valneva

Advancing Vaccines for Better Lives

Company Presentation – July 2019

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Valneva – Highlights and key information

+ **Valneva is a biotech company** developing and commercializing vaccines for infectious diseases with major unmet needs
  - › > €100m product sales revenues[1]
  - › Cash flow positive[1]

+ **Specializes in important, high value niches**
  - › Travel vaccines
  - › Technological competence on vector-transmitted diseases

+ **Focused R&D programs in development including**
  - › the only Lyme disease vaccine in clinical development today
  - › a unique, differentiated chikungunya vaccine candidate

+ **International footprint** with approximately 480 employees
  - › Locations in EU and North America for Manufacturing, R&D, and Sales & Marketing

2018 Revenues: €113.0m
2019 Rev. Guidance: €125-135m

Cash: €81.7m (as of Dec. 31, 2018)

Ticker: EPA – VLA

1 In 2018: https://www.valneva.com/en/investors-media/news/2019#310

Valneva's mid-term strategy

To become the leading commercial stage vaccine biotech

Commercial Products

Growing product sales revenues to €200m and beyond

R&D

Investing in innovative R&D programs to address major unmet needs

Financial

Use proceeds from commercial business to fund R&D; raise capital for major R&D programs as required

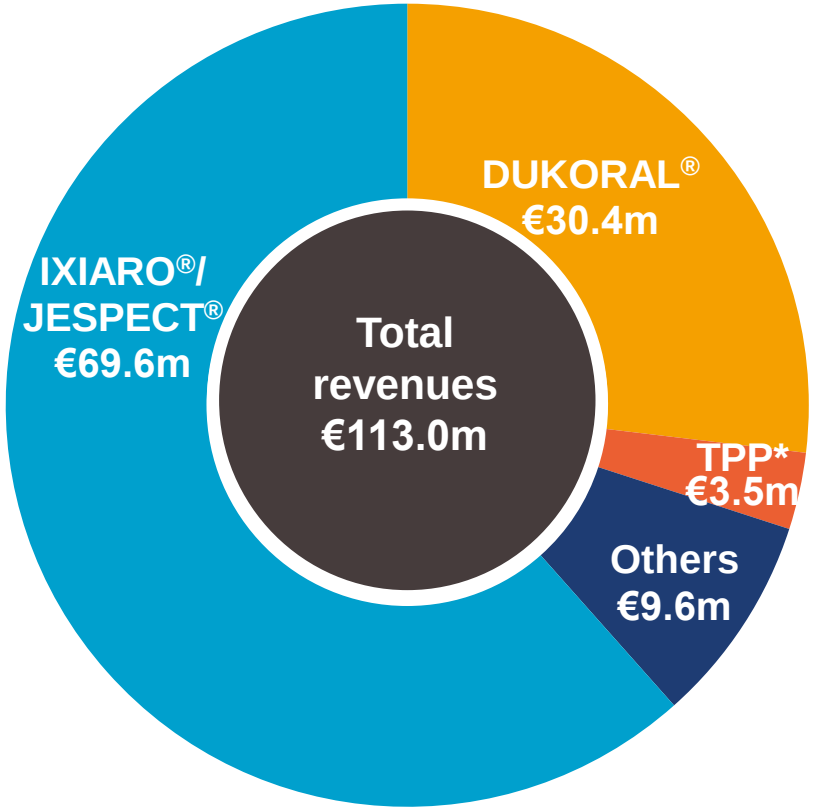
Strategic Growth

Organic growth complemented by targeted acquisition and licensing strategies

Valneva's profitable commercial business funds R&D programs

Product sales growth 2017-2018 16% (CER);
Repeated double-digit sales growth expected 2018-2019

2018 Full-year results



Product sales
€103.5m

Direct sales
81.2%

Gross
margin
60.7%

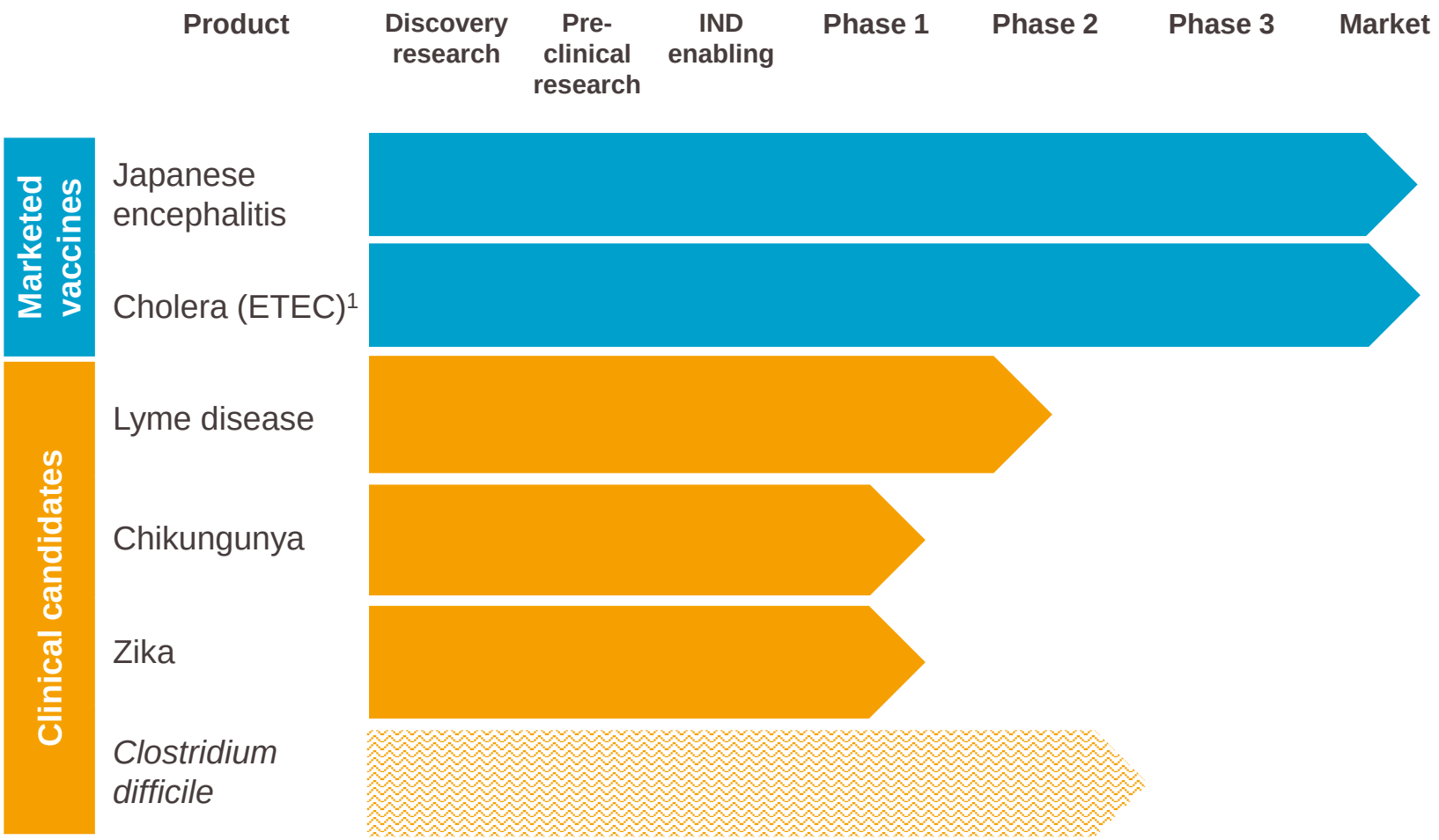
Cash
generated
€16.3m

CER: at constant exchange rates;
**Third party products sold by Valneva's commercial organization*

Innovative R&D pipeline in areas of major unmet need

Valneva's R&D pipeline

Focusing on vaccines with major unmet need



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

IXIARO®/JESPECT®

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

IXIARO®/JESPECT®

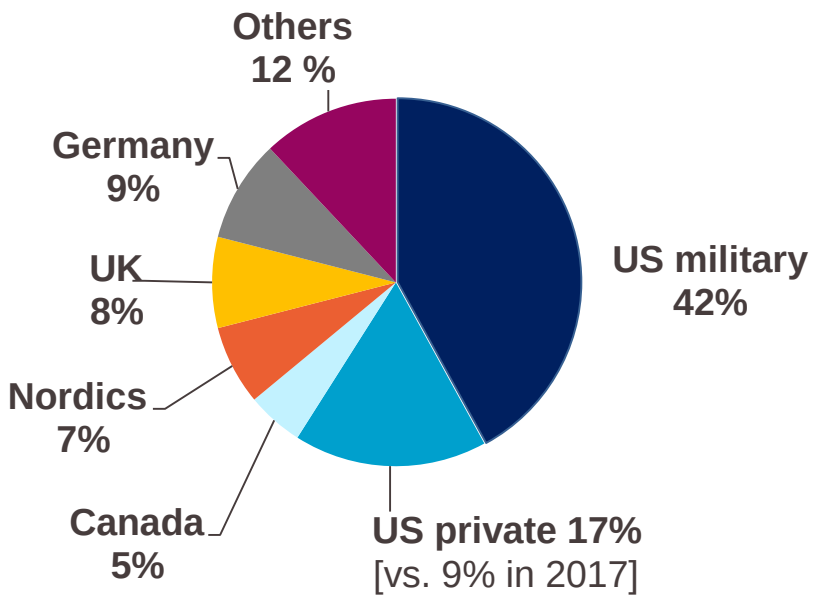
+ **Designed to protect travelers and military against JE, the leading cause of viral neurological disease & disability in Asia**
+ Indicated for active immunization against JE in **adults, adolescents, children and infants** aged two months and older[1]

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

IXIARO®/JESPECT®: US accounts for >50% of sales

2018 product sales analysis



Growth expected to be 15% CER or more in 2019

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 eterotoxigenic *Escherichia coli* (ETEC)**[1]

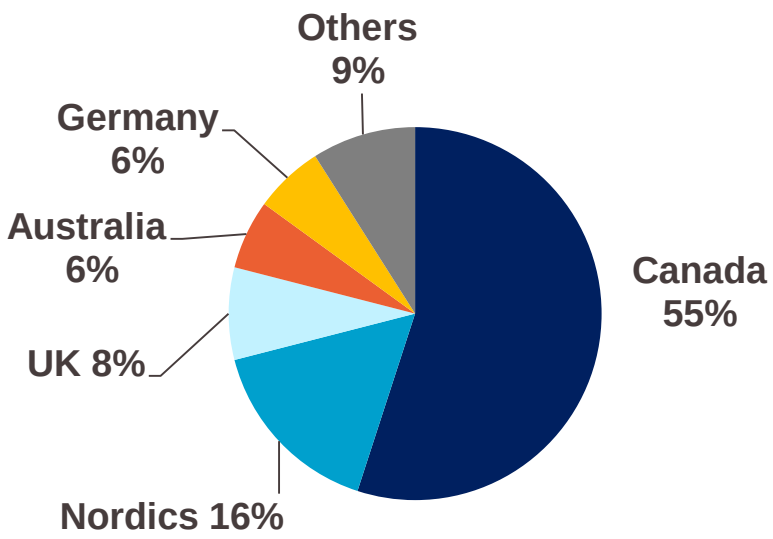
+ **Designed to protect adults and children** from two years of age who will be visiting endemic areas

Commercial position

+ In several markets, including EU, currently indicated to protect against 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 and primarily for cholera only

DUKORAL®: Canada accounts for >50% of sales

2018 product sales analysis

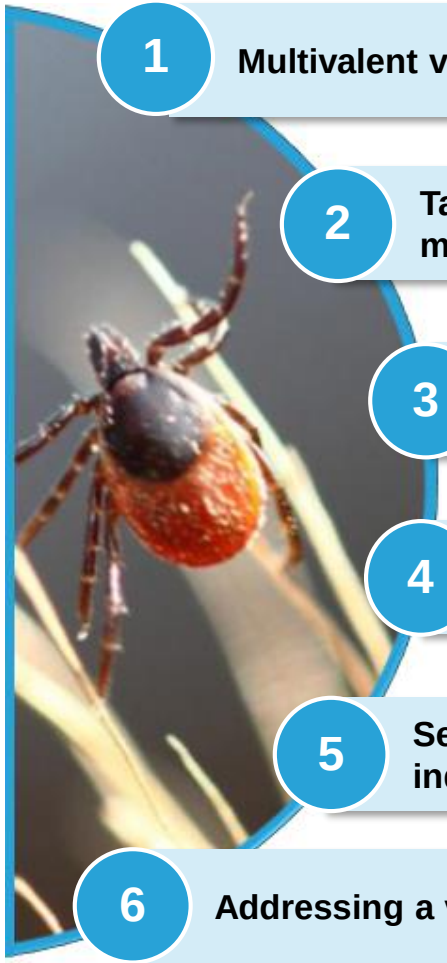


Revenues to grow by up to 5% CER[4] in 2019

__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; 4 CER: at constant exchange rates

Lyme disease is a serious unmet medical issue

VLA15 is the only vaccine candidate in clinical development today



1. **Multivalent vaccine (six serotypes) to protect against Lyme disease in N. America and Europe**
2. **Targets OspA of Lyme borrelia, preventing spirochetes from migrating through the tick's mid-gut – an established and proven Mode of Action for a Lyme disease vaccine**
3. **Safe and immunogenic with excellent boosterability in Phase 1 studies[1]**
4. **Currently in Phase 2 with clear development path for US and EU licensure; FDA Fast Track Designation granted**
5. **Semi-generic manufacturing process with three fusion proteins expressed in *e. coli* – Final industrialization for Phase 3 already anticipated**
6. **Addressing a very significant market opportunity**

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

Overview of Lyme disease

Severe tick-transmitted infection with high prevalence in N. America & Europe

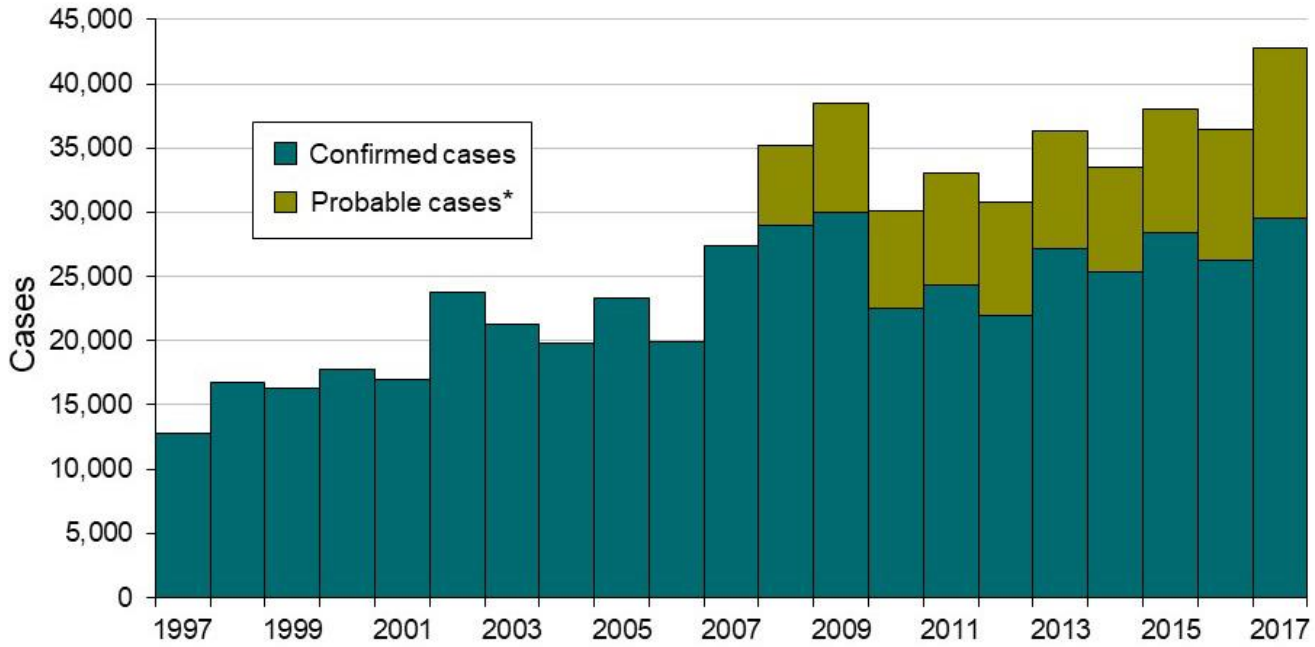
- Tickborne disease (Vector-Ixodes ticks)
- Caused by *Borrelia burgdorferi* spirochete (resides in gut of tick – migrates to salivary gland – enters host during feeding)
- Early signs and symptoms (3-30 days after tick bite) include flu-like sympthoms[1] and Erythema migrans rash[2]
- Left untreated, can spread to joints (arthritis), heart (carditis) and cause neurological problems
- Diagnosed by clinical symptoms, exposure to known endemic area, and lab tests
  - › Treatment: antibiotics (doxycycline, amoxicillin, or cefuroxime axetil)

1 *Fever, chills, headache, fatigue, muscle and joint aches, swollen lymph nodes;* ***2*** *Occurs in approx. 70-80% of infected persons.*

Lyme disease epidemiology

The most common vector-borne illness in the Northern hemisphere

Annual Reported Cases of Lyme Disease in the US[1]



- **Lyme disease has seen a marked increase in reported cases, driven by:**
  - Climate change contributing to increased tick and host populations
  - Longer tick breeding seasons
  - Increasing awareness and healthcare follow-ups

Estimated Cases

- **~ 300,000 cases in US (p.a.)[2]**
- **~ 200,000 cases in EU (p.a.)[3]**
- Most-affected US regions:
  - 95% of US cases in 2016 occurred in Northern US states
- Key age Groups:
  - 17.3% of cases occur in 5-14 years
  - 36.6% of cases occur in 40-64 years

1 https://www.cdc.gov/lyme/why-is-cdc-concerned-about-lyme-disease.html; 2 https://wwwnc.cdc.gov/eid/artickle/21/9/15-0417_article; 3 Estimated from available national data. Number largely underestimated based on WHO Europe Lyme Report as case reporting is highly inconsistent in Europe and many LB infections go undiagnosed; ECDC tic-borne-diseases-meeting-report; 4 Climate change influences on the annual onset of Lyme disease in the United States; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4631020/;

VLA15: Phase 2 – Optimizing dose and schedule

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

Phase 2
820 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**

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 Primary phase (initiated June 2019[2])

+ 2 selected dose levels (adjuvanted) chosen after run-in phase, placebo
+ 450 healthy volunteers (18 to 65 years)
+ Schedule: 0, 1, 2 months

135 µg w/ alum	180 subjects
180 µg w/ alum	180 subjects
Placebo	90 subjects

VLA15-202 Secondary phase (initiated July 2019[3])

+ 2 selected dose levels (adjuvanted) chosen after run-in phase, placebo
+ 250 healthy volunteers (18 to 65 years)
+ Alternative schedule: 0, 2, 6 months

135 µg w/ alum	100 subjects
180 µg w/ alum	100 subjects
Placebo	50 subjects

__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

Lyme vaccine candidate VLA15 – next steps

Current outline for Phase 3 clinical development plan*

Phase 2 expected to provide first data by mid-2020

- Initial Data: Day 85 after short schedule: dose determination
- Alternative schedule data expected late 2020
- Booster studies with additional 12 months follow-up

Phase 3 could be initiated 2021/2022

- Large-scale efficacy study needed: either combined US/EU or two trials
- Efficacy being followed for two tick seasons
- Target BLA/MAA filing after first tick season
- Phase 3 may include adolescents (12 years+) in addition to adults
- First pediatric data expected at point of licensure
- Overall Phase 3 duration of approximately three years

**Subject to development progress, regulatory concurrence and company funding*

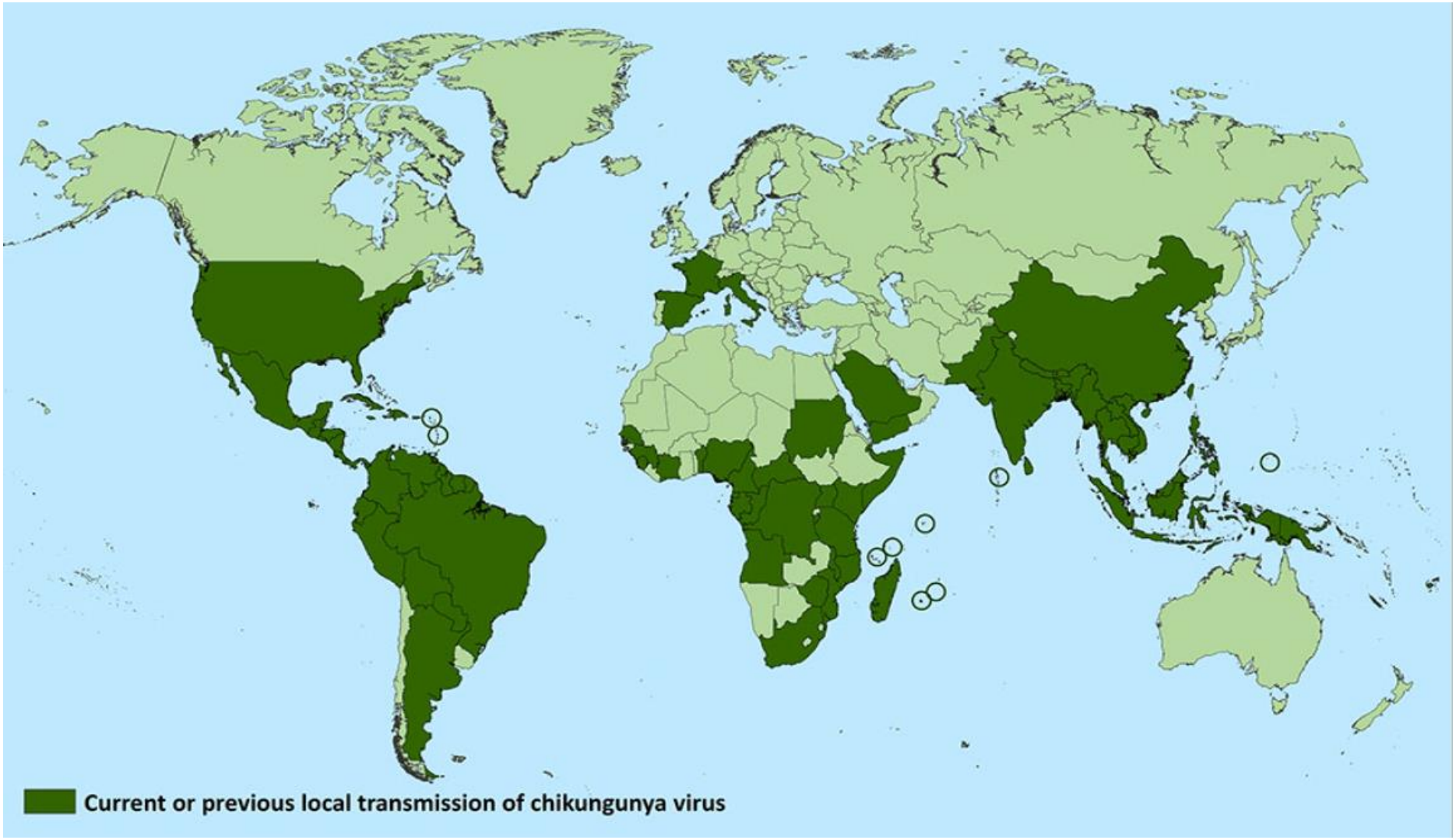
Chikungunya is a severe, emerging outbreak disease
VLA1553 is a unique, differentiated single-shot vaccine candidate

1. Currently no preventive vaccines or effective antiviral treatments exist for chikungunya
2. VLA1553 is a monovalent, single dose, live attenuated[1] prophylactic vaccine targeting chikungunya virus neutralization
3. Excellent immunogenicity and safety in Phase 1 with first hints on efficacy[2]
4. Currently in Phase 1 (follow-up) – Acceleration directly into pivotal trial under evaluation; FDA Fast Track Designation granted
5. Full-scale drug substance manufacturing process established at in-house FDA licensed facility
6. Addressing a very significant market opportunity

__1__ CHIKV LR2006-OPY1 infectious clone was attenuated by deleting large part of gene coding nsP3 (alphavirus-replicase; __2__ Valneva Reports further Positive Results for its Chikungunya Vaccine Candidate; Photo credit: James Gathany (source)

Chikungunya epidemiology

Countries and territories where chikungunya cases have been reported (as of May 29, 2018)[1]



1 https://www.cdc.gov/chikungunya/geo/index.html

Chikungunya Phase 1 study (VLA1553-101) – Interim results

Excellent immunogenicity and safety profile up to Month 7[1]

Immunogenicity

- 100% Seroconversion Rate (SCR)[2] achieved at Day 14 after a single vaccination in all dose groups[1]
  - SCR fully sustained at 100% after six months[1]
- Single vaccination of VLA1553 is sufficient to induce sustaining, high titer, neutralizing antibodies[1]

Excellent immunogenicity profile after single vaccination

Safety

- Generally safe in all dose groups
- Well-tolerated in 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 (AESIs) up to Month 7[1]

Excellent safety profile in low and medium doses

1 Valneva Reports further Positive Results for its Chikungunya Vaccine Candidate; 2 SCR defined as proportion of subjects achieving a CHIKV-specific neutralizing antibody titre as NT_{50} ≥ 20; 3 As occurs with other live-attenuated vaccines

VLA 1553: Development considerations and steps

Outline for potential accelerated clinical development plan*

- **FDA Fast Track granted to VLA1553 vaccine candidate**
- **Phase 1 first unblinded data reported May 2019**
  - Day 28 safety and immunogenicity after single dose
  - Viremia data at Days 3, 7 and 14 post-vaccination
  - Month 6 safety and immunogenicity data providing information on antibody persistence
  - Month 7 re-vaccination safety, immunogenicity and viremia data as early indicator of efficacy
- **Supporting non-clinical experiments in preparation/process**
  - Mosquito transmission studies
  - NHP study addressing biodistribution
  - Passive transfer study in NHPs to develop correlate of protection using human sera from VLA1553-101

Aiming for accelerated approval procedure at FDA*

**Subject to development progress, regulatory concurrence and company funding*

Financial outlook

Continued double-digit sales growth, higher R&D investment to support clinical development

	2018	2019
Product sales revenues	€103.5m	€115m - €125m
Total revenues	€113.0m	€125m - €135m
R&D investments	€25.3m	€35m - €40m
Gross margin	60.7%	> 60%
Net operating margin[1]	24.1%	25% - 35%
EBITDA	€13.1m	€5m - €10m

1 Net operating margin is based on the P&L for the Commercial Products segment including an allocation (56%) of G&A costs from Corporate Overheads and Amortisation of Intangibles related to IXIARO®

Corporate Governance and Shareholder Structure

Management Board

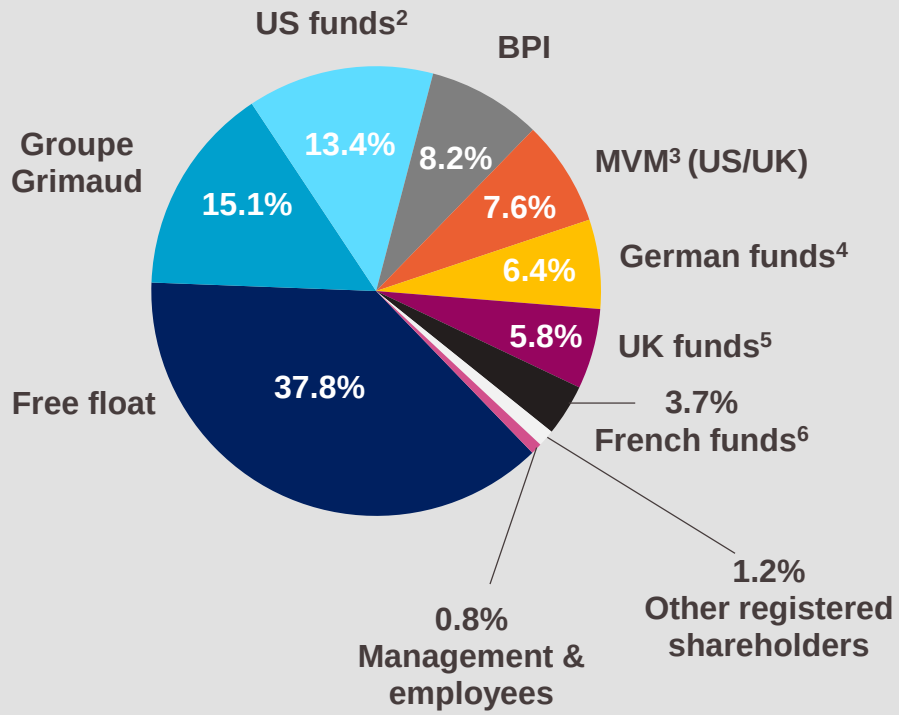
+ **Thomas Lingelbach**, *President & CEO*
+ **Franck Grimaud**, *President & CBO*
+ **David Lawrence**, *CFO*
+ **Wolfgang Bender, MD, PhD**, *CMO*
+ **Frédéric Jacotot**, *General Counsel & Corporate Secretary*

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)
+ **Balaji Muralidhar, MD, PhD** (UK)
+ **Sandra E. Poole** (US)

Stock Information

+ Primary listing = Euronext (Paris)
+ Number of ordinary shares: 90.9m
+ Shareholder structure[1]:



1 Estimates as of May 2019, based on ordinary share capital; 2 Combined positions of 11 U.S.-based funds managed by Deerfield Partners, Armistice Capital, Artisan Partners L.P., New Leaf, General American, Granite Point and others; 3 Funds managed by MVM Life Science Partners; 4 Combined positions of DWS Investment, Apus Capital, Apo Asset Management, Lupus alpha, Medical Strategy, Hauck & Aufhäuser, CD-Ventures, and Deutsche Apotheker; 5 Combined positions of Highclere, AXA Investment Managers Ltd., and Abingworth LLP; 6 Combined positions of CDC Entreprises Valeurs Moyennes, AXA Paris, La Banque Postale AM, AG2R, PRO BTP, Chaussier Gestion, and Mandarine Gestion.

Recent and upcoming newsflow in 2019

On track to deliver 15-20% CER product sales growth expected in 2019

Successful outcome of Phase 2 run-in for Lyme disease vaccine candidate (VLA15)
- DSMB has cleared two dosage levels for further clinical development

Excellent Phase 1 data for chikungunya vaccine candidate (VLA1553) reported
- Aiming for accelerated development strategy

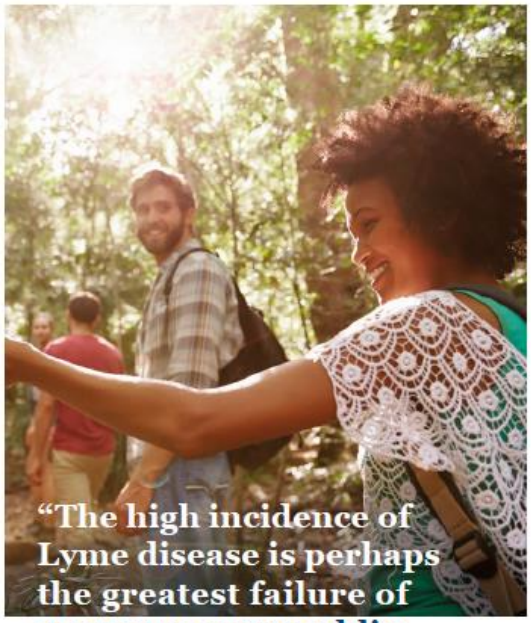
Valneva regains control of R&D and full flexibility to find best partners

Valneva's R&D day on July 9th in New York

Appendices

Vaccination against Lyme disease

Justification for a Lyme 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**

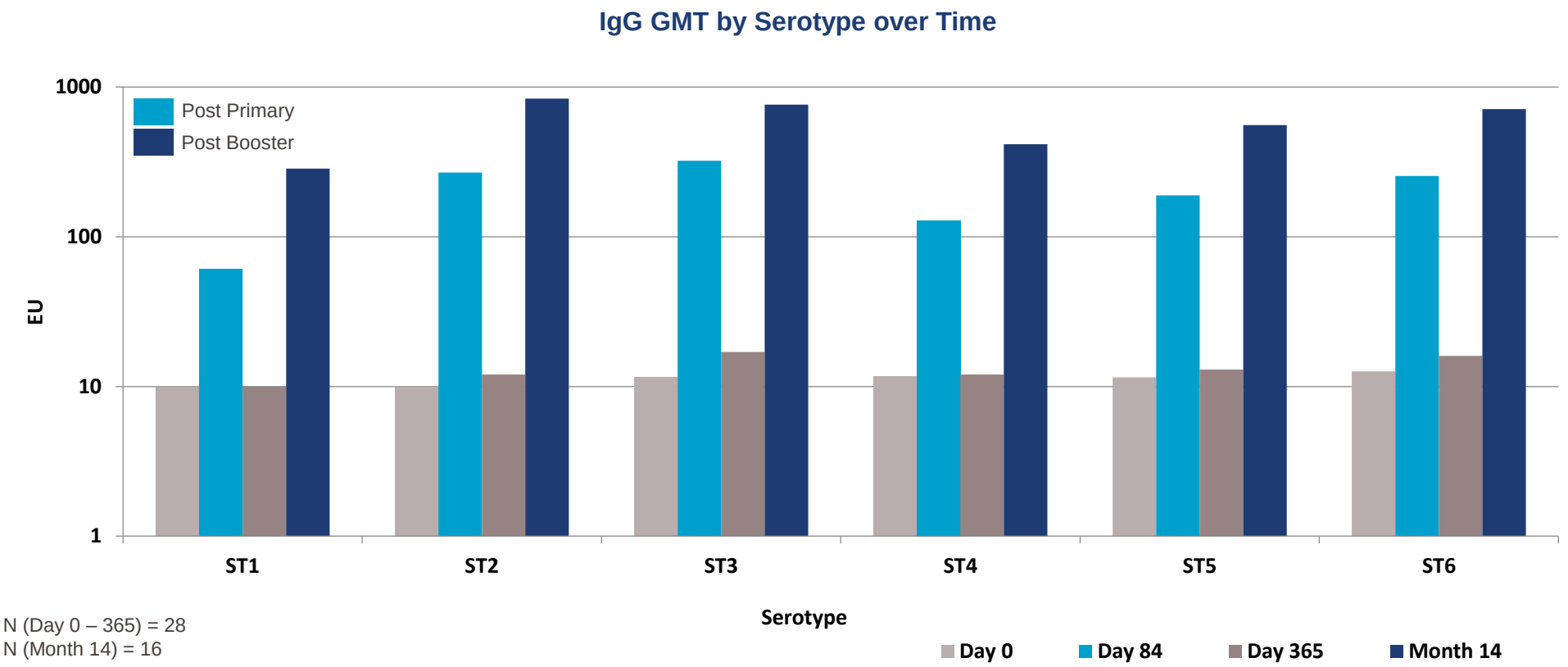
- **Other preventive measures have not been shown to work on a public health scale**

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

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

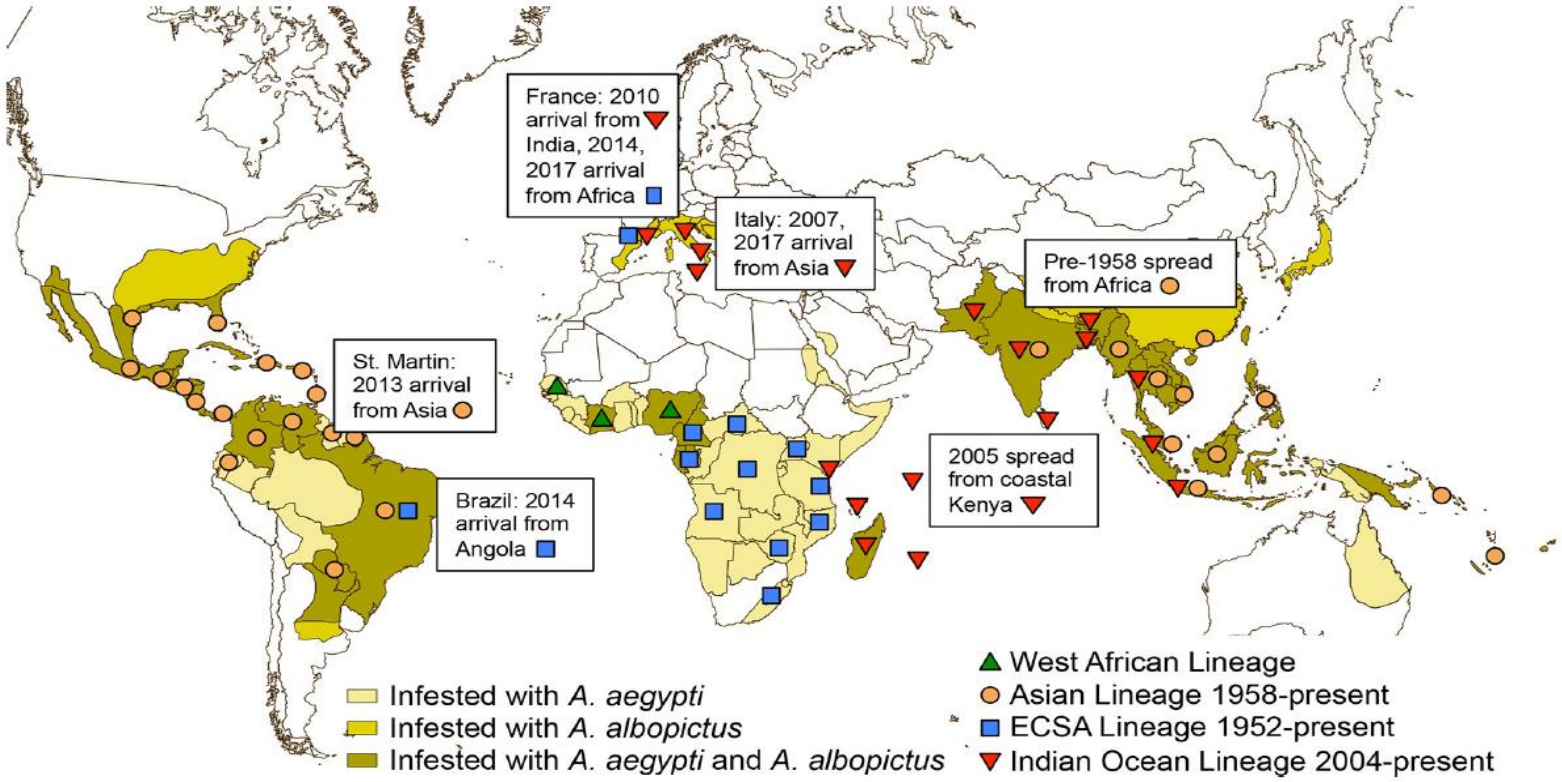


Fig 1. World map with countries where autochthonous (locally initiated) chains of CHIKV transmission have been identified. Data from World Health Organization (http://www.who.int/emergencies/diseases/chikungunya/en/) and Pan American Health Organization (https://www.paho.org/hq/index.php?option=com_topics&view=article&id=343&Itemid=40931&lang=en).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

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

Rezza & Weaver 2019

VLA84: Unpartnered *Clostridium difficile* vaccine candidate

Vaccine targeting healthcare-associated diarrhea, an increasing threat to the elderly in a $1 billion market[1]

Clostridium difficile (C. diff)

- **Single most common pathogen of acute healthcare-associated infections in the US[2] (~ 450,000 cases of annually and ~ 30,000 deaths[3])**
- **~ 172,000 cases in EU member states per year[4]**
- **Targeting primary prevention of *C. difficile***
  - Current antibiotic treatments have significant limitations with recurrence in ~20% of cases[5]

Valneva's vaccine candidate VLA84

- **One of two late stage vaccine candidates**
- **Modern, recombinant single subunit-toxin antigen (CTAB) expressed in e. coli w/o adjuvants**
- **Potential distinct competitive advantages on industrialization/future manufacturing**

Phase 2 completed

- **Phase 3 ready**
- **Highly immunogenic in all age groups tested (strong immune responses to both C. diff toxins A & B)**
- **Good safety and tolerability profile confirmed**
- **Comparable immunological profile to other CDI clinical programs targeting primary prevention of CDI**

New development & partnering approach

- **Potential partners hesitant about level of Phase III investment required and investment-risk proposition**
- **VLA to use first CDI vaccine approval and consider "Head to Head" non-inferiority Phase 3 on immunological correlate**
- **New approval expected to substantially improve investment-risk proposition for own or partnered development to market**

Source picture: www.123rf.com; ***1*** *VacZine Analytics Clostridium difficile prophylactic vaccines Market View, January;* ***2*** *Magill S, Edwards J R, Bamberg W et al. Multistate Point-Prevalence Survey of Health Care–Associated Infections. New England Journal of Medicine 2014;370:1198-208;* ***3*** *Lessa et al, Burden of Clostridium difficile Infection in the United States. N Engl J Med 2015;372:825-34.* ***4*** *Clostridium difficile infection in Europe. A CDI Europe Report.;* ***5*** *Leffler et al, Clostridium difficile infection. N Engl J Med 2015;372:1539-48;*

Thank you
Merci
Danke
Tack

valneva