Valneva Announces U.S. FDA Approval of World's First Chikungunya Vaccine, IXCHIQ®

November 13, 2023

valneva

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IXCHIQ® is approved by the U.S. Food & Drug Administration (FDA) and is indicated for the prevention of disease caused by chikungunya virus (CHIKV) in individuals 18 years of age and older who are at increased risk of exposure to CHIKV. Continued approval of IXCHIQ® in the United States is contingent upon verification of clinical benefit in confirmatory studies. Regulatory review of the VLA1553 chikungunya vaccine candidate remains ongoing in other jurisdictions, and approval by the FDA does not guarantee approval in other jurisdictions, on similar terms or at all.

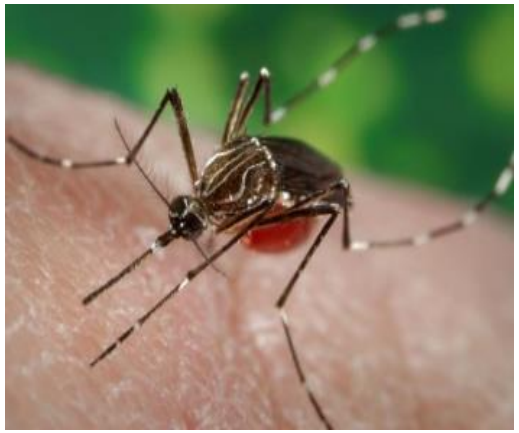
IXCHIQ®

The world’s first licensed chikungunya vaccine[1]

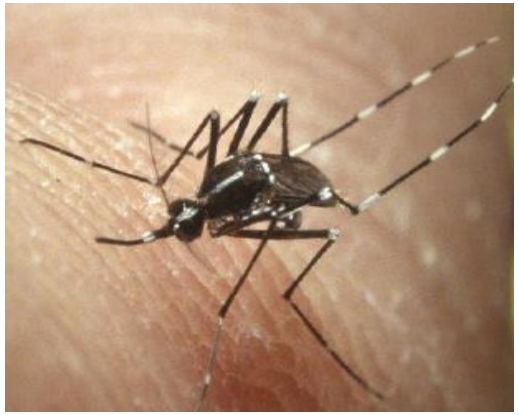
1 Please refer to the full Prescribing Information: https://www.fda.gov/media/173758/download

Chikungunya: A Major Public Health Threat

Mosquito-transmitted disease with potentially debilitating consequences



Aedes aegypti



Aedes albopictus

- Transmitted by ***Aedes*** mosquitoes[1]
- Often causes **large, explosive outbreaks**, affecting one-third to three-quarters of the population[1]; difficult to predict next outbreaks[2]
- **Outbreaks** have occurred in Asia, Africa and across Latin America[1]; potential to occur in the U.S. and Europe[2,3]
- Recent outbreak in Paraguay[4] with PAHO issuing an **epidemiological alert** for the Americas[5]

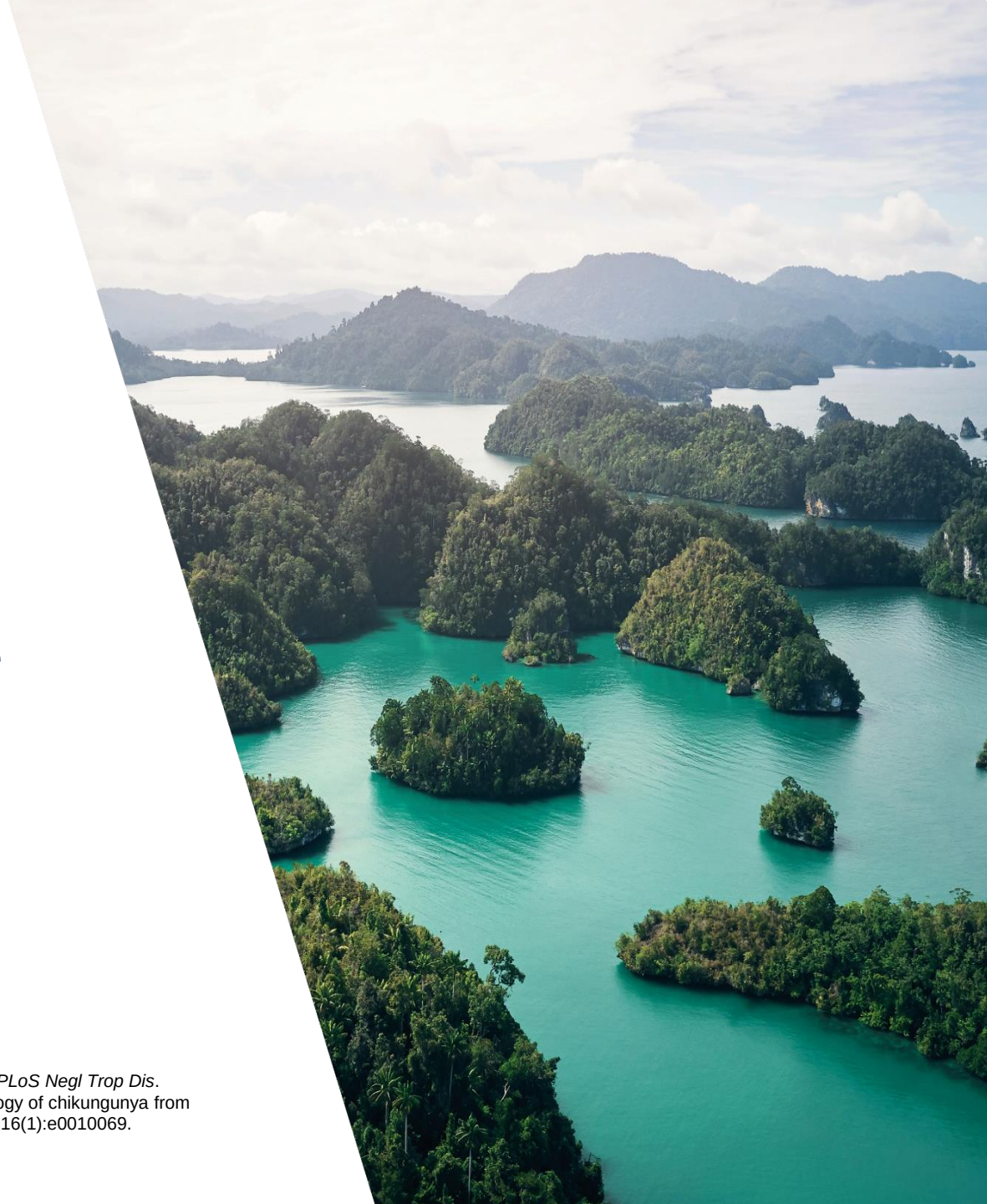
No curative treatment – No other vaccines available

1. Staples et al. CDC Yellow Book 2020, Chapter 4; 2. Bettis et al, PLOS Neglected Tropical Diseases 16(1): e0010069; 3. Silva LA et al. J Clin Invest. 2017 Mar 1;127(3):737-749; 4 PAHO provides guidance to countries in response to increased chikungunya cases; 5 Epidemiological Alert: Chikungunya increase in the Region of the Americas

Over 3/4 of the world's population lives in areas at risk of Chikungunya Virus (CHIKV)

- The areas of greatest risk for travelers are thought to be **the Americas**, **parts of Africa, and Southeast Asia**[1,2]

- Returning infected travelers can trigger local outbreaks (e.g. **Southern U.S./Europe**)[2]



1. Puntasecca CJ, King CH, LaBeaud AD. Measuring the global burden of chikungunya and Zika viruses: a systematic review. *PLoS Negl Trop Dis*. 2021;15(3):e0009055. doi:10.1371/journal.pntd.0009055; **2**. Bettis AA, L'Azou Jackson M, Yoon IK, et al. The global epidemiology of chikungunya from 1999 to 2020: a systematic literature review to inform the development and introduction of vaccines. *PLoS Negl Trop Dis*. 2022;16(1):e0010069. doi:10.1371/journal.pntd.0010069

High Disease Burden & Health-Economic Impact

43% **of CHIKV patients suffer from chronic chikungunya**

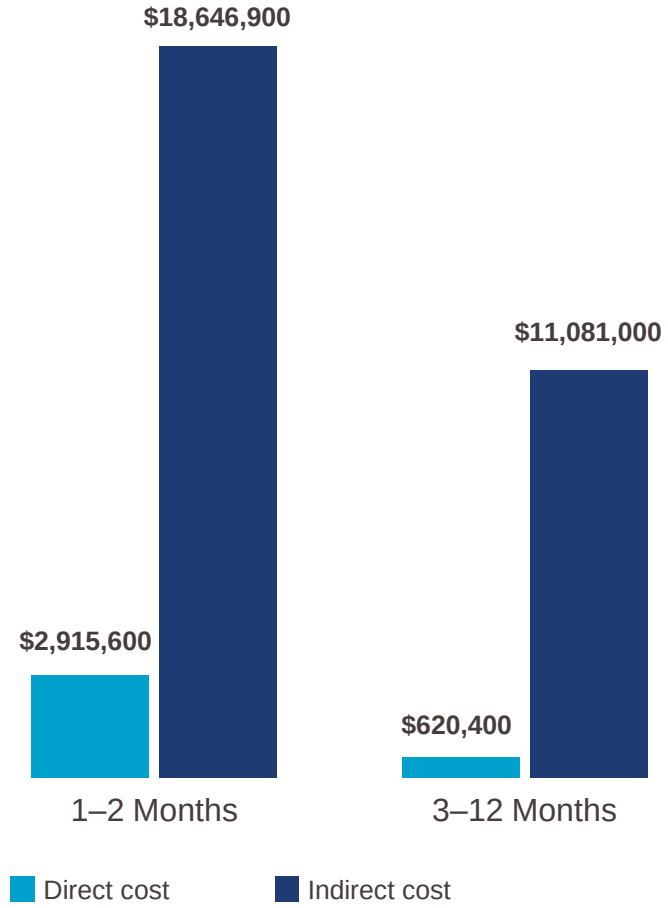
- Potentially debilitating effects may last from months to years
- Many who experience severe infection never fully recover[1,2]

1. Puntasecca CJ, King CH, LaBeaud AD. Measuring the global burden of chikungunya and Zika viruses: a systematic review. *PLoS Negl Trop Dis*. 2021;15(3):e0009055. doi:10.1371/journal.pntd.0009055; **2.** Paixão ES, Rodrigues LC, da Conceição M, et al. Chikungunya chronic disease: a systematic review and meta-analysis. *Trans R Soc Trop Med Hyg*. 2018;1123(7):301-316. doi:10.1093/trstmh/try063

CHIKV infections carry an economic burden

Combination of hospital-related costs and loss of productivity

- Includes direct and indirect costs:
  - Direct: outpatient visits, testing, and medications
  - Indirect: loss of productivity due to absenteeism, and years lived with disability
- Outbreak in the U.S. Virgin Islands (2014-15): estimated direct healthcare costs were $2.9 million for the first 2 months and $0.6 million for 3–12 months following the outbreak
- The total estimated cost associated with the outbreak ranged from $14.8 to $33.4 million (approximately 1% of gross domestic product)



CHIKV = chikungunya virus.
Feldstein LR, et al. PLoS Negl Trop Dis. 2019;13(7):e0007563.

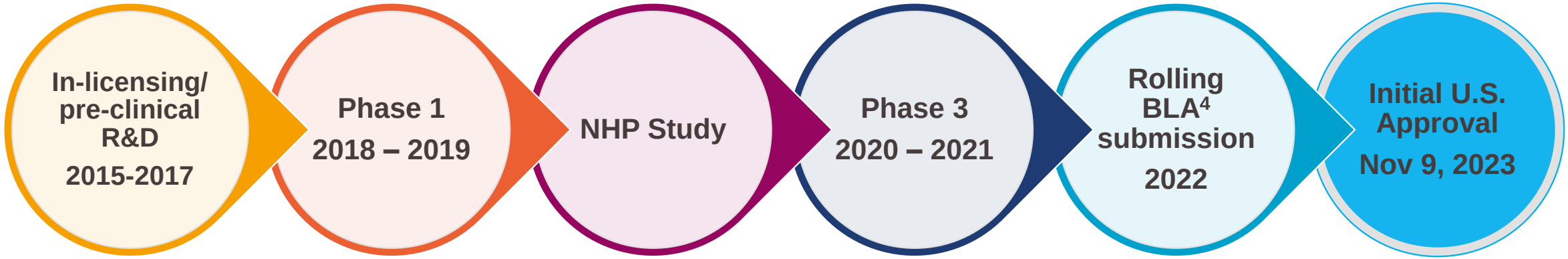
CHIKV Associated With Significant Psychosocial and Quality of Life (QoL) Burden

The post-CHIKV vicious circle[1-5]

1. Simon F. CISTM16. **2.** Soumahoro MK, et al. PLoS One. 2009;4:e7800. **3.** Ramachandran V, et al. PLoS One. 2012;7:e51519. **4.** Marimoutou C, Medicine (Baltimore). 2012;91:212-919. **5.** Simon F, et al. Médecine et maladies infectieuses. 2015;45:243-263.

IXCHIQ®: The 3rd Vaccine Valneva has brought from early R&D to approval[1]

Meticulous Development Leveraging our Strengths in Development and Manufacturing



Collaboration with Peter Liljeström/ Karolinska Institutet

Efficacy and 12-mo persistence in NHPs[1]

Proof of concept for product development

100% SRR[2] by Day 14; sustained 12mo.

Safety profile supported Phase 3 progression

FDA Fast Track

CEPI[3] funding

Protection in passive transfer model

Established immunological surrogate and Phase 3 endpoint

98.9% SRR by Day 28; sustained 12mo.

Positive lot-to-lot consistency results

Partnership with Instituto Butantan

EMA PRIME / FDA Breakthrough Designations

Initiated August 2022; completed December 2022

Accepted February 2023

Accelerated Approval pathway

Adults aged 18+

Priority Review Voucher

ACIP[5] recommendation expected Feb 2024

1. Non-human primates; **2.** Sero-response rate; 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.** Coalition for Epidemic Preparedness Innovations; **4.** Biologics license application; **5**. Advisory committee on immunization practices

VLA1553: Clinical Data Highlights[1,2,5]

Live-attenuated CHIKV vaccine demonstrates rapid and long-lasting immunity with a single shot

Immunogenicity Data

- 99% Seroresponse[3] Rate (SRR) after a single vaccination
- Immunogenicity profile maintained over time: 99% SRR after 12 months[4]
- Older adults (≥ 65 years) achieved similar SRR and neutralizing antibody titers as younger adults (<65 years)[1,4]
- 100% SRR after 14 days and sustained to Month 12[2]
- Adolescent trial met primary endpoint[5]: highly immunogenic in baseline-negative individuals; 99% SRR

Safety Data

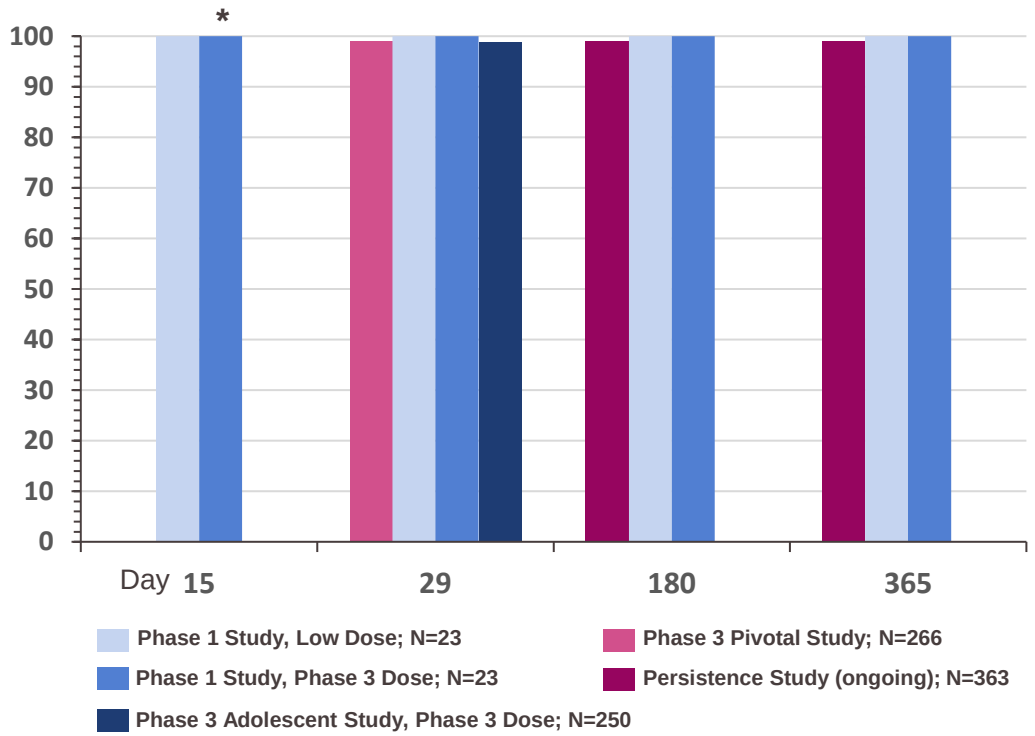
- VLA1553 was generally well tolerated among the >3,600 adults and 754 adolescents evaluated for safety
- Pivotal Safety Data[1]:
  - ~50% of study participants had solicited systemic adverse events, most commonly headache, fatigue and myalgia
  - Majority of solicited adverse events mild or moderate. 2.0% of study participants reported severe solicited adverse events, most commonly fever.
- Adolescent trial in Brazil suggests favorable safety profile regardless of previous CHIKV infection[6]

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 Pivotal Phase 3 Immunogenicity Data in Adolescents for its Single-Shot Chikungunya Vaccine Candidate; **6.** Valneva Reports Positive Initial Phase 3 Safety Data in Adolescents for its Single-Shot Chikungunya Vaccine Candidate

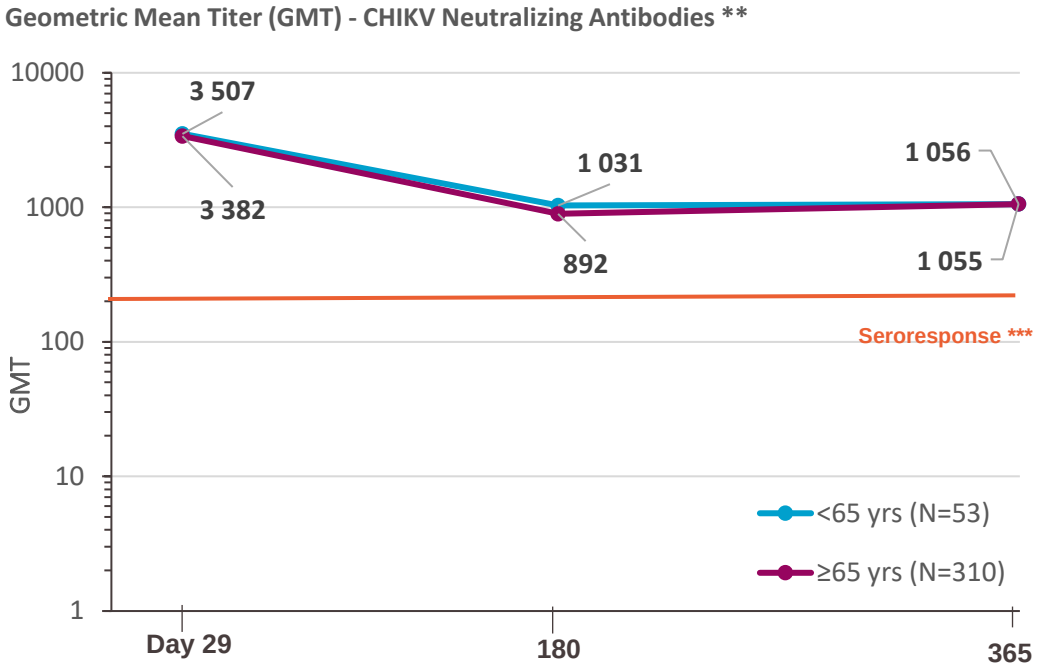
VLA1553 Induces Early and Sustained Response Regardless Of Age

High seroresponse rates across studies

Seroresponse sustained at highest levels up to Month 12



Comparable titers in younger and older adults

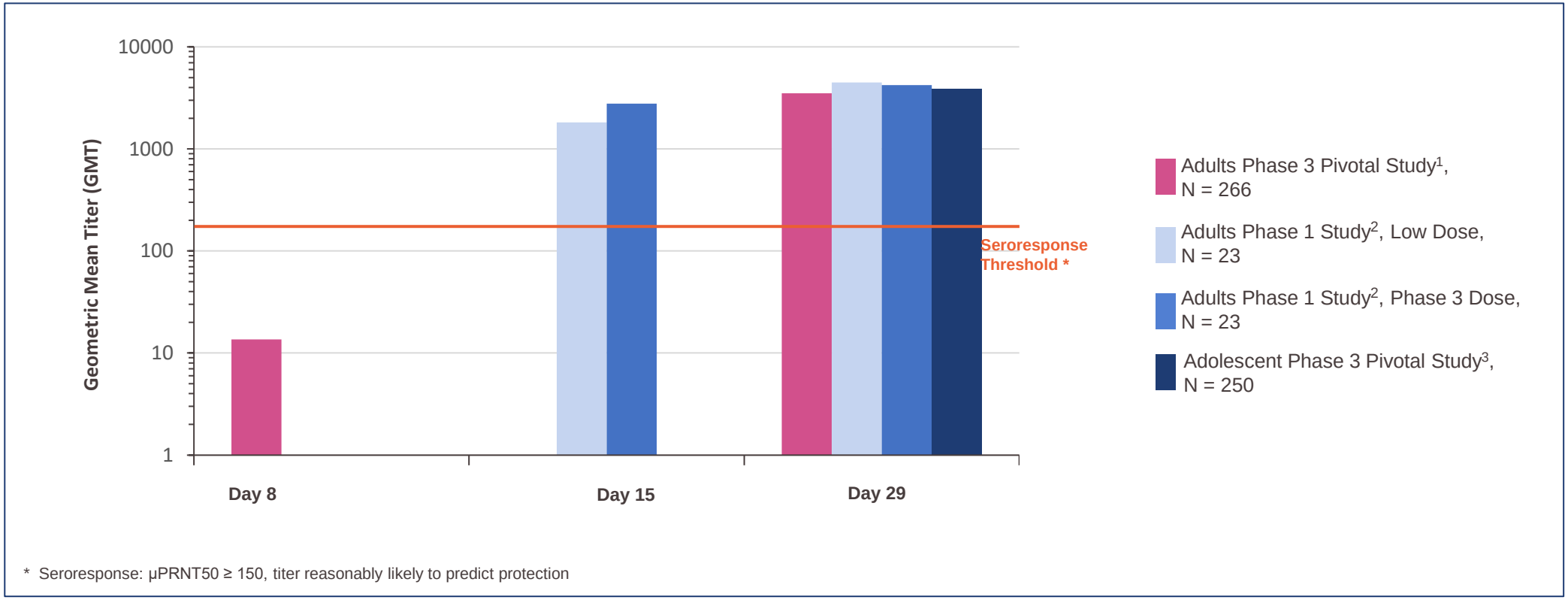


** Persistence Study, Whole Sample Population
*** Seroresponse : µPRNT50 ≥ 150, titer reasonably likely to predict protection

***** 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

VLA1553: Fast and Robust Induction of Neutralizing CHIKV Antibodies

High neutralizing antibody titers at Day 15 in Phase 1; by Day 29 for pivotal trial endpoint



* Seroresponse: µPRNT50 ≥ 150, titer reasonably likely to predict protection

Note: All GMT used same, validated µPRNT assay

1. Valneva Successfully Completes Pivotal Phase 3 Trial of Single-Shot Chikungunya Vaccine Candidate; **2.** 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; **3.** Valneva Reports Positive Pivotal Phase 3 Immunogenicity Data in Adolescents for its Single-Shot Chikungunya Vaccine Candidate

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 > 12 years of age in endemic areas of Brazil	**Pragmatic randomized controlled effectiveness and safety study in adults in an endemic country (n ~ 20.000)**
▪ To estimate the efficacy 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), ~450 cases / 890 controls ▪ Municipality selection based on CHIKV risk, test infrastructure ▪ Pilot vaccination period to ensure est. >15% vaccination coverage – Safety evaluation (incidence of medically attended AESIs) (n ~ 5000) – Serosurvey (Pre-exposure assessment)	▪ To assess efficacy 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) for severe chikungunya-like adverse reactions and prolonged arthralgia ▪ Statutory requirement[3] for well-controlled clinical investigation introduced to address potential biases associated with an observational design
2025 – 2028 (including pilot phase)	**2025 - 2029**

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

Chikungunya Global Market Segments

Global market for chikungunya vaccines estimated to exceed $500 million per year by 2032[1]

Segments Targeted Directly by Valneva

Travelers from Non-Endemic Regions

Travel vaccine for individuals travelling to areas with risk of chikungunya

Military from Non-Endemic Regions

Vaccine for troops stationed in areas with risk of chikungunya

Outbreak Preparedness Non-Endemic Regions

Vaccine in areas in response to / at risk for a domestic outbreak

Segments Targeted via Partnership

Endemic Region Use

Vaccine in endemic / LMIC markets, Targeted via **CEPI / Instituto Butantan Partnership**

CHIKV identified in >100 countries across five continents

1. VAMV005. Chikungunya virus vaccines. Global demand analysis. Feb 2020

IXCHIQ® Fits Perfectly Within our Existing Commercial Infrastructure

High-caliber team with significant experience in the vaccine space

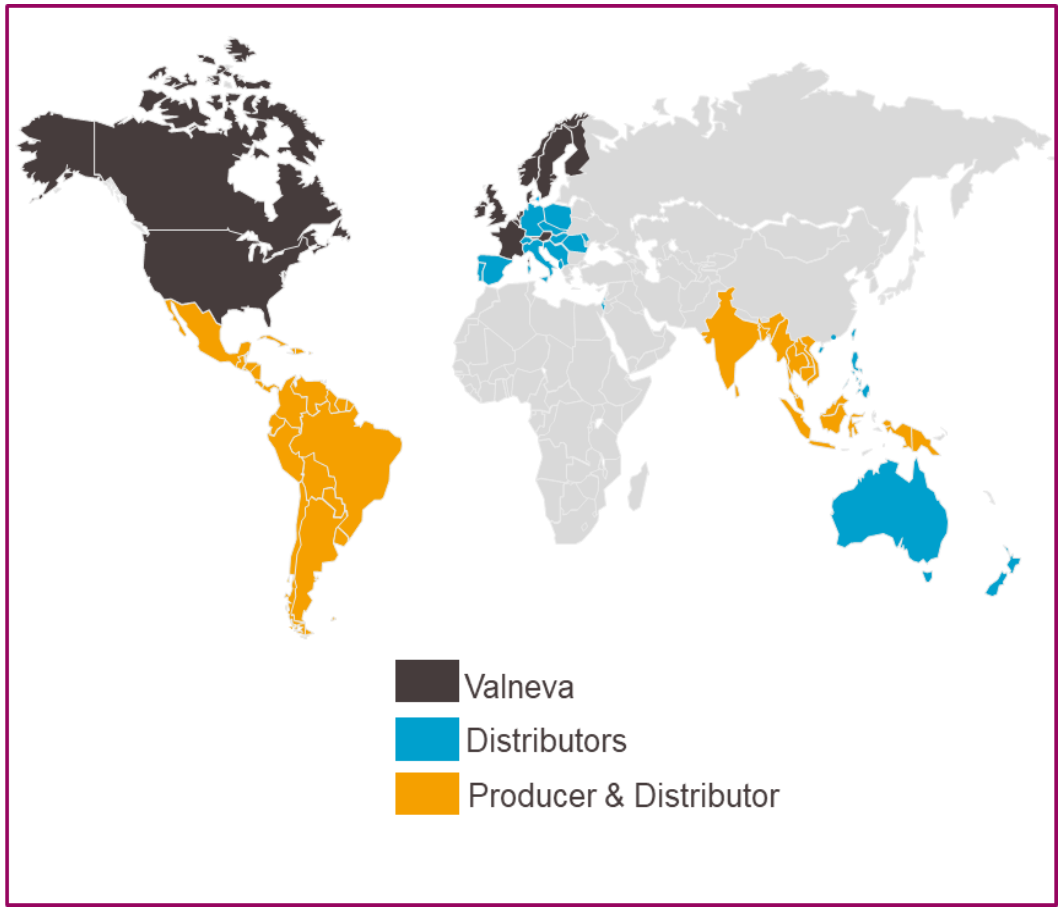
Highly experienced teams with deep expertise in vaccine market segments

Commercial infrastructure in most key markets; footprint extended through distribution partners

Integrated sales, marketing, medical and access/government affairs capabilities focused on increasing awareness and unlocking brand potential

Leverage data-driven insights and digital tools to enhance commercial capabilities

Commercial Footprint



IXCHIQ® Key Features and Differentiators

IXCHIQ® (CHIKUNGUNYA VACCINE, LIVE)

Indicated for the prevention of disease caused by chikungunya virus (CHIKV) in individuals 18 years of age and older who are at increased risk of exposure to CHIKV

- We expect to benefit by being first to market with a potentially best-in-class vaccine
- We believe we have a differentiated and competitive product characterized by a strong and durable immunological response from a single injection
- No overall differences in immunogenicity between younger and older adults (65+ years old)
- Generally well tolerated among the >3,600 adults and 754 adolescents evaluated for safety[1]

1. Please refer to the full Prescribing Information for contraindications, warnings, and other important information: https://www.fda.gov/media/173758/download

Preparing for Global Market Launches

Planned Additional and Future Regulatory Processes[1]

IXCHIQ® : Valneva

United States

- Initial approval for adults
- Priority Review Voucher

Adolescent study expected to support label expansion

Canada

- Filed NDS[2] May 2023

Expect review completion mid-2024[3]

Adolescent study expected to support label expansion

Europe/UK

- Filed marketing application with EMA[4] October 2023[5]
- Granted accelerated assessment by EMA's CHMP[6]

Expect MHRA[7] submission in 2024 via reliance route

Additional Markets

Countries with established travelers' or endemic markets

Instituto Butantan

Brazil

First potential approval/ launch in chikungunya-endemic country

IXCHIQ® filing H1 2024; potential licensure 2025

Complete Tech Transfer and VLA1555 filing; potential licensure 2025

Additional LATAM/other LMICs[9]

Prioritization in 2024: First submission in 2024

WHO pre-qualification

1. IXCHIQ® is not currently approved in any other country or jurisdiction outside of the U.S.; **2**. New drug submission; **3**. Based on Health Canada's performance standards of approx. 300 days from acceptance; **4.**. European Medicines Agency; **5.** Valneva Submits Chikungunya Vaccine Marketing Application to EMA and Announces CHMP Accelerated Assessment; **6.** Committee for Medicinal Products for Human Use; **7.** Medicines and Healthcare Products Regulatory Agency; **8.** Pre-filing processes are ongoing and can take approximately 12 months from filing acceptance to potential approval; **9.** Low-and-middle-income countries

Thank you

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Q&A