thank you
Merci
Danke
Tack

valneva