# Advancing Vaccines for Better Lives

Company Presentation
April 2020

valneva

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# Valneva's Value Proposition

## Integrated business model with valuable commercial and R&D assets

### Commercial Business

**Total sales revenues €129.5m[1] in 2019; +25% vs. 2018**

IXIARO®
- Only licensed JE vaccine for travelers, Military in North America, CAN, EU
- Sales approaching €100m[1]

DUKORAL®
- Cholera (LT-ETEC) vaccine, licensed in CAN, EU, ROW
- Sales > €30m[1]

**Recent transactions underline major valuation disconnect**
BN product acquisition from GSK @ 4.5x revenue

### R&D

**Lyme vaccine in Phase 2 with data reading out from mid-2020**

US/EU market opportunity of ~$1bn per annum
- Only program in clinical development
- Commercial/development partner tbc (expected by year end)

**Chikungunya vaccine entering Phase 3 in Q4 2020**

Global market opportunity of ~$0.5bn per annum
- Huge synergy with existing infrastructure
- Possible Priority Review Voucher upside

**R&D provides upside for shareholders**
Two unique vaccines with low R&D risk profile to be launched in the next 3-4 years

**1** All 2019 results are unaudited

# Valneva: A specialty vaccine company focused on prevention against diseases with major unmet medical needs

**€85m–€115m product sales[1]**
~ €40m US military
€85-95m Private market

**€64.4m cash**
$85m debt facility secured early 2020

**~ 65% gross margin**
~ 80% direct sales

**~ 500 people**
Four main sites
Six in-market commercial teams

**1** 2020 Guidance from Press Release: Valneva Provides Business Update on COVID-19 Situation;

# Lyme Disease Vaccine – VLA15

# Lyme Disease is a Massively Important Health Issue – Media Attention Spiked Again in January 2020

**No approved options that can protect humans against Lyme disease**

**Analysis suggests a Lyme vaccine in the US and EU could have peak revenue potential of more than ~$1b[1]**

**Lyme disease cases may rise 92 per cent in US due to climate change (New Scientist)[2]**

**1** Lyme Disease. L.E.K. interviews, research and analysis, 2 https://www.newscientist.com/article/2232705-lyme-disease-cases-may-rise-92-per-cent-in-us-due-to-climate-change/

# VLA15 – Key Value Driver in 2020 and Beyond

## The only Lyme disease vaccine candidate in clinical development today

1. Multivalent vaccine (six serotypes) to protect against Lyme disease in N. America and Europe
2. Phase 2 interim data (primary endpoint) expected mid-2020
3. FDA Fast Track Designation granted
4. Established and proven Mode of Action for a Lyme disease vaccine
5. Favorable safety profile and no associated safety concerns in Phase 1 studies[1]
   Phase 2 run-in (higher dosages than Phase 1) confirmed favorable safety profile of VLA15

1 Valneva PR: Valneva Reports Positive Initial Booster Data and Final Phase 1 Data for its Lyme Disease Vaccine Candidate

# VLA15: Phase 2 – Optimizing Dose and Schedule

## Observer-blind, randomized, placebo-controlled, Phase 2 studies conducted in the US and EU[1]

**Phase 2**
***819 subjects in two studies***
Primary objective: Safety and immunogenicity data four weeks after completed schedule
Secondary objectives: Long-term immunogenicity and safety data

Study **VLA15-201** with run-in phase

Study **VLA15-202**

**Enrollment completed for both studies**

### VLA15-201 Run-in phase (completed June 2019[2])

- Conventional schedule, higher dose
- **3 adjuvanted dose levels, placebo**
- **120 healthy volunteers** (18 to 40 years)

| | |
|---|---|
| 90 µg w/ alum | 30 subjects |
| 135 µg w/ alum | 30 subjects |
| 180 µg w/ alum | 30 subjects |
| Placebo | 30 subjects |

### VLA15-201 (initiated June 2019[2]): Schedule 0, 1, 2 months

- **2 adjuvanted dose levels** (135 µg and 180 µg) chosen after run-in phase, placebo
- **453 healthy volunteers** (18 to 65 years)
- **9 sites in the US and Europe**

### VLA15-202 (initiated July 2019[3]): Schedule 0, 2, 6 months

- **2 adjuvanted dose levels** (135 µg and 180 µg) chosen after run-in phase, placebo
- **246 healthy volunteers** (18 to 65 years)
- **5 sites in the US**

**1** VLA15-201 only (ClinicalTrials.gov Identifier: NCT03769194); Phase 2 subjects are baseline seropositive (10%) or seronegative (90%); **2** Valneva PR: Valneva Reports Successful Outcome of Phase 2 Run-In for its Lyme Disease Vaccine Candidate; **3** Valneva PR: Valneva Initiates Second Phase 2 Study for its Lyme Disease Vaccine Candidate VLA15 ; VLA15-202 ClinicalTrials.gov Identifier: NCT03970733

# VLA15 Phase 2 Progressing Extremely Well
## – Clinical development overview

**Patient recruitment for both Phase 2 studies completed September 2019**

**Phase 2 first data due mid-2020**

- Initial data: Day 85 after base immunization schedule expected mid-2020

**Phase 3 initiation planned in 2021/2022**

- Two placebo-controlled Phase 3 efficacy studies
  - 8,000 subjects in each of US and Europe
  - Based on current estimates of Lyme disease incidence rates in order to demonstrate efficacy of the vaccine in Lyme endemic regions in the U.S. and Europe
- Detailed plans for Phase 3 entry to be discussed with FDA based on Phase 2 data
- Timing depends on schedule, tick season(s), Phase 2 data and other factors

*Subject to development progress, regulatory approvals and company funding

# Chikungunya Vaccine – VLA1553

# Chikungunya is a Growing and Enduring Problem

**Currently there is no vaccine or any treatment options for chikungunya**

**Global market including endemic regions (see below)**
**Traveller vaccine market at up to €250m[1]**

**2019 - 2020: outbreaks[2] in Africa (Djibouti, Ethiopia, Kenya, Sudan), Asia (Philippines, Thailand), and South America (Brazil, Colombia)**

**1** Chikungunya. L.E.K. interviews, research and analysis for traveler vaccine market., 2 *Djibouti, Ethiopia, Kenya, Sudan; Philippines, Thailand; Brazil, Colombia*

# VLA1553 – Key Growth Driver for Future Valneva Sales

## The only single-shot vaccine candidate against chikungunya today

1. VLA1553 is a monovalent live attenuated[1] prophylactic vaccine targeting chikungunya virus neutralization
2. Currently no preventive vaccines or effective antiviral treatments exist for chikungunya
3. FDA Fast Track Designation granted. Priority Review Voucher eligible
4. Phase 1 complete. Accelerated Approval Pathway confirmed with potential Phase 3 start in Q4 2020
5. Seamless fit with existing commercial and manufacturing capabilities as a plug-and-play asset
6. Up to $23.4 million (€20.3 million) awarded to Valneva for R&D by CEPI

**1** CHIKV LR2006-OPY1 infectious clone was attenuated by deleting large part of gene coding nsP3 (alphavirus-replicase; Photo credit: James Gathany (source)

# Chikungunya Phase 1 Study (VLA1553-101) – Final Results

## Sustained immunogenicity with single shot for over one year

### Immunogenicity

**100% Seroconversion Rate (SCR)[1] achieved at Day 14 after a single vaccination in all dose groups[2]**

**SCR sustained at 100% after 13 months** with no decline in neutralizing antibody titers in the groups after a single vaccination[2]

***Excellent immunogenicity profile after single vaccination***

### Safety[2]

**Generally safe in all dose groups**

**Well-tolerated at the low and medium doses**

- Superior safety profile, including viremia, in low and medium doses compared to highest dose

**Excellent local tolerability**

**No adverse events of special interest (e.g. chikungunya infection related) and no vaccine related Serious Adverse Events (SAEs) up to Month 13**

***Excellent safety profile in low and medium doses[2]***

**1** SCR defined as proportion of subjects achieving a CHIKV-specific neutralizing antibody titre as $NT_{50} \geq 20$; **2** Valneva Reports Excellent Final Phase 1 Results for its Chikungunya Vaccine Candidate, Confirms Plans

# VLA1553 – Excellent Data and Progressing Rapidly

## Status and clinical development overview

**Positive End of Phase 2 FDA meeting (EoP2)**

- Detailed Phase 3 design confirmation expected
- Confirmation for the Accelerated Approval Pathway already received
- Excellent Phase 1 previously reported

**Additional non-clinical studies requested by FDA fully completed**

- Mosquito transmission studies
- NHP study addressing biodistribution
- Passive transfer study in NHPs to develop surrogate of protection using human sera from VLA1553-101

**Awaiting detailed protocol review with FDA before initiating Phase 3 in Q4 2020**

# Commercial Products

# IXIARO®/JESPECT®

## Only vaccine against Japanese encephalitis (JE) in US, Canada and Europe

### IXIARO®/JESPECT®

- **Designed to protect travelers and military against JE, the leading cause of viral neurological disease and disability in Asia**
- Indicated for active immunization against JE in **adults, adolescents, children and infants** aged two months and older[1]

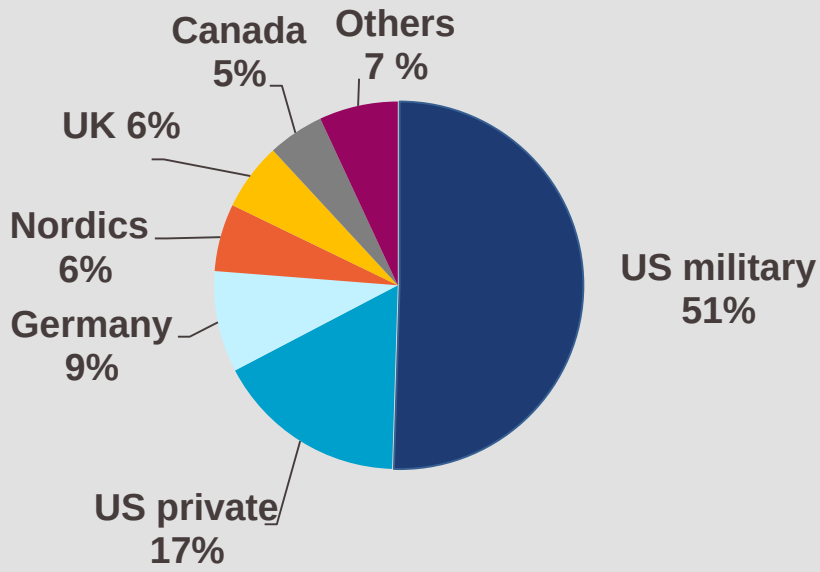
**Commercial position**

- Currently, **no effective treatment for the disease**
- **The only approved vaccine available for US, EU and Canadian travelers**
- Supply agreement in place with US military and strong track record of repeat contracts
- Limited competition - local producers exist in endemic regions and mainly serve public markets

### North America driving growth

*FY '19 product sales analysis*

**€94.1m**




**1** Indications differ by country - Please refer to Product / Prescribing Information (PI) / Medication Guide approved in your respective countries for complete information, incl. dosing, safety and age groups in which this vaccine is licensed. The currently available presentation for IXIARO® can be used in children from 3 years of age. Prior to availability of the new presentation, no attempt should be made to adjust the syringe volume or to administer a 0.25mL/3µg dose in children less than 3 years of age.

# DUKORAL®

## Only cholera (ETEC[1]) vaccine approved in EU, Canada and Australia

### DUKORAL®

- **For the prevention of diarrhea caused by *Vibrio cholera* and/or heat-labile toxin producing enterotoxigenic *Escherichia coli* (ETEC)**[1]
- **Designed to protect adults and children** traveling to endemic areas

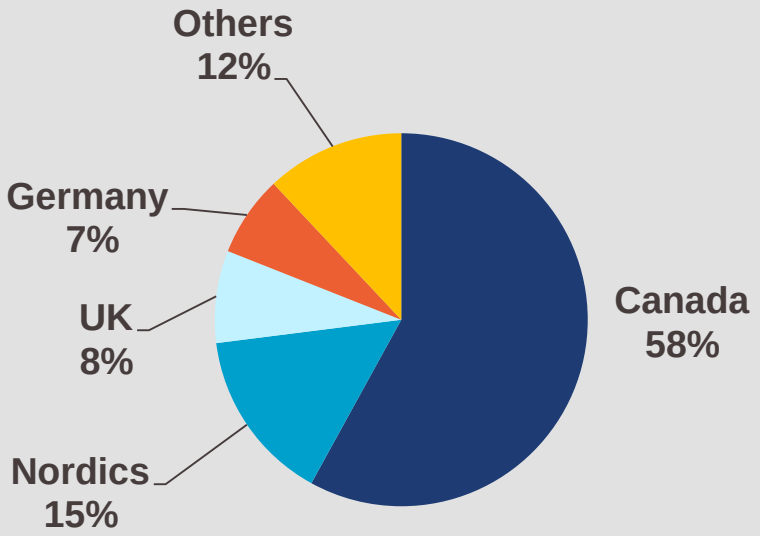
**Commercial position**

- In several markets, incl. EU, indicated for cholera only
- **Only approved cholera vaccine available for Canadian, European and Australian travelers**
  - ~3-5 million cholera cases, 100,000-120,000 deaths/year[2]
  - ~5-18 million reported ETEC cases/year[3] (ETEC is the most frequent form of traveler's diarrhea)
  - WHO pre-qualification widely used in other countries
  - Asian manufacturers predominantly serve local markets

### Canada remains our key market

*FY '19 product sales analysis*

**€31.5m**




**1** Indications differ by country - Please refer to Product / Prescribing Information (PI) / Medication Guide approved in your respective countries for complete information, incl. dosing, safety and age groups in which this vaccine is licensed, ETEC = Enterotoxigenic Escherichia coli (E. Coli) bacterium; **2** WHO cholera factsheet February 2014; **3** Lundkvist J, Steffen R, Jonsson B. Cost-benefit of WC/rBS oral cholera vaccine for vaccination against ETEC-caused travelers' diarrhea. J Travel Med 2009; 16(1):28-34;

# Valneva's Management and Advisory Team – Dedicated to Deliver VLA's Vision

## Experienced international team

### Management Board

- **Thomas Lingelbach –** President & CEO (center)
- **Franck Grimaud –** President & CBO (2nd from left)
- **David Lawrence** – CFO (2nd from right)
- **Wolfgang Bender, MD, PhD** – CMO (left)
- **Frédéric Jacotot** – General Counsel & Corporate Secretary (right)

### Supervisory Board

- **Frédéric Grimaud** (France), *Chairman*
- **Lisa Shaw-Marotto** (US), *Vice Chairperson, Chair – Nomination & Compensation Committee*
- **James Sulat** (US), *Chair – Audit Committee*
- **Anne-Marie Graffin** (France)
- **Alexander von Gabain, Prof., PhD** (Austria)
- **Thomas Casdagli** (UK)
- **Sandra E. Poole** (US)

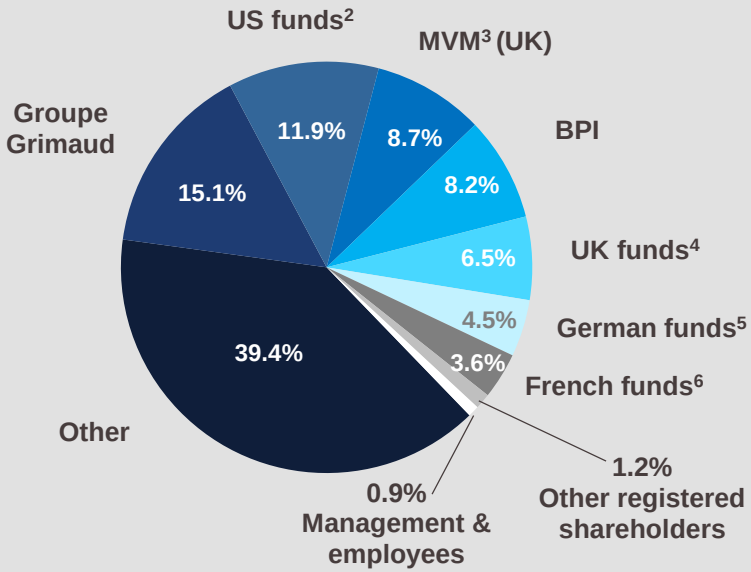
### Scientific Advisory Board

- **Ralf Clemens, MD, Ph.D.,** *Chair*
- **Norman W. Baylor, Ph.D.**
- **Anna Durbin, MD**
- **Alain Munoz, MD, Ph.D.**
- **George R. Siber**
- **Stanley Plotkin, MD**

# VLA has strengthened its institutional shareholder base with blue-chip healthcare investors including US

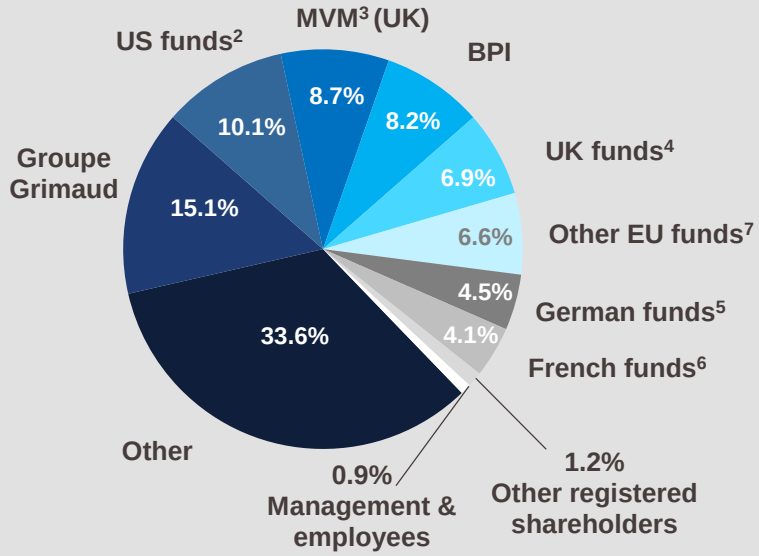
## November 2019

- Number of ordinary shares: 90.9m
- Shareholder structure[1]:




## January 2020

- Number of ordinary shares: 90.9m
- Shareholder structure[1]:




## Capital strategy

- Leveraging commercial business for non-dilutive funding to complement equity capital
- Intended Nasdaq listing to co-fund late-stage Lyme disease program development

**1** Estimates based on ordinary share capital; **2** Combined positions of U.S.-based funds managed by Deerfield Partners, Armistice Capital, New Leaf, General American, Granite Point and others; **3** Funds managed by MVM Life Science Partners; **4** Combined positions of Highclere, AXA Investment Managers Ltd. and Abingworth LLP; **5** Combined positions of Apus Capital, Apo AM, Lupus alpha, and others; **6** Combined positions of AXA Paris, CDC Entreprises Valeurs Moyennes and others; **7** Combined positions of 10 funds based in Liechtenstein, the Netherlands, Austria, Luxembourg, and Switzerland.

# 2020 Key Newsflow

**Lyme disease vaccine candidate VLA15**

- **First Phase 2 data expected mid-2020**

**Chikungunya vaccine candidate VLA1553**

- **Phase 3 initiation (Detailed design and timing pending FDA confirmation)**

**New IXIARO® contract with the U.S. Department of Defense expected H1 2020**

**US IPO update during H2 2020**

Thank you
Merci
Danke
Tack

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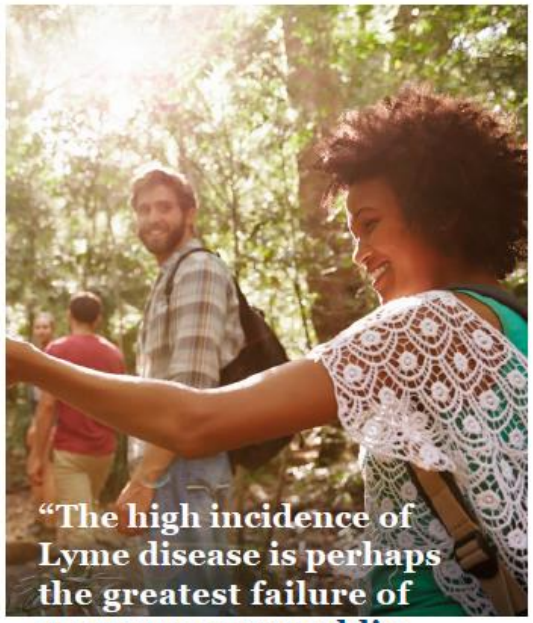
# Appendix

# Vaccination against Lyme Disease

## Justification for a Lyme vaccine




— STANLEY A. PLOTKIN
Emeritus Professor of the Wistar Institute at the University of Pennsylvania and inventor of the Rubella vaccine

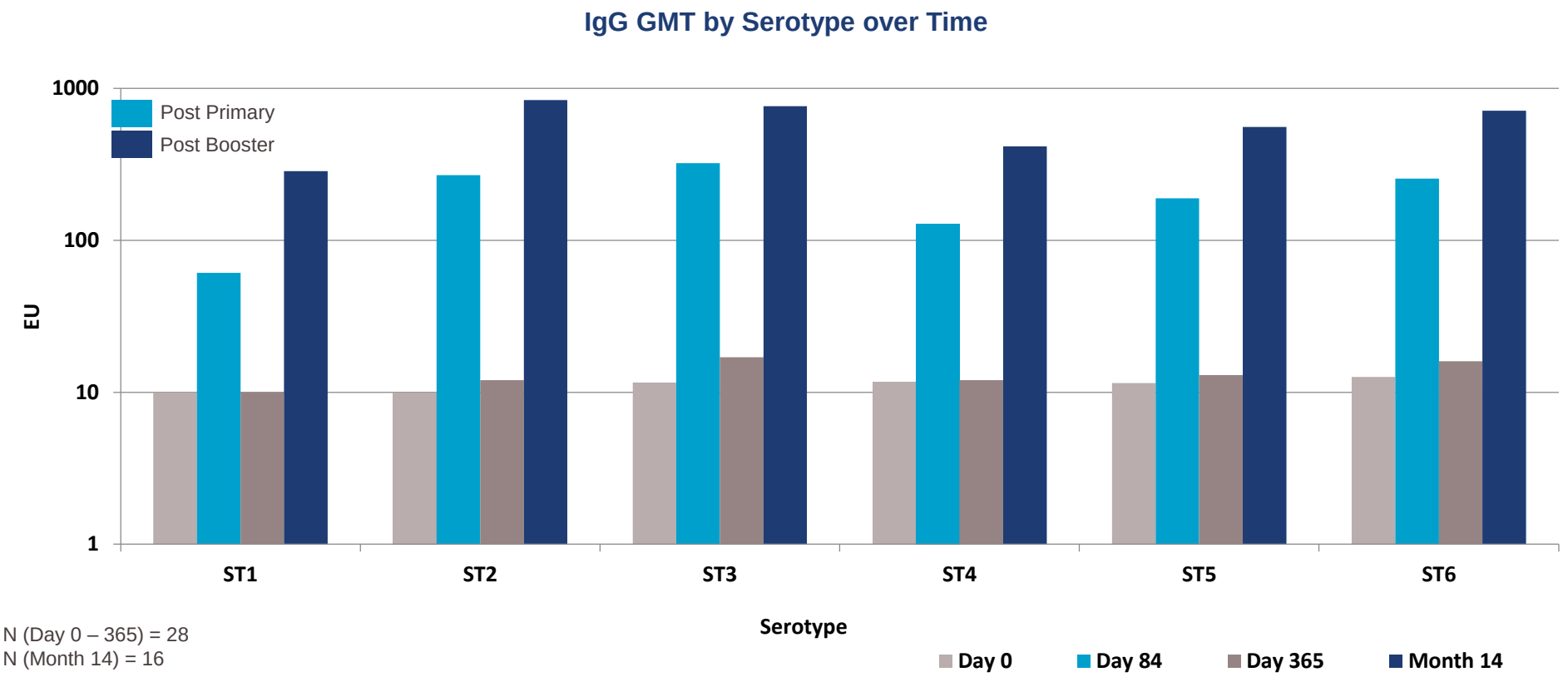
- Vaccination with OspA has been proven to work in the past (Lymerix®, ImuLyme®)
- **Disproven postulate[1], restrictive recommendations and corporate decisions resulted in there being no Lyme vaccine available for humans since 2002**
- **Delayed or inadequate treatment can lead to disabling sequelae**
- **Disease footprint widens[2]**
- **Direct medical costs in the US estimated up to $1.3 billion[3] – indicating an attractive health economical benefit**
- **Other preventive measures have not been shown to work on a public health scale**

**1** Steere et al. CID 2011: 52 (Suppl3) S259; **2** New Scientist, Lyme disease is set to explode and we still don't have a vaccine; March 29, 2017 https://www.newscientist.com/article/mg23431195-800-lyme-disease-is-set-to-explode-and-you-cant-protect-yourself/ ; **3** Adrion, E. et al PLOS ONE Feb 2015

# Lyme Phase 1 Study (VLA15-101) – Immunogenicity

## GMT for highest adjuvanted dose group between 61 (ST1) and 269 (ST2), substantial booster effect

**IgG GMT of Highest Adjuvanted Group (90µg + Alum) Before and After Primary Series and Booster Dose**




N (Day 0 – 365) = 28
N (Month 14) = 16

# Chikungunya: Vector Prevalence and Disease Outbreaks

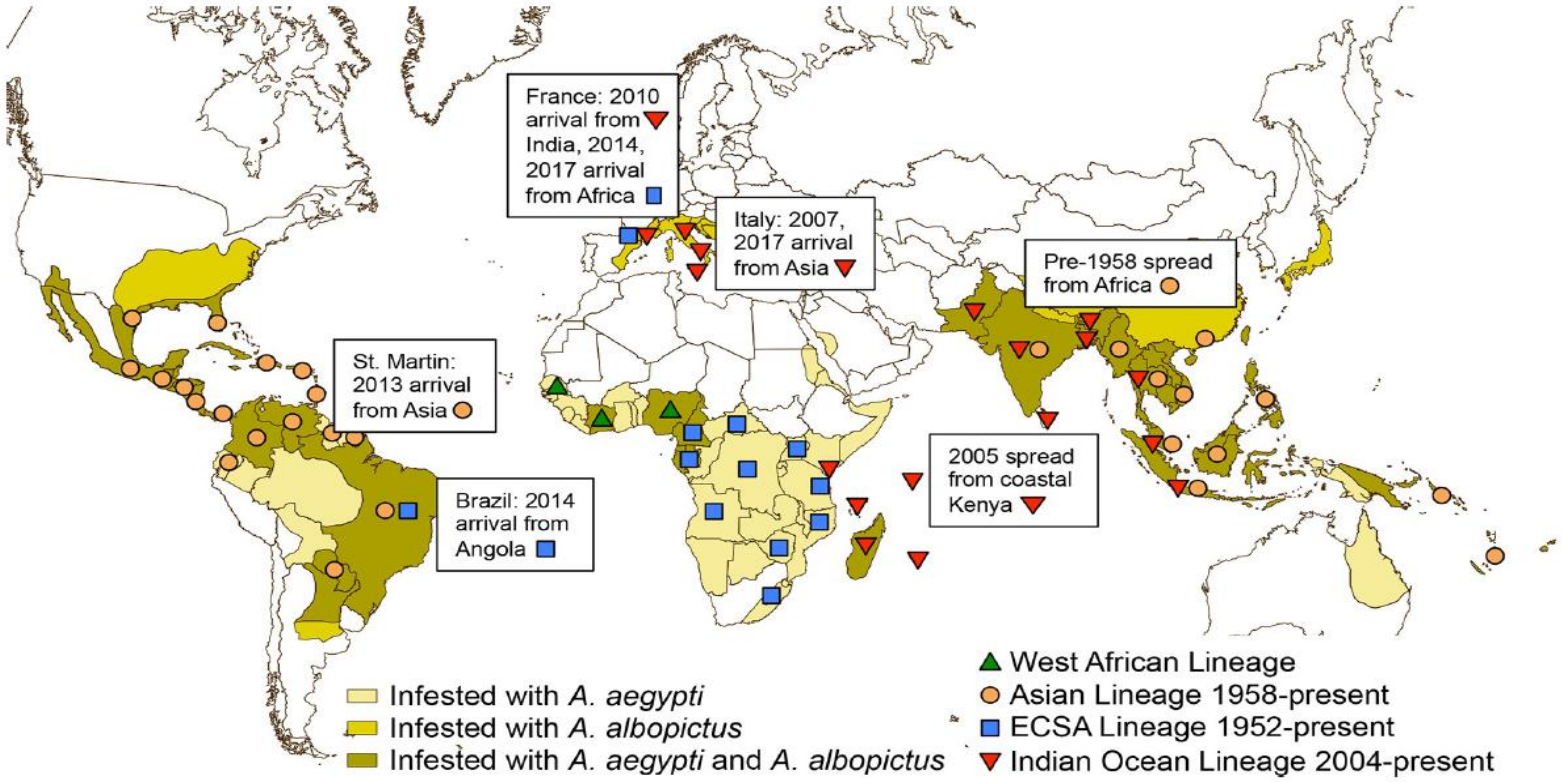



**Fig 1. World map with countries where autochthonous (locally initiated) chains of CHIKV transmission have been identified.** Data from World Health Organization (http://www.who.int/emergencies/diseases/chikungunya/en/) and Pan American Health Organization (https://www.paho.org/hq/index.php?option=com_topics&view=article&id=343&Itemid=40931&lang=en). CHIKV, chikungunya virus.

https://doi.org/10.1371/journal.pntd.0006919.g001

*Rezza & Weaver 2019*

# VLA1553 is Expected to be Highly Differentiated

## Competition overview

| | Valneva | Emergent (Paxvax) | Themis |
|---|---|---|---|
| *Vaccine candidate* | Monovalent, single dose, live-attenuated vaccine candidate | Virus-like particle (VLP) vaccine | Measles-vectored Chikungunya vaccine (MV-CHIK), Live-recombinant vaccine |
| *Schedule* | Single-shot - Day 0 | 2 shots - Day 0 & 28 | 2 shots - Day 0 & 28 |
| *Development stage* | Phase 1 in US complete (manuscript in preparation)<br>No Phase 2 trial needed (single shot efficacy) | Phase 2 completed | Multiple Phase 2 studies<br>- 2x completed (in EU/PR)<br>- 1 recruiting<br>- 1 active, not recruiting |
| *Duration of protection* | 100% seroconversion at **13 months** following single-dose administration | 6 months | 6 months |
| *Phase 3 Guidance* | **Pivotal trial (Phase 3) initiation planned Q4 2020** | 2020 | 2020 |

**1** PR Emergent BioSolutions Announces Interim Results From Phase 2 Study Evaluating CHIKV-VLP, Chikungunya Virus Vaccine Candidate (Link) + Detailed study results Emergent/Paxvax' Phase 2 clinical trial results (Link), **2** PR Themis Bioscience Publishes Compelling Phase 2 Results for Lead Vaccine Candidate against Chikungunya Fever in The Lancet (Link) + Themis' Phase 2 clinical trial results: (Link), **3** PR Valneva reports further positive results for its chikungunya vaccine candidate (Link),

# VLA1553 Key Differentiators

## The only single-shot vaccine candidate for chikungunya today

**Rapid onset of long-lasting protection**

- Single vaccination is sufficient to induce sustaining, high titer, neutralizing antibodies

**Cross-protection potential against globally circulating strains**

**“Intrinsic human viral challenge” provided first indication of efficacy**

**Full-scale drug substance manufacturing process established at existing in-house FDA licensed facility**

- Product is lyophilized, optimized storage conditions

**Regulatory approval will be based on an immunological surrogate[1] (Accelerated Approval Pathway)[2]**

**Manufacturing and commercial infrastructure to produce and commercialize VLA1553 already in place**

**1** Immune marker reasonably likely to predict clinical benefit, as an immunogenicity endpoint in lieu of a clinical endpoint to infer vaccine effectiveness; **2** Press Release: Valneva Reports Positive End-of-Phase 2 Chikungunya Meeting with the U.S. FDA; Sets Stage for Phase 3 Study

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