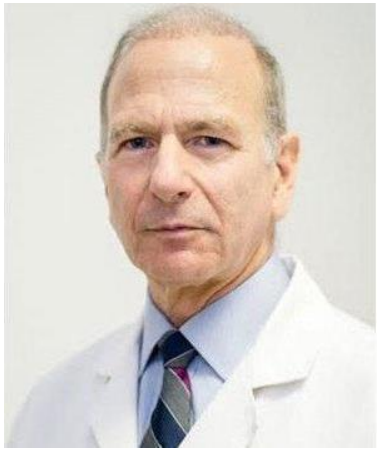
KOL Presentation on the Threat of Chikungunya Virus

Investor Webcast
May 25, 2022

Today's Agenda

Welcome and Introduction	**Joshua Drumm, Ph.D.** *VP Global Investor Relations, Valneva*
Chikungunya In Depth	**Bradley A. Connor, M.D.** *World-renowned expert in tropical medicine and gastroenterology*
VLA1553 Update	**Juan Carlos Jaramillo, M.D.** *Chief Medical Officer, Valneva*
Q&A	**Joined by:** **Peter Bühler;** *Chief Financial Officer, Valneva* **Katrin Dubischar;** *VP, Chikungunya Program Director, Valneva*

Speaker Introductions



Bradley A. Connor, M.D.

- Clinical Professor of Medicine at the Weill Cornell Medical College
- Attending Physician at the New York Presbyterian Hospital – Cornell Campus
- Founder and Medical Director of the New York Center for Travel and Tropical Medicine
- NYC Site Director for the CDC's Emerging Infectious Disease network
- Past president of the International Society of Travel Medicine (ISTM)

Juan Carlos Jaramillo, M.D.

- Experienced R&D leader with broad expertise
- Daiichi Sankyo – SVP, market access and medical affairs; SVP, head of global market access and pricing
- Grünenthal – SVP, medical affairs and clinical development
- Previous roles at GlaxoSmithKline

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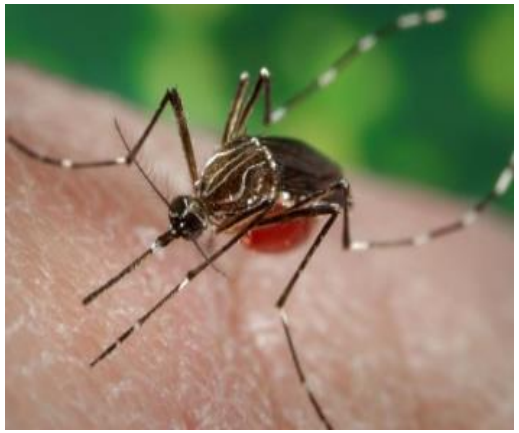
This presentation presents information about VLA1553, an investigational vaccine candidate that has not been approved for use and has not been determined by any regulatory authority to be safe or effective.

The Threat of Chikungunya Disease

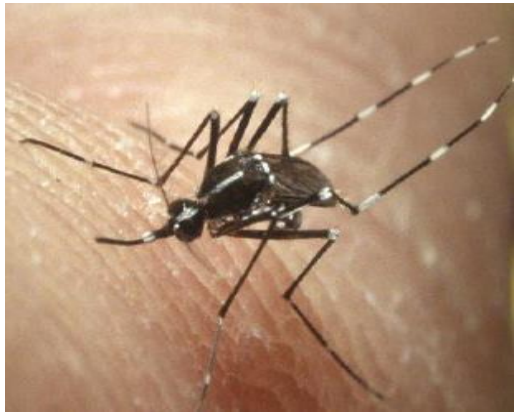
Bradley Connor, M.D.

Chikungunya: a major public health threat

Mosquito-transmitted disease with potentially debilitating consequences



Aedes aegypti



Aedes albopictus

- Chikungunya virus (CHIKV) is transmitted by *Aedes* mosquitoes[1]
- Often causes large, explosive outbreaks with high attack rates, 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] with the potential for it to happen in the U.S. and Europe[2,4]
- Highest areas of risk of infection for travelers include the Americas, parts of Africa, and Southeast Asia[3]
- Returning infected travelers can trigger local transmission in areas where relevant mosquitoes are established (e.g. Southern U.S./Europe)[2]
- High burden of disease: outbreaks can have substantial health-economic impact; infection can progress to severe chronic symptoms in many patients[4]

No cure; treatment is symptomatic and supportive only

Without a vaccine, prevention is limited to protection against mosquito bites and vector control

1. Staples et al. CDC Yellow Book 2020, Chapter 4 . 2. Bettis et al, PLOS Neglected Tropical Diseases 16(1): e0010069. 3. Lindsey et al *Am J Trop Med Hyg*. 2018;98(1):192-197. doi:10.4269/ajtmh.17-0668 4. Silva LA et al. J Clin Invest. 2017 Mar 1;127(3):737-749.

High acute morbidity: can lead to chronic, incapacitating effects

Lasting months to years in a high proportion of patients

Acute Phase (up to 97%)[1]

- Symptoms typically begin 3-7 days after being bitten by an infected mosquito[1]
  - Fever and joint pain / joint inflammation, other systemic manifestations[1-4]
  - Joint symptoms are typically severe and can be debilitating[1]
- Viremic for 5-10 days[2,3]
- Acute symptoms typically resolve in 7-10 days[1]
- Sub-acute post-viremic state (6-21 days) can occur[3,4]
  - Persistent articular symptoms
  - Tenosynovitis and bursitis

Chronic Phase (4% to 78%)[5,6]

- Pattern similar to Rheumatoid Arthritis
  - Characterized by peripheral spondylarthritis, undifferentiated arthritis, fibromyalgia, neuropathic chronic pain
- Fatigue is another main persistent symptom, can last for months to years[7,8]
- Risk factors for developing chronic symptoms:[(6,9)]
  - >45 years of age
  - High viral load during acute phase
  - Severe immunologic response in post-viremic phase
- Chronic disease negatively impacts quality of life and ability to work

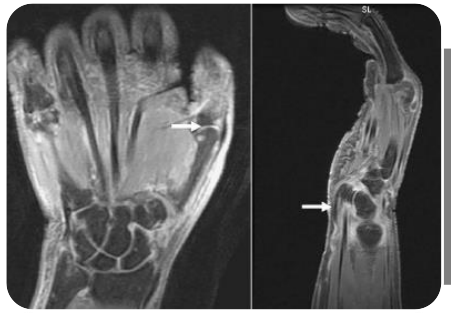
Chikungunya means “to become contorted” in Kimakonde, describing sufferers’ stooped appearance

1. Staples et al. CDC Yellow Book 2020, Chapter 4. 2. Rudolph KE, et al. Am J Trop Med Hyg. 2014;90:882-891. 3 Suhrbier A et al. Nat Rev Rheumatol. 2012;8:420-429. 4. Stalkowsky F et al. PLoS one 2009;4:e7603-e7603. 5. Rodríguez-Morales AJ et al . Arthritis Care Res 2016;68:849-58 6. Martí-Carvajal A et al. PLoS One 2017;12:e0179028 7. Manimunda SP, et al. Trans R Soc Trop Med Hyg 2010; 104: 392–99. 8. Soumahoro MK, et al. PLoS One 2009;4:e7800. 9. Zaid A et al. Arthritis Rheumatol 2018;70:484-95

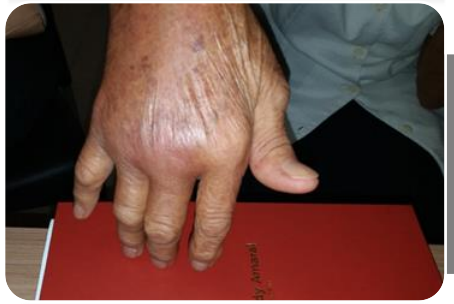
Chronic Chikungunya negatively impacts quality of life

Persistent rheumatologic disease

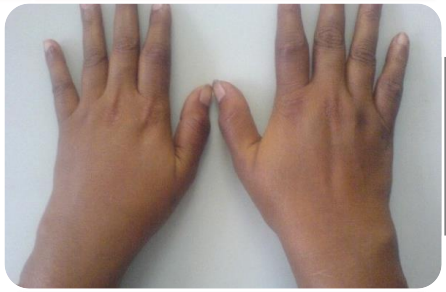
Post-CHIKV Rheumatism - 2 forms -	Effect of Arthritis/Polyarthritis	Impact on Quality of Daily Life
Mechanical musculoskeletal disorders	Long-term joint pain	• **Rising from chair** • **Walking** • **Picking up objects** • **Opening a bottle** • **Self care** • **Physical impact on leisure time and limitations on activity**
	Stiffness after immobility[1,4]	
	Multiple joints affected, ie, spine, shoulder, elbow, wrist, hand, hip, knee, ankles, feet	
Chronic inflammatory arthritis	Can be triggered by change in temperature and physical effort[5]	
	May require surgery	



Carpitis and thumb arthritis (left) – Multiple tenosynovitis of fingers and wrist (right)[1]



2 years after CHIKV infection: Intense arthritis of metacarpophalangeal joints and wrist[3]



Symmetrical inflammatory polyarthritis[2]

1. Fabrice S, et al. Medicine: 2007;86:123-137. 2. Mohan A, et al. Indian J Dermatol. 2010; 55: 54–63. 3. Amaral J, et al. Viruses. 2019;11:289. 4. Tritsch S. et al. J Rheum. 2020;47:1267-74. 5. Schilte C. et al. PLOS Negl Trop Dis. 2013;7:e2137.

Chikungunya symptoms mimic Dengue/Zika, spread by the same vectors[1-3]

Similar clinical presentation may result in underdiagnosis

- Atypical presentations of Chikungunya may also be seen in persons with respiratory, cardiovascular, and neurological comorbidities[3,4]
- Lack of disease awareness has obscured the true public health impact of Chikungunya[4,5]
- Cross-reactivity with other alphaviruses has resulted in reduced specificity of clinical diagnosis resulting in less optimal outcomes for infected patients due to delays in disease-specific treatment[4, 6]

Disease	Dengue	CHIK	Zika
Fever	++++	+++	+++
Myalgia/Arthralgia	+++	++++	++
Edema in Limbs	—	—	++
Maculopapular Exanthema	++	++	+++
Retro-Orbital Pain	++	+	++
Conjunctivitis	—	+	+++
Lymphadenopathy	++	++	+
Hepatomegaly	—	+++	—
Bleeding	+	—	—

1. https://www.cdc.gov/chikungunya/hc/diagnostic.html, accessed 30 August 2020. 2. Staples et al. CDC Yellow Book 2020, Chapter 4. 3. Economopoulou A, et al. 2009;137:534-41; 4. https://www.biomedcentral.com/about/press-centre/science-press-releases/03-03-2016, accessed 9 August 2020. 5. https://www.who.int/news-room/fact-sheets/detail/chikungunya, accessed 3 September 2020. 6. Horwood, 2015.

Common predictors of severe disease

Age[1-2]

- Very young, particularly neonates
- Older adults (≥65 years), particularly the elderly

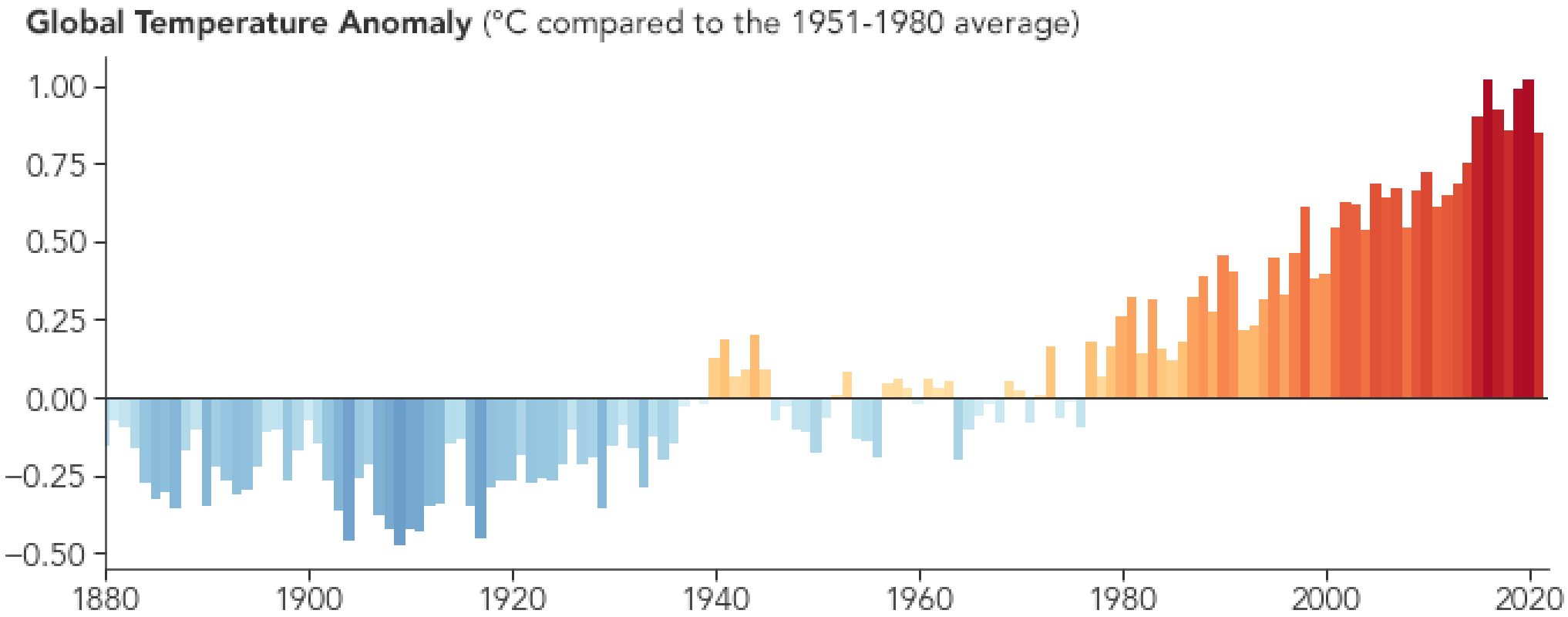
Comorbidities[1-4]

+ Hypertension
+ Diabetes mellitus
+ Heart disease
+ Chronic kidney disease (CKD)

People at risk for more severe disease include newborns infected around the time of birth, older adults, and people with chronic medical conditions

1. Economopoulou A, et al. Epidemiol Infect. 2009;137:534-41. 2. https://www.cdc.gov/chikungunya/symptoms/index.html, accessed 3 August 2020. 3. Cerbino-Neto et al. Rev Soc Bras Med Trop. 2020;53: e04312019. 4. Da Silva G, et al. Am J Trop Med Hyg. 2018;99:1327-1330.

Earth’s continued warming trend

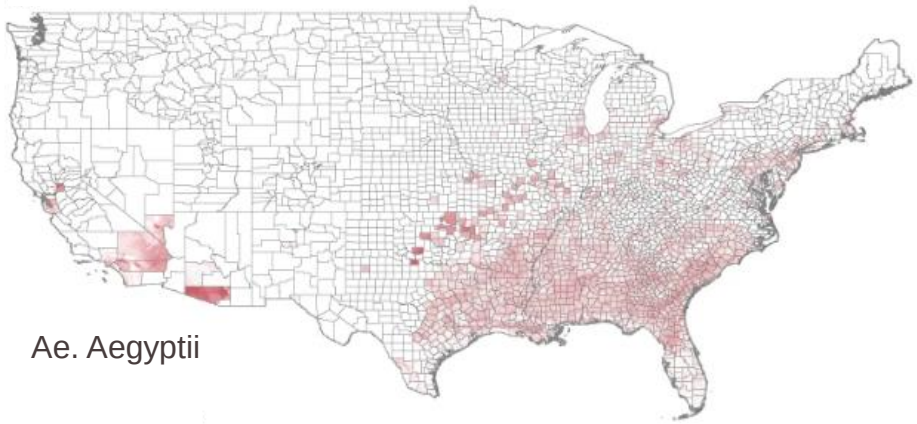


Source: https://earthobservatory.nasa.gov/images/149321/2021-continued-earths-warming-trend

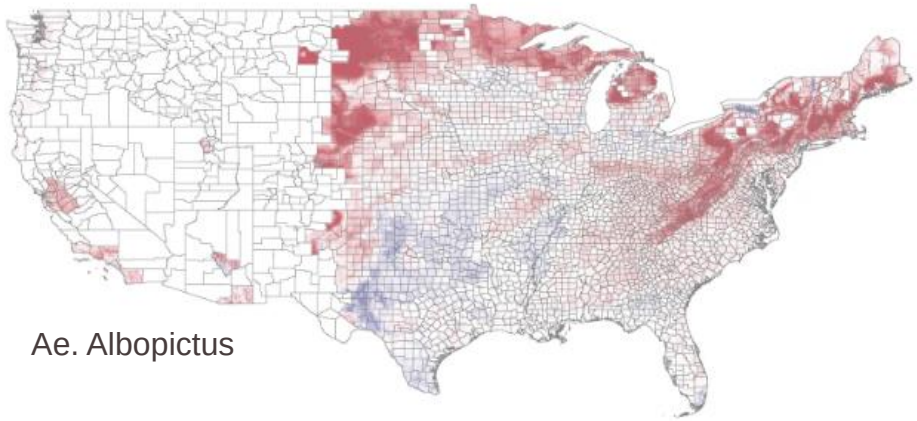
Expansion of Aedes mosquitoe habitat due to climate change

Large areas of U.S. and southern Europe expected to be affected by *Aedes* mosquitoes

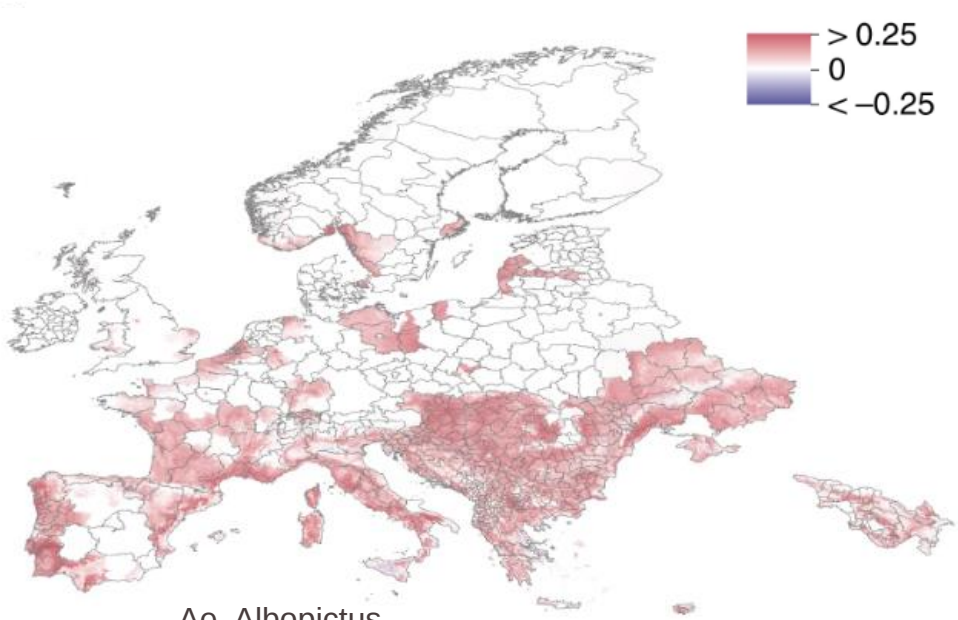
Expected expansion (red) and contraction (blue) of mosquito population between 2020 and 2050



Ae. Aegyptii



Ae. Albopictus



Ae. Albopictus

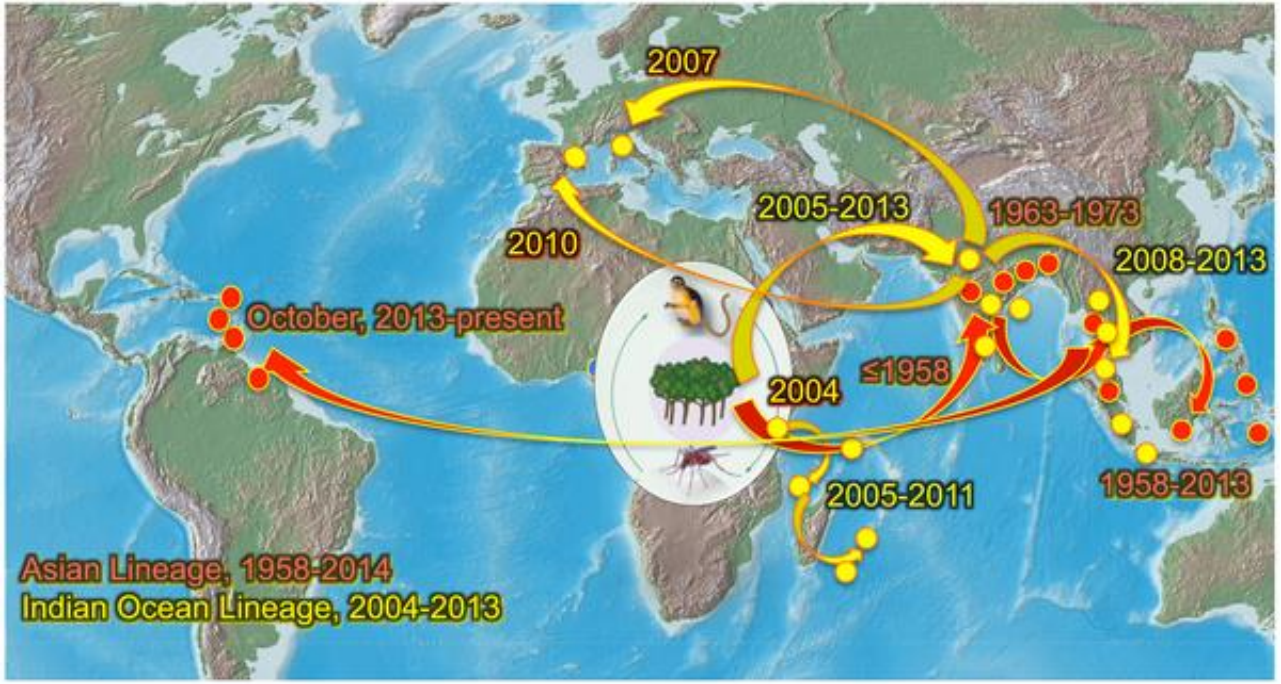
Growing outbreak risk:
CHIKV may spread in the warmer regions where *Aedes* are established[1]

Kraemer, M.U.G., Reiner, R.C., Brady, O.J. *et al.* Past and future spread of the arbovirus vectors *Aedes aegypti* and *Aedes albopictus*. *Nat Microbiol* 4, 854–863 (2019). https://doi.org/10.1038/s41564-019-0376-y

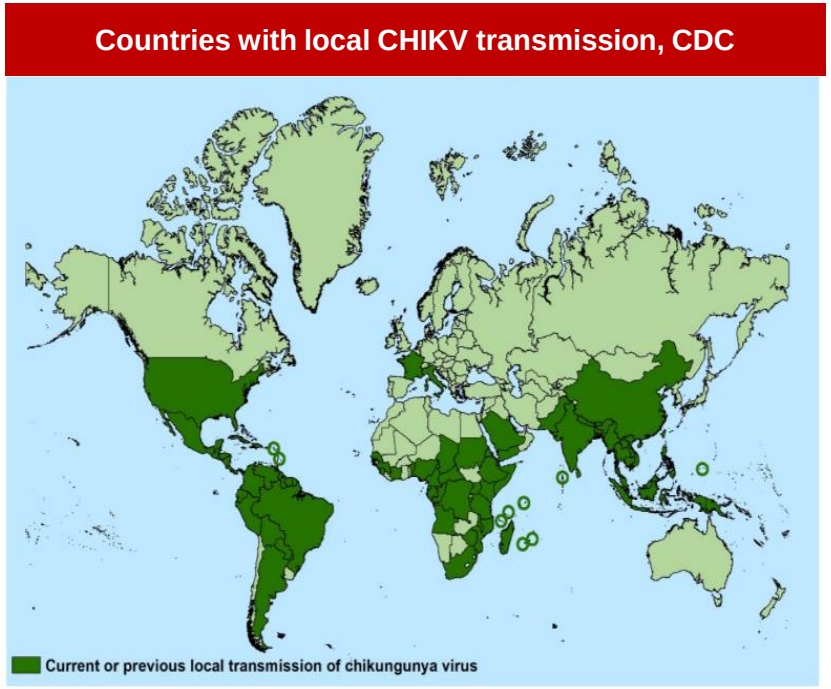
The global spread of Chikungunya

>3.2 million cases reported since introduction into the Americas in 2013[1]

Spread of the Asian lineage (red) and the Indian Ocean lineage (yellow) from Africa[2]



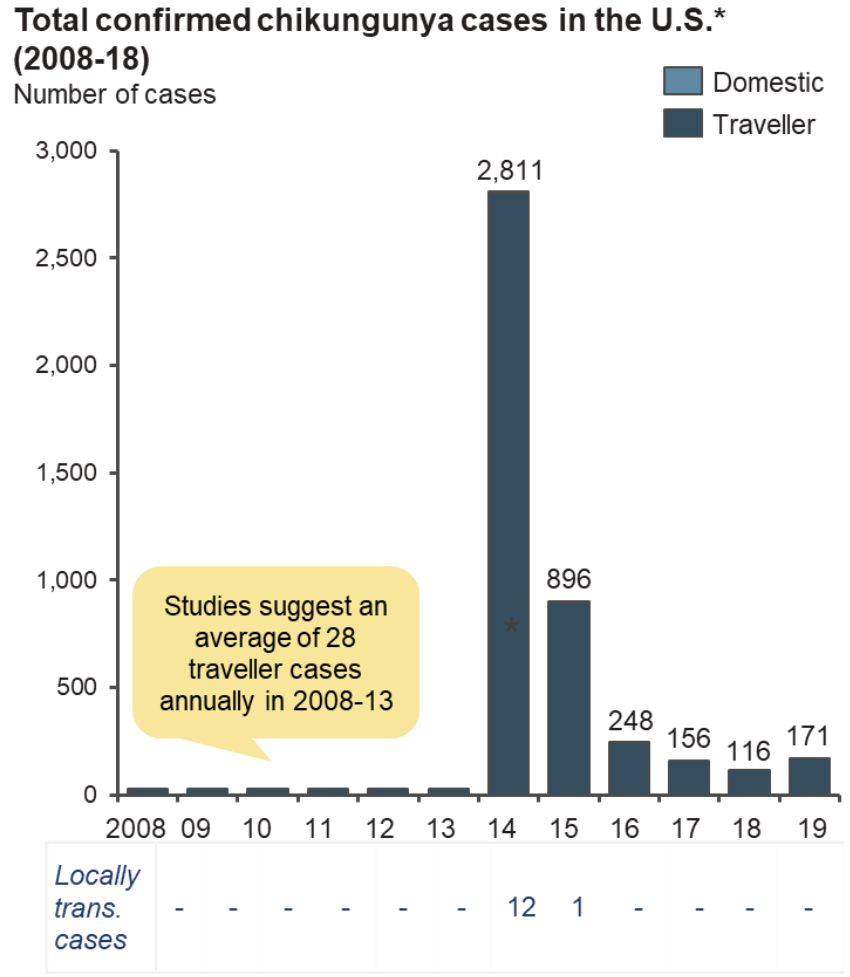
Transmission reported in over 100 countries[3]



1. PAHO/WHO data: Number of reported cases of chikungunya fever in the Americas. https://www.paho.org/data/index.php/en/mnu-topics/chikv-en/550-chikv-weekly-en.html. Last accessed 17 Mar 2022; 2. Weaver SC (2014) Arrival of Chikungunya Virus in the New World: Prospects for Spread and Impact on Public Health. PLOS Neglected Tropical Diseases 8(6): e2921; 3 Guzzetta et al. BMC Medicine (2020) 18:226 https://doi.org/10.1186/s12916-020-01674-y 4 Staples et al. CDC Yellow Book 2020, Chapter 4.

Chikungunya cases in the U.S.

- Rarely identified in U.S. travelers prior to 2008
- From 2008–2013, an average of 28 cases/year in the U.S.
  - All travelers to affected areas in Asia, Africa, or Indian Ocean
  - None resulted in known local transmission in the U.S.
- In late 2013, the first local transmission in the Americas was identified in the Caribbean
- Since 2014:
  - >4,000 reported cases among U.S. travelers
  - 13 documented cases of local transmission in the U.S. (12 in Florida and 1 in Texas)
  - >5,000 reported cases of local transmission in Puerto Rico
- The CDC estimates that *Aedes aegypti* and *Aedes albopictus* mosquitos are currently present in 39 states



*Chikungunya became a nationally notifiable condition in 2015

1. CDC Arboviral Diseases Branch, Division of Vector-Borne Diseases. Chikungunya in the United States, April 8, 2015

Chikungunya cases in the EU

Expanding *Aedes* mosquito habitat creates risk for outbreaks

- In 2019, 15 countries reported 516 cases of chikungunya virus disease, of which 421 (82%) were confirmed
- France reported the highest proportion of cases (21%), followed by the United Kingdom (18%) and Germany (17%)
- One third of the cases were reported in July, August or September. *(Vector season in Europe)*

Expanding Aedes mosquito habitats create risk for outbreaks

- e.g. Italy: 414 cases between Jun-Nov 2017[2]

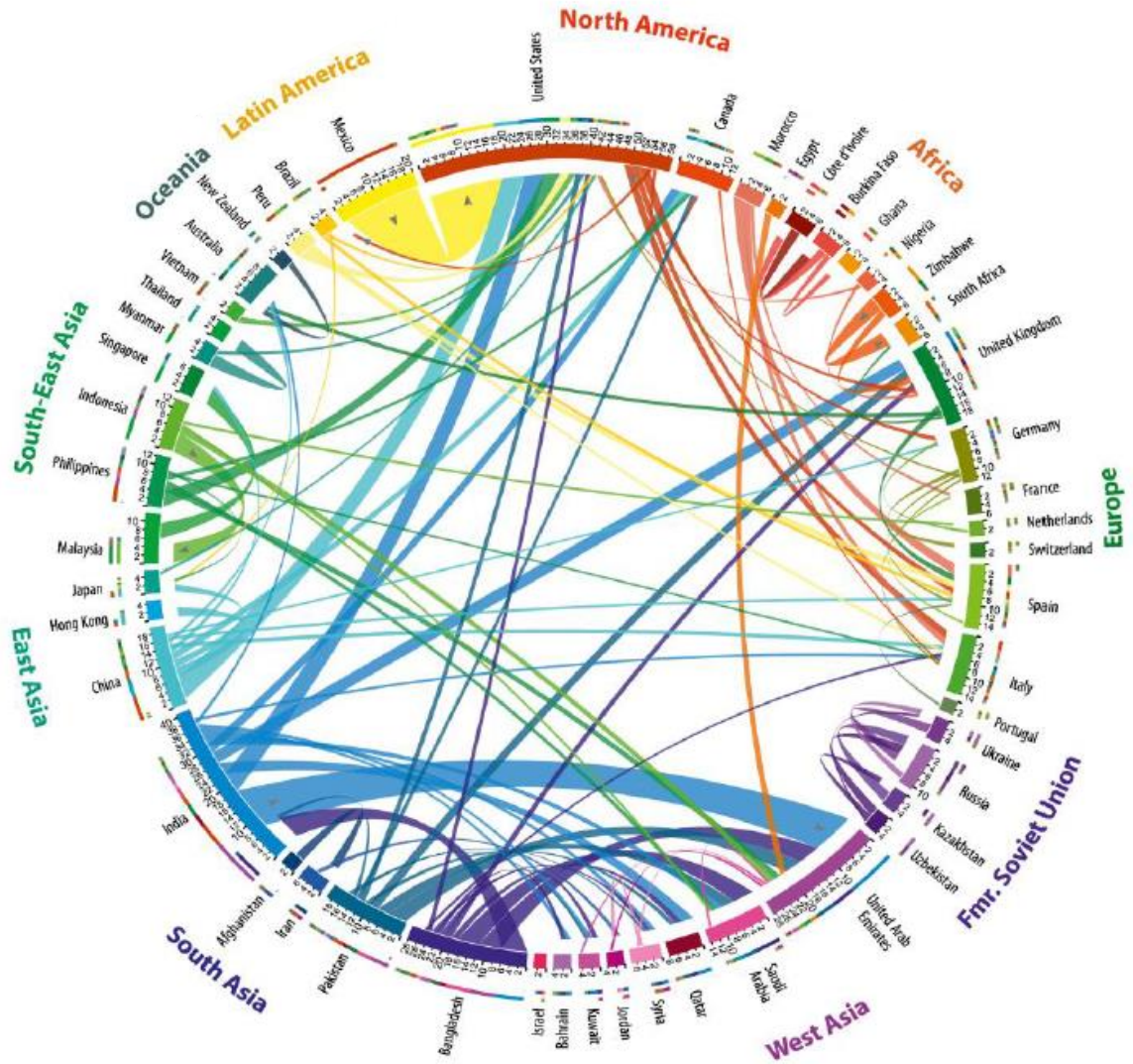
Figure 1. Distribution of chikungunya virus disease cases by country, EU/EEA, 2019

Source: Country reports from Austria, Belgium, Croatia, Czechia, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom.

https://www.ecdc.europa.eu/sites/default/files/documents/chikungunya-annual-epidemiological-report-2019.pdf; 2.Guzzetta et al. BMC Medicine (2020) 18:226 https://doi.org/10.1186/s12916-020-01674-y

Added risk: human migration and visiting friends and relatives

In addition to other travelers (business, tourists) and military



The possibility for CHIKV to cause future global outbreaks is substantial and growing…

…lack of disease awareness obscures its true public health impact[2,3]

1 Murphy et al. 2014; 2. https://www.biomedcentral.com/about/press-centre/science-press-releases/03-03-2016, accessed 9 August 2020; 3. https://www.who.int/news-room/fact-sheets/detail/chikungunya,

ECDC recognizes the CHIKV threat and need for vigilance

… The last outbreaks were in 2017 in France (n=17 cases) and in Italy (n=282 cases) [5]. **Vector-borne transmission events involving chikungunya virus within the EU/EEA are expected in areas where Aedes albopictus is established and when environmental conditions are suitable for vector activity and virus replication (roughly from early summer to mid-autumn) [6].**

Public health implications

Vigilance regarding travel-related cases of chikungunya virus disease and other Aedes-borne infections remains essential. Public health authorities in the EU/EEA should consider raising awareness among clinicians and travel clinic specialists about the risk related to such diseases, especially when and where vector-borne secondary transmission may take place [6]. The detection of an autochthonous case in the EU/EEA should trigger epidemiological and entomological investigations to assess the size of the transmission area and the potential for onward transmission, and to guide vector control measures.

Chikungunya is without a cure and limited treatment options

There is no vaccine to prevent or medicine to treat chikungunya virus[1,2]	**Treatment for symptoms can include rest, fluids, and use of analgesics and antipyretics[2]**	**Physical activities tend to aggravate the joint inflammatory process, contributing to local wear and thus to prolonging the clinical condition[3]**	**Treatment of the acute phase is limited to painkillers and nonsteroidal anti-inflammatory drugs (NSAIDs)[4]**

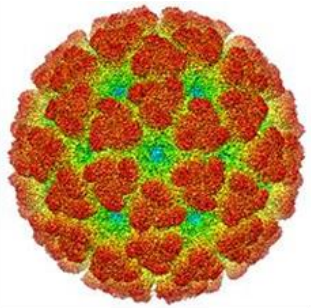
Persistent joint pain may benefit from use of[2]:

- Anti-inflammatories/inflammatory mediators: NSAIDs, corticosteroids, DMARDS, biologics
- Physical and occupational therapy
- Psychological support
- Surgery may be required – tendon release to joint replacement

1. Thiberville SD, et al. Antiviral Res; 2013;99:345-370. 2. Staples et al. CDC Yellow Book 2020, Chapter 4. 3. Da Cunha RV, Trinta, KS. Mem Inst Oswaldo Cruz, Rio de Janeiro. 2017;112:523-531. **4 Simon et al. Curr Infect Dis Rep. 2011;13:218-228.**

The high unmet medical need is a strong rationale to develop preventative strategies

Lack of disease awareness has obscured the true public health impact



Chikungunya virus

- Since its discovery in 1952, CHIKV has spread worldwide to cause large, explosive outbreaks that often overwhelm local healthcare systems
- The mosquito vector habitat continues to expand with climate change, posing increased outbreak risk in warmer areas of U.S. and Europe
- The acute phase is often severe, and chronic, debilitating symptoms associated with rheumatism can last up to ~6 years in some patients
- There are no specific drug treatments or preventive measures for chikungunya virus disease

Source: Halstead S 2015, Silva et al., 2016, WHO, CDC

Juan Carlos Jaramillo, M.D.
Chief Medical Officer

Valneva in Summary

Fully integrated specialty vaccine company focused on development and commercialization of **prophylactic vaccines for infectious diseases** with significant unmet medical need

- **Highly specialized and targeted approach to development of unique prophylactic vaccines**
- **Advanced pipeline of differentiated clinical-stage assets** designed to address large target populations
- **Highly experienced leadership team with vaccine development and regulatory expertise;** clear demonstrated ability of rapidly moving new vaccines through the clinic to commercialization
- **Highly developed, nimble and sophisticated manufacturing infrastructure**
- **Specialist sales infrastructure: Two commercialized vaccines; distribution rights for 3rd-party vaccines**

Valneva has an advanced clinical pipeline of investigational vaccine candidates and three approved products[1]

[1] As of May 6, 2022, VLA2001 has been granted emergency use authorization by the Bahraini NHRA and Conditional Marketing Authorization by the UK MHRA. [2] VLA15 received Fast Track designation from the FDA. [3] VLA1553 received Fast Track designation from the FDA, PRIME designation from the European Medicines Agency and is also potentially eligible for a U.S. Priority Review Voucher. [4] 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

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VLA1553*: single shot Chikungunya vaccine candidate

Most clinically advanced Chikungunya vaccine program Worldwide (Phase 3 completed)

1. Single shot, live attenuated[1] prophylactic vaccine targeting chikungunya virus neutralization
2. Final pivotal Phase 3 results and lot-to-lot data reported; Adolescent Phase 3 trial initiated in January 2022; FDA Pre-submission process commenced in Q2 2022
3. Granted FDA Breakthrough Therapy, Fast Track and EMA PRIME; Potentially eligible for FDA Priority Review Voucher
4. Up to $23.4 million awarded to Valneva for R&D by CEPI; Partnership with Instituto Butantan for LMICs
5. Excellent fit with existing commercial and manufacturing capabilities
6. Global market, including endemic regions, estimated to exceed $500 million by 2032[2]

Note: Photo credit: James Gathany. **1** CHIKV LR2006-OPY1 infectious clone was attenuated by deleting large part of gene coding nsP3 (alphavirus-replicase); **2** VacZineAnalytics Chikungunya virus vaccines Global demand analysis. February 2020.

*VLA1553 is an investigational chikungunya vaccine candidate and is not approved for use in the United States or any other jurisdiction

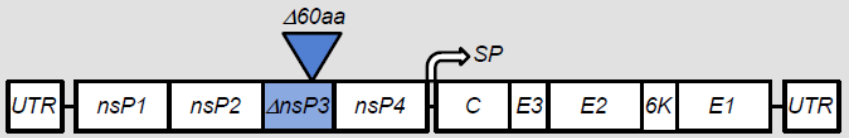
VLA1553: live-attenuated design

Attenuation via genetic deletion

CHIKV Δ5nsP3 (VLA1553)

- Based on La Réunion strain of East Central South African genotype (Indian Ocean lineage)
- Cross-protective immunity against other CHIKV genotypes (e.g. Asian isolate)

Vaccine construct



Attenuation

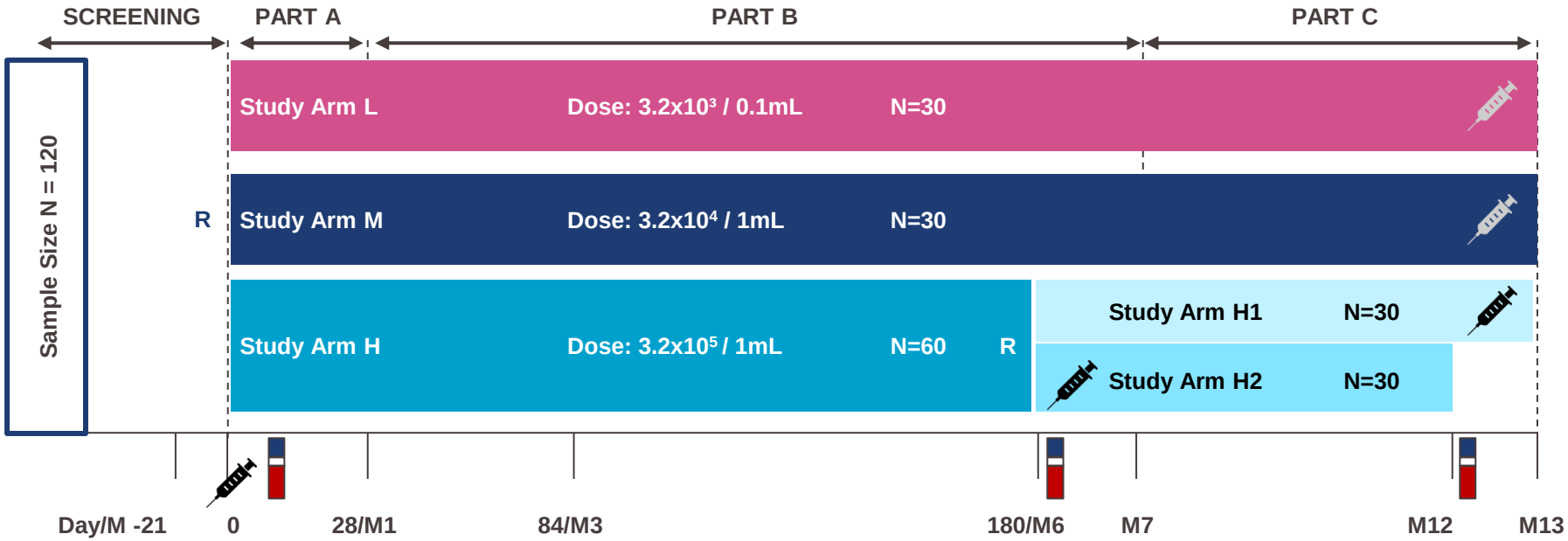
- **60 aa deletion in gene encoding non-structural protein nsP3 (viral replicase complex)**
  - Results in reduced replication as compared to CHIKV parent clone
  - No change of deletion detectable after up to 20 passages on Vero cells
  - Reversion to wild-type is impossible

Hallengärd *et al*., 2013. J Virol 88(5):2858-66

*VLA1553 is an investigational chikungunya vaccine candidate and is not approved for use in the United States or any other jurisdiction

Phase 1 trial led to direct progression into Phase 3

- Observer-blinded, randomized, multicenter, dose escalation study
- Study Population: 120 healthy volunteers aged 18 to 45 years
- Dosage: low (L); medium (M); high (H)
- Immunization route: intramuscular



Safety including viremia on Days 0/3/7/14 post-vaccination

Re-vaccination at Month 6 and12 with the highest dose (homologous viral challenge)

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Summary of Phase 1 clinical data

Results published in *The Lancet Infectious Disease*[1]

Safety Results

- No safety concerns identified by independent data safety monitoring board
- Very few localized adverse events
- Systemic adverse events included short-term fever, headache and fatigue, muscle pain
- No vaccine related Serious Adverse Events or Adverse Events of Special Interest

Profile supported Phase 3 progression with medium dose

Immunogenicity Results

- 100% seroconversion rate achieved at Day 14 after a single vaccination in all dose groups; fully sustained at 100% by Month 12
- A single vaccination of VLA1553 was sufficient to induce sustaining, high-titer, neutralizing antibodies at all dose levels one year after priming
- Upon Re-Vaccination ("Challenge"):
  - — No anamnestic response
  - — No vaccine-strain viremia

Highly immunogenic after single vaccination

1 Wressnigg et al. 2020; Lancet Infect Dis 20:1193-1203

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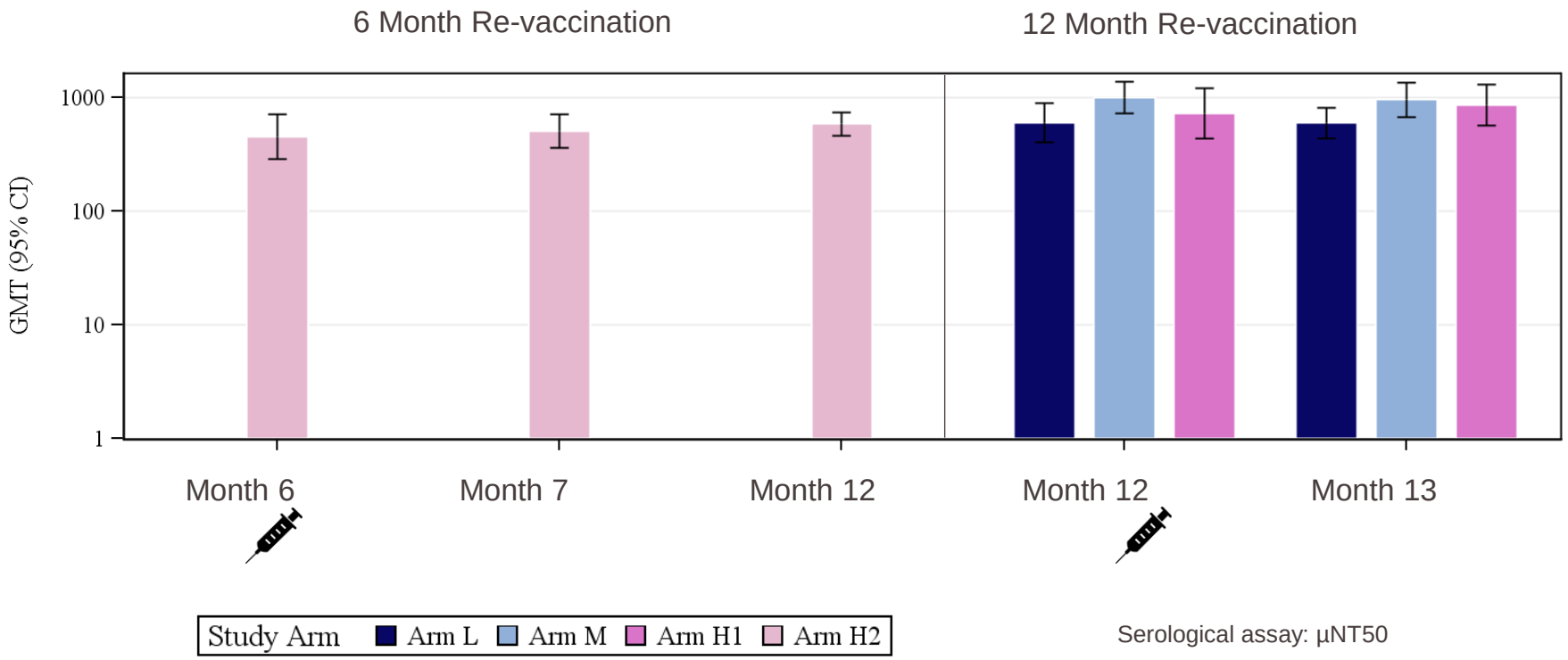
First indications of potentially sterilizing immunity after single-shot vaccination[1]

Absence of an anamnestic immune response following re-vaccination “challenge”

CHIKV-specific neutralizing antibodies do not increase after re-vaccination (i.e. homologous viral challenge)[2]



1 Sterilizing immunity = immune response where neutralizing antibodies are able to bind and prevent free virus from infecting cells in the body; 2 Wressnigg et al. 2020; Lancet Infect Dis 20:1193-1203

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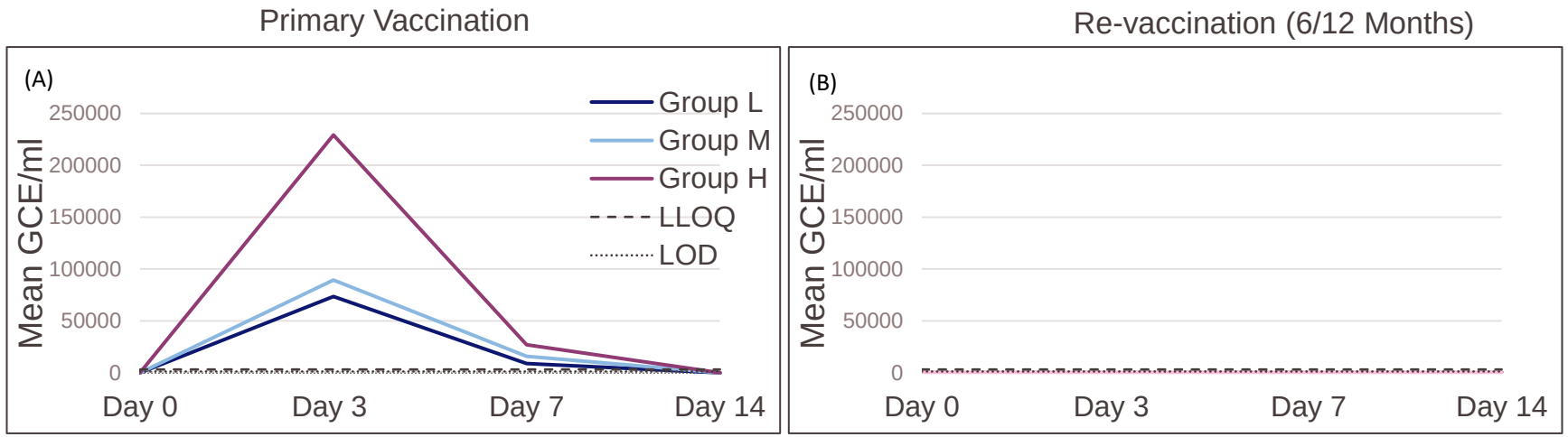
First indications of potentially sterilizing immunity after single-shot vaccination[1]

Absence of viremia following re-vaccination “challenge”

Short-lived viremia observed after a single dose is completely abolished following re-vaccination



Mean Genome Copy Equivalents (GCE) / mL
Limit of Detection (LOD): 1087 GCE/mL,
Lower Limit of Quantification (LLOQ): 3261 GCE/mL.
Time points with no available results in the treatment group are plotted at 0

Re-vaccination results reflect observations from prior studies with non-human primates (NHPs)[2]

1 Wressnigg et al. 2020; Lancet Infect Dis 20:1193-1203; **2** Roques *et al.* 2017. JCI Insight.2(6):e83527 (vaccinated NHPs challenged with wild type CHIKV)

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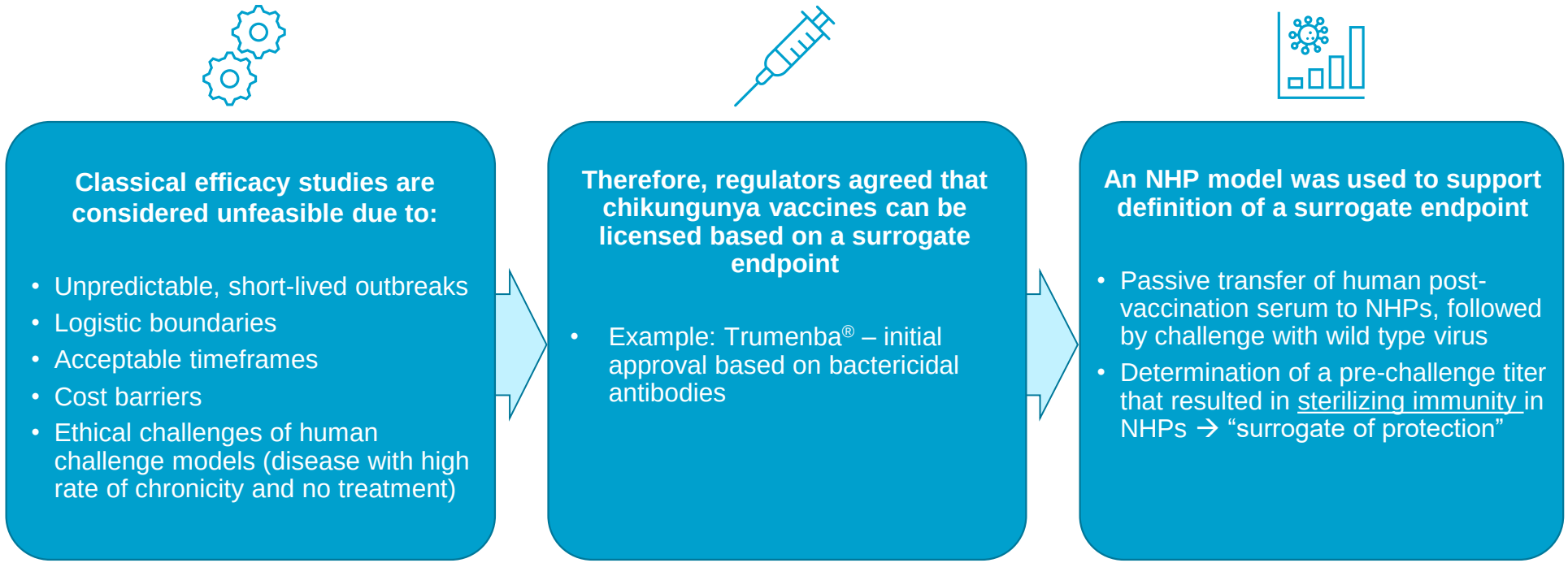
Defining a surrogate of protection against chikungunya virus[1]

Establishing a Phase 3 surrogate endpoint that could support FDA accelerated approval



The Result:

- Human Phase 1 sera protected NHPs in passive transfer model
- Surrogate titer established that conferred sterilizing immunity in NHPs; further supported by sero-epidemiological study[2]
- Surrogate neutralizing antibody titer agreed upon with FDA as Phase 3 endpoint under the accelerated approval pathway

1 A neutralizing antibody titer that resulted in sterilizing immunity against CHIKV in non-human primates; 2 Yoon et al. 2015

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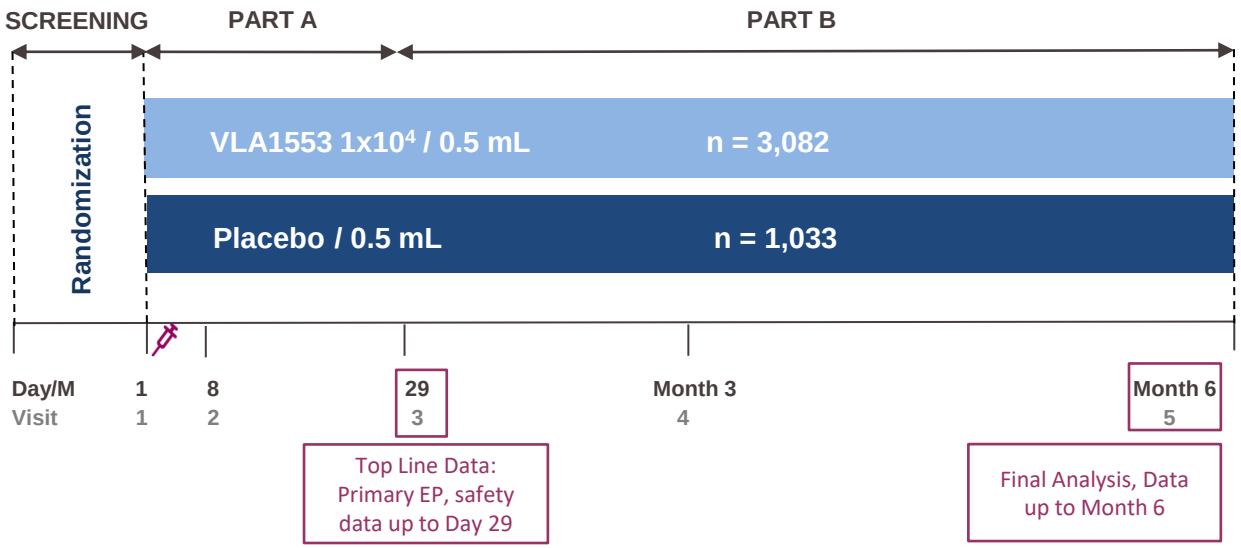
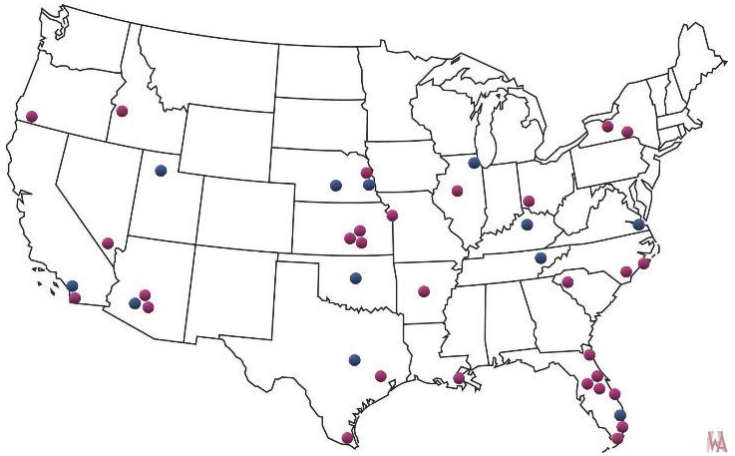
Pivotal trial design: VLA1553-301

Multicenter, randomized, placebo-controlled double-blind trial in 4,115 adults

- Primary Endpoint: Proportion of participants with a seroprotective CHIKV neutralizing antibody level*
- Immunogenicity subset: first 500 participants enrolled at selected sites
- Solicited adverse events captured for 10 days following vaccination



n = number of participants in the safety population



Blue = Immunogenicity sites
Purple = Non-Immunogenicity sites
(i.e. not enrolling participants within the immunogenicity subset)

* Determined by µPRNT (Micro Plaque Reduction Neutralization Test) for baseline negative subjects 28 days post-vaccination. Seroprotective = having achieved the specific level of neutralizing antibodies agreed with FDA as a surrogate of protection based on non-human primate studies

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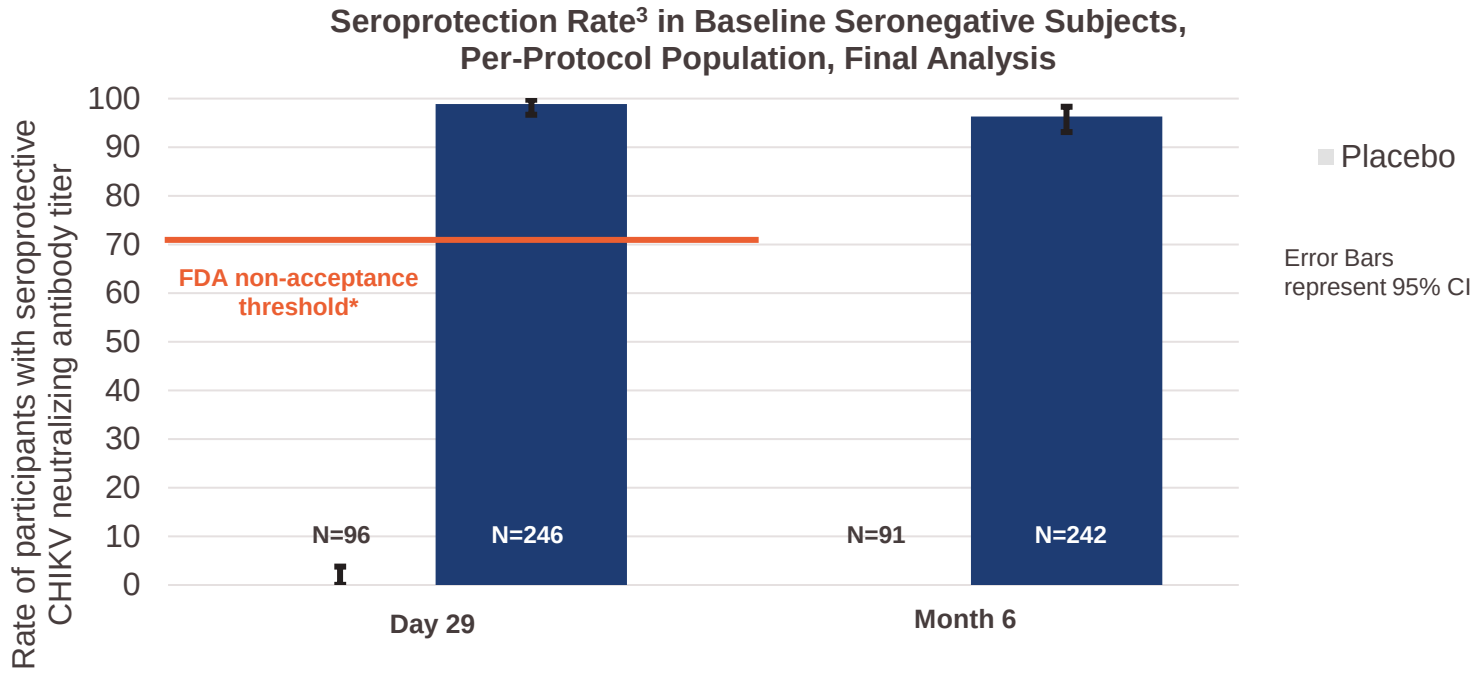
VLA1553 Met Primary Endpoint in Phase 3

Induced seroprotection[1] in 98.9% of participants; exceeding FDA threshold[2]



- Seroprotection rate (SPR) was 98.9% [95% CI: 96.7-99.8], vs placebo 0% [95%CI 0.0 – 3.8]
- High SPR rate was maintained after six months at 96.3%
- Robust data, confirmed in older adult population (≥65)
- VLA1553 was generally well tolerated among the 3,082 participants evaluated for safety

1 Protective CHIKV neutralizing antibody levels; 2 The lower bound of the 95% Confidence Interval for the SPR at Day 29 in the VLA1553 group needed to exceed 70% Neutralizing antibody titers determined using a µPRNT$_{50}$ assay; 3 The proportion of participants with a seroprotective CHIKV neutralizing antibody level, determined by µPRNT (Micro Plaque Reduction Neutralization Test) for baseline negative subjects 28 days post-vaccination

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Key conclusions from the pivotal study

Immunogenicity Results

- VLA1553-301 met its primary endpoint
- Seroprotective[1] levels of antibodies in 98.9% of participants after a single vaccination
- Immunogenicity profile maintained. GMT stayed well above the seroprotective[1] level of antibodies in 96.3% of participants at Day 180
- Vaccine also confirmed to be immunogenic in older adults (≥ 65 years), who achieved similar seroprotection rates and neutralizing antibody titers as younger adults (<65 years)

Safety Results

- VLA1553 was generally well tolerated among the 3,082 subjects evaluated for safety
- An independent Data Safety Monitoring Board continuously monitored the study and identified no safety concerns
- The majority of solicited adverse events were mild or moderate and resolved within three days. 2.0% of study participants reported severe solicited adverse events, most commonly fever.
- Approximately 50% of study participants experienced solicited systemic adverse events, most commonly headache, fatigue and myalgia

1 A seroprotective CHIKV neutralizing antibody level, determined by µPRNT (Micro Plaque Reduction Neutralization Test) for baseline negative subjects 28 days post-vaccination

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VLA1553 partnerships and non-dilutive funding

Collaboration with CEPI and Instituto Butantan to enhance accessibility

July 2019: Coalition for Epidemic Preparedness Innovations (CEPI) funding

- Granted up to $23.4 million for late-stage development of a single-dose chikungunya vaccine, with support from the European Union's Horizon 2020 program

January 2021: Instituto Butantan, agreement for the development, manufacturing and marketing of VLA1553 in Low and Middle Income Countries (LMICs)

- Valneva will transfer its chikungunya vaccine technology to Instituto Butantan
- In addition to providing commercial access to LMICs, Instituto Butantan will provide certain clinical and Phase 4 studies that Valneva will use to meet additional regulatory requirements in developed markets

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VLA1553 development outlook

First and only program to meet its Phase 3 trial endpoint worldwide

Completed pivotal clinical trials

- Met all Phase 3 immunogenicity and safety endpoints
- Results confirmed by final lot-to-lot consistency trial results (VLA1553-302)

Additional studies initiated

- Antibody persistence follow-up trial (VLA1553-303) fully enrolled: 361 volunteers from the VLA1553-301 trial will be followed annually for at least five years
- Adolescent Phase 3 trial initiated in January 2022 to support potential label expansion and licensure in Brazil, funded by CEPI

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VLA1553 regulatory outlook

Pre-submission process with FDA commenced in Q2 2022

- Expect to start biologics license application (BLA) submission in H2 2022

The sponsor of the first chikungunya vaccine approved in the U.S. will be eligible to receive a Priority Review Voucher[1]

- Can potentially be monetized; PRVs recently selling for ~$110 million[2]

FDA regulatory designations	EMA regulatory designation
▪ Fast Track (2018) ▪ Breakthrough Therapy (2021)	▪ PRIority MEdicine (PRIME) (2020)

1 https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/tropical-disease-priority-review-voucher-program; 2 https://investors.biomarin.com/2022-02-09-BioMarin-Sells-Priority-Review-Voucher-for-110-Million, https://bridgebio.com/news/bridgebio-pharma-sells-rare-pediatric-disease-priority-review-voucher-for-110-million-and-defers-principal-payment-on-senior-debt-by-two-years/

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Chikungunya vaccine market and expected target populations

Global market estimated to exceed $500 million by 2032[1]

Target market segments include:

Non-endemic areas: e.g. U.S., EU, CA	Endemic use
▪ Travelers ▪ Military ▪ Outbreak preparedness	▪ LMICs (Instituto Butantan / CEPI) ▪ Key non-LMIC endemic areas

Excellent fit with Valneva's global manufacturing and commercial infrastructure

- FDA-approved vaccine[2] virus manufacturing facility in Livingston, Scotland
- Experienced commercial team with deep expertise in the travel vaccine market

1 includes endemic regions; 2 For production of Valneva's Japanese Encephalitis Virus Vaccine IXIARO®

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VLA1553*: single shot Chikungunya vaccine candidate

Most clinically advanced Chikungunya vaccine program Worldwide (Phase 3 completed)

1. Single shot, live attenuated[1] prophylactic vaccine targeting chikungunya virus neutralization
2. Final pivotal Phase 3 results and lot-to-lot data reported; Adolescent Phase 3 trial initiated in January 2022; FDA Pre-submission process commenced in Q2 2022
3. Granted FDA Breakthrough Therapy, Fast Track and EMA PRIME; Potentially eligible for FDA Priority Review Voucher
4. Up to $23.4 million awarded to Valneva for R&D by CEPI; Partnership with Instituto Butantan for LMICs
5. Excellent fit with existing commercial and manufacturing capabilities
6. Global market, including endemic regions, estimated to exceed $500 million by 2032[2]

Note: Photo credit: James Gathany. **1** CHIKV LR2006-OPY1 infectious clone was attenuated by deleting large part of gene coding nsP3 (alphavirus-replicase); **2** VacZineAnalytics Chikungunya virus vaccines Global demand analysis. February 2020.

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Q&A Session