valneva

R&D INVESTOR DAY 2019

NEW YORK, JULY 9

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Today's Speakers

Thomas LINGELBACH

Chief Executive Officer
Valneva

David LAWRENCE

Chief Financial Officer
Valneva

Wolfgang BENDER, MD, PhD, MPH, MHA, DTMP

Chief Medical Officer
Valneva

Stanley A. PLOTKIN, MD

Emeritus Professor,
Wistar Institute
University of Pennsylvania

Agenda

1. **Introduction** – Thomas Lingelbach
2. **Company Strategy** – David Lawrence
3. **Lyme disease and VLA15**
   - › Lyme disease – Dr. Stanley A. Plotkin
   - › Valneva's vaccine candidate, VLA15 – Thomas Lingelbach
4. **Chikungunya and VLA1553**
   - › Chikungunya – Dr. Stanley A. Plotkin
   - › Valneva's vaccine candidate, VLA1553 – Dr. Wolfgang Bender
5. **Q&A**
6. **Closing Remarks**
7. **Appendix**

INTRODUCTION

THOMAS LINGELBACH
CHIEF EXECUTIVE OFFICER

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

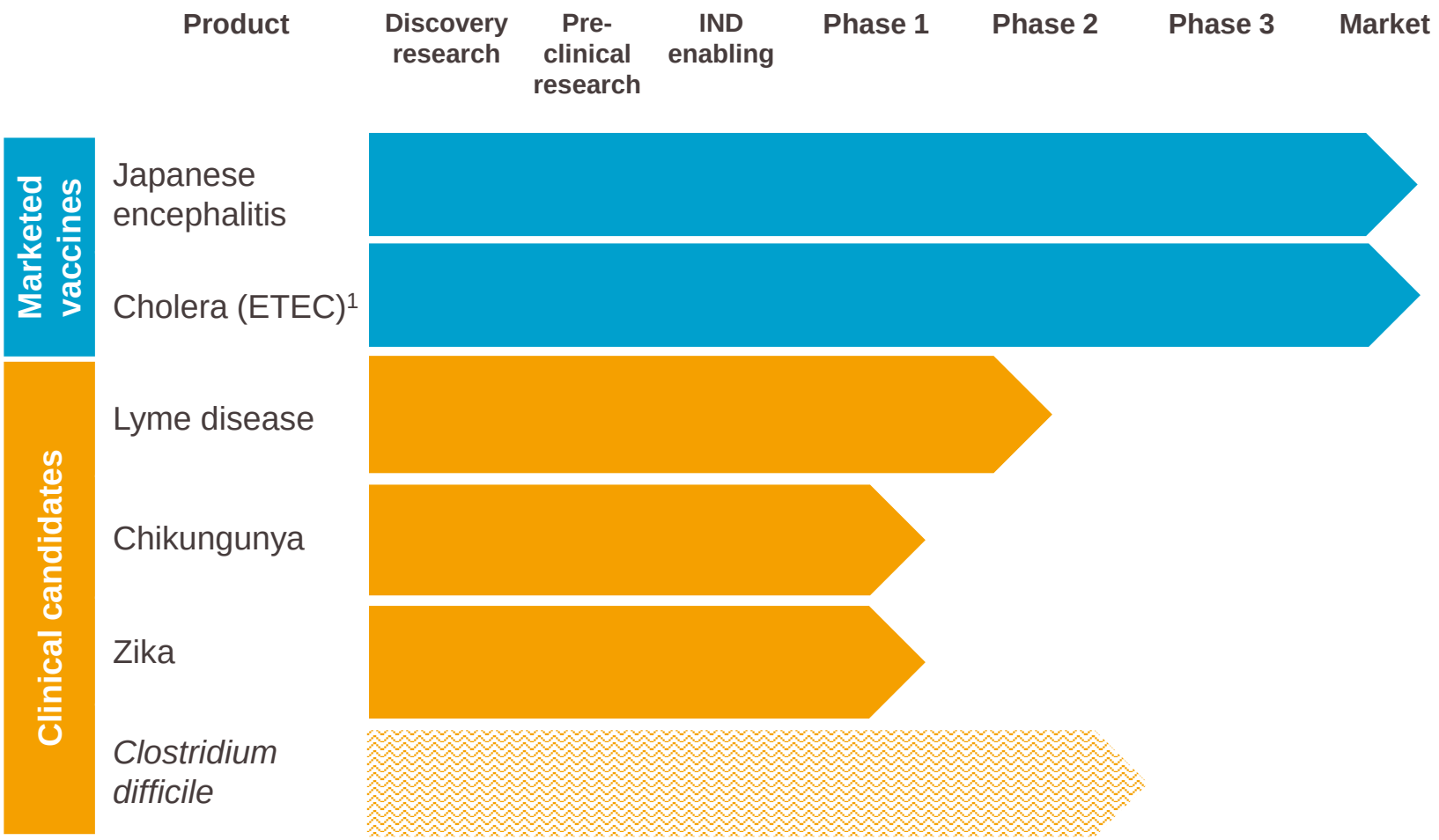
Cash: €81.7m (as of Dec. 31, 2018)

Ticker: EPA – VLA

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

Valneva's 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

COMPANY STRATEGY

DAVID LAWRENCE
CHIEF FINANCIAL OFFICER

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

Capital Formation Strategy

Access Best Capital Market to Fund Lyme Vaccine Development

Step 1 - Strengthen Shareholder Base; add Blue Chip US Investors

→ **How?** PIPE (€50m September 2018)

Step 2 – Raise R&D Funding

→ **How?** Potential NASDAQ Listing (>€100m)

Key Enablers –

+Lyme:

- Execute development plan
- Report Phase II data
- Ongoing FDA dialogue

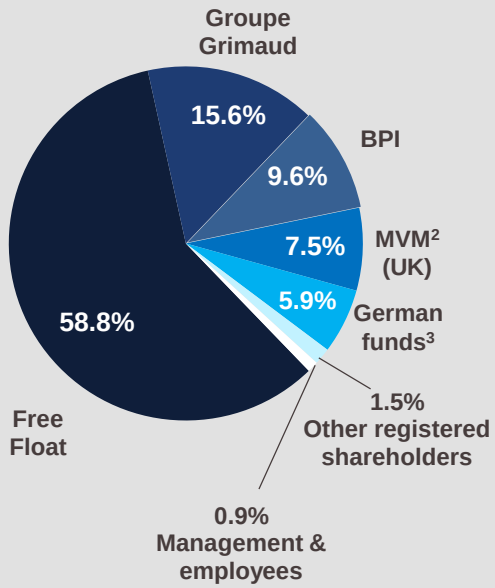
+Business:

- Prepare for IPO
- SOX analysis, Delist Vienna, etc.
- Deliver on earnings guidance
- Regain control of R&D

VLA continuously strengthening its institutional shareholder base with blue-chip healthcare investors

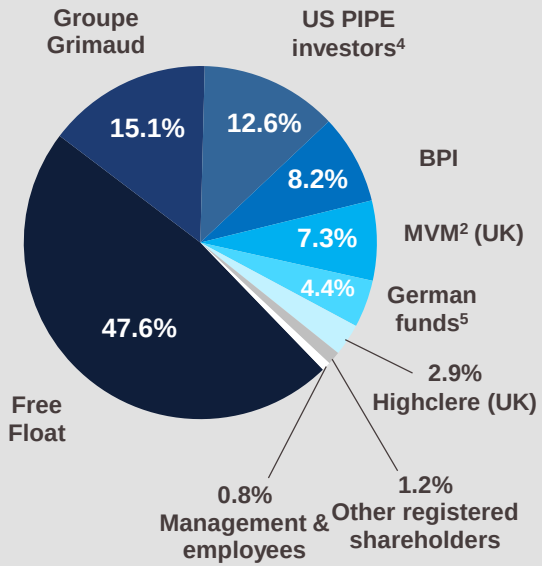
January 2018

+ Number of ordinary shares:77.6m
+ Shareholder structure[1]:



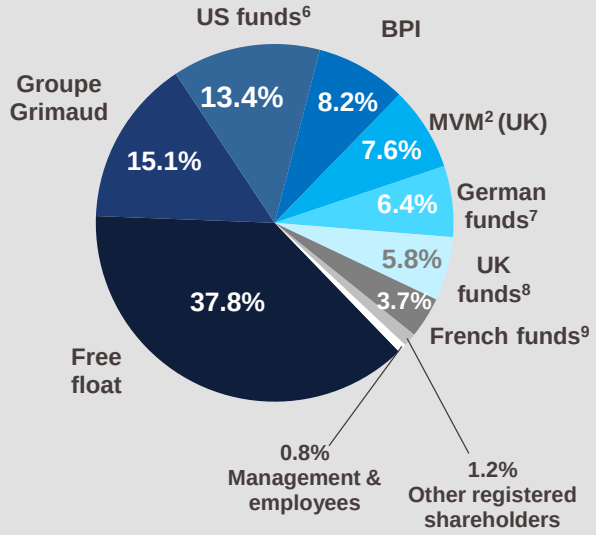
October 2018

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



May 2019

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



1 Estimates based on ordinary share capital; **2** Funds managed by MVM Life Science Partners; **3** Combined positions of 10 Germany-based funds managed by Apus Capitral, Apo Asset Management, Lupus alpha, CD-Ventures, SK Vermögensverwaltung, Hauck & Aufhäuser, and others; **4** Combined positions of U.S.-based participants in Valneva's September 2018 private placement; **5** Combined positions of Apus Capital, Lupus Alpha, Apo Asset Management, CD-Ventures, and Medical Strategy; **6** 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; **7** Combined positions of DWS Investment, Apus Capital, Apo Asset Management, Lupus alpha, Medical Strategy, Hauck & Aufhäuser, CD-Ventures, and Deutsche Apotheker; **8** Combined positions of Highclere, AXA Investment Managers Ltd., and Abingworth LLP; **9** Combined positions of CDC Entreprises Valeurs Moyennes, AXA Paris, La Banque Postale AM, AG2R, PRO BTP, Chaussier Gestion, and Mandarine Gestion.

LYME DISEASE

STANLEY A. PLOTKIN, MD
Professor Emeritus
Wistar Institute
University of Pennsylvania

Prospects for a New (or old) Vaccine Against Lyme Disease

by

Stanley A. Plotkin

I have no financial interest
in new Lyme Disease
or Chikungunya vaccines
and receive no honoraria
from Valneva.

Case History of Alec P. (1)

- 35 yr. old living in Chester Co., PA
- Walks his dog
- Developed an erythematous rash behind knee
- Physician called it cellulitis, treated it locally

Case History of Alec P. (2)

- Out with his dog one day, Alec collapsed and was unresponsive
- Neighbor called 911
- Med-tech measured heart rate of 35/minute
- Experienced cardiologist at local hospital suspected Lyme
- Put in cardiac pacemaker and started intravenous cephalosporin

Lyme Disease

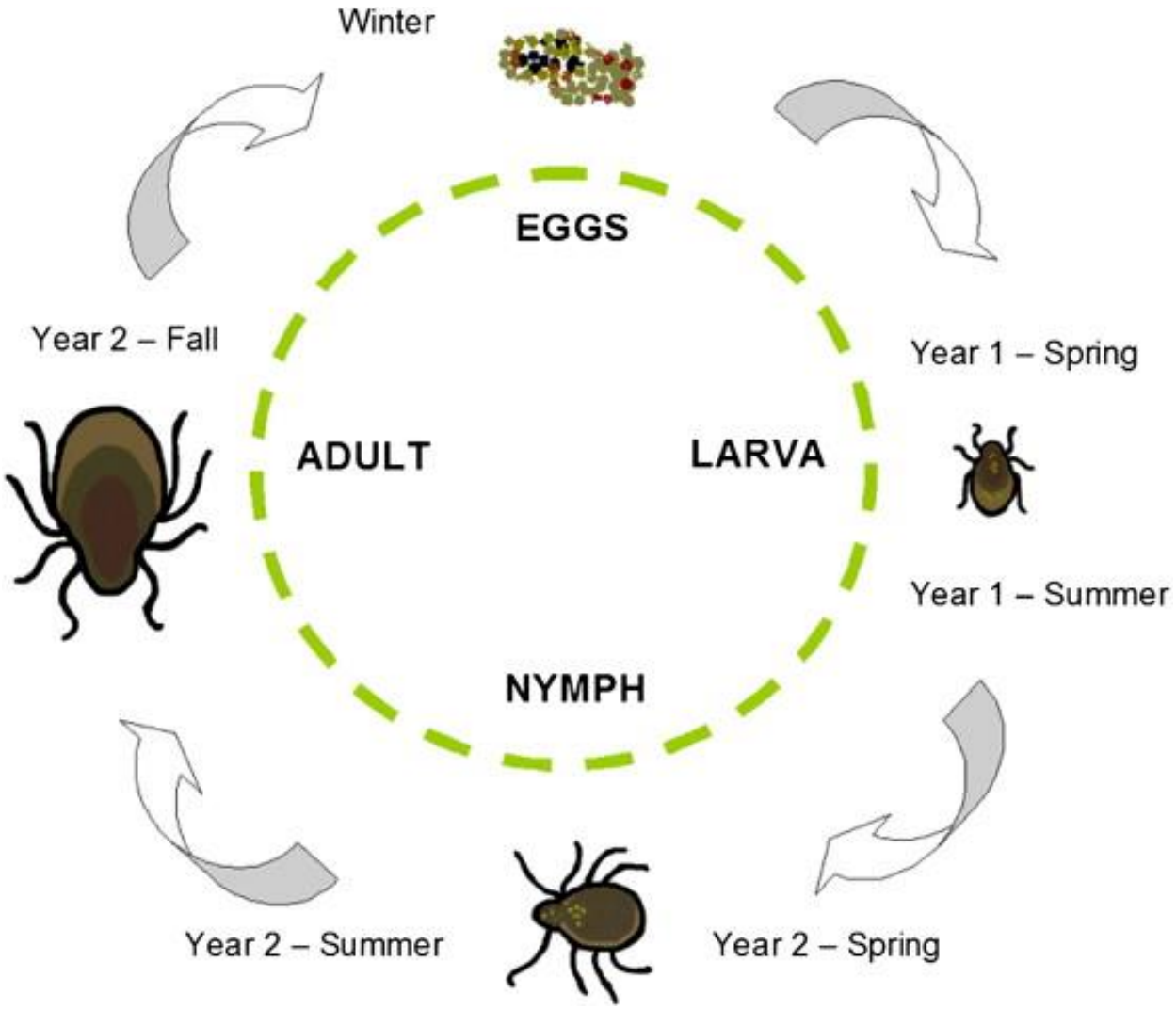
- Tickborne disease – *Ixodes scapularis* predominant in Eastern U.S. *Ixodes ricinus* in Europe
- Caused by *Borrelia burgdorferii* spirochete – resides in gut of tick, migrates to salivary gland and enters host during tick feeding
- Early symptoms – fever, headache, fatigue, erythema migrans rash (70-80%), arthralgia, myalgia
- 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)

Lyme Borrelia

Skin Lesions Caused by Lyme

Fig 1. Life cycle of *Ixodes* ticks. Illustration courtesy of Chinmoy Bhate, MD.



J Am Acad Dermatol. 2011 Apr;64(4):619-36; quiz 637-8. doi: 10.1016/j.jaad.2010.03.046.

Lyme disease: Part I. Advances and perspectives.

Bhate C[1], Schwartz RA.

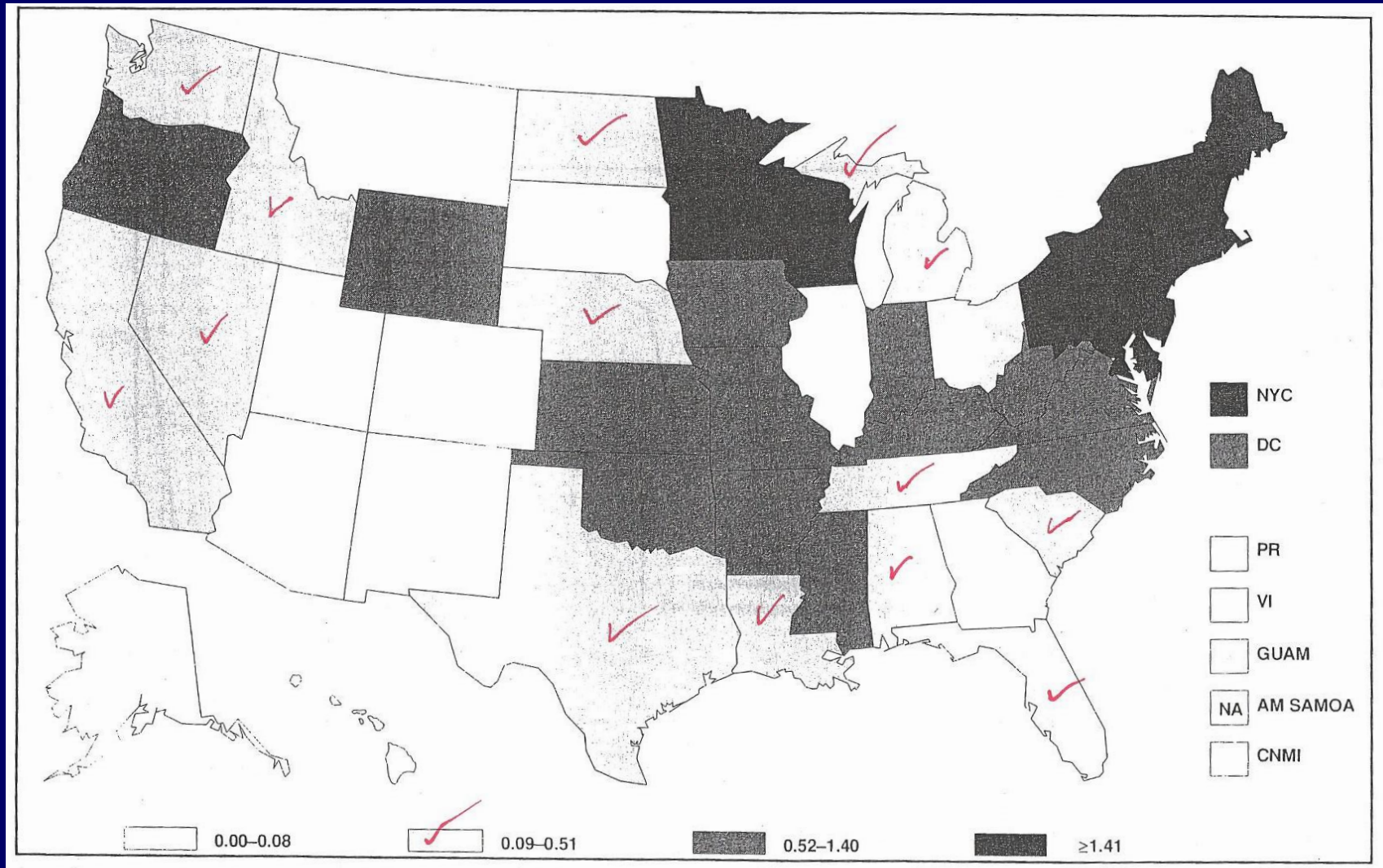
Advice to Avoid Lyme Disease

(Philadelphia Inquirer)

- Avoid wooded areas with high grass
- Walk on trails only
- Use DEET repellents
- Treat clothing with permethrin
- Shower within two hours after walk
- Full body tick check
- Check pets for ticks
- Dry clothes in high heat

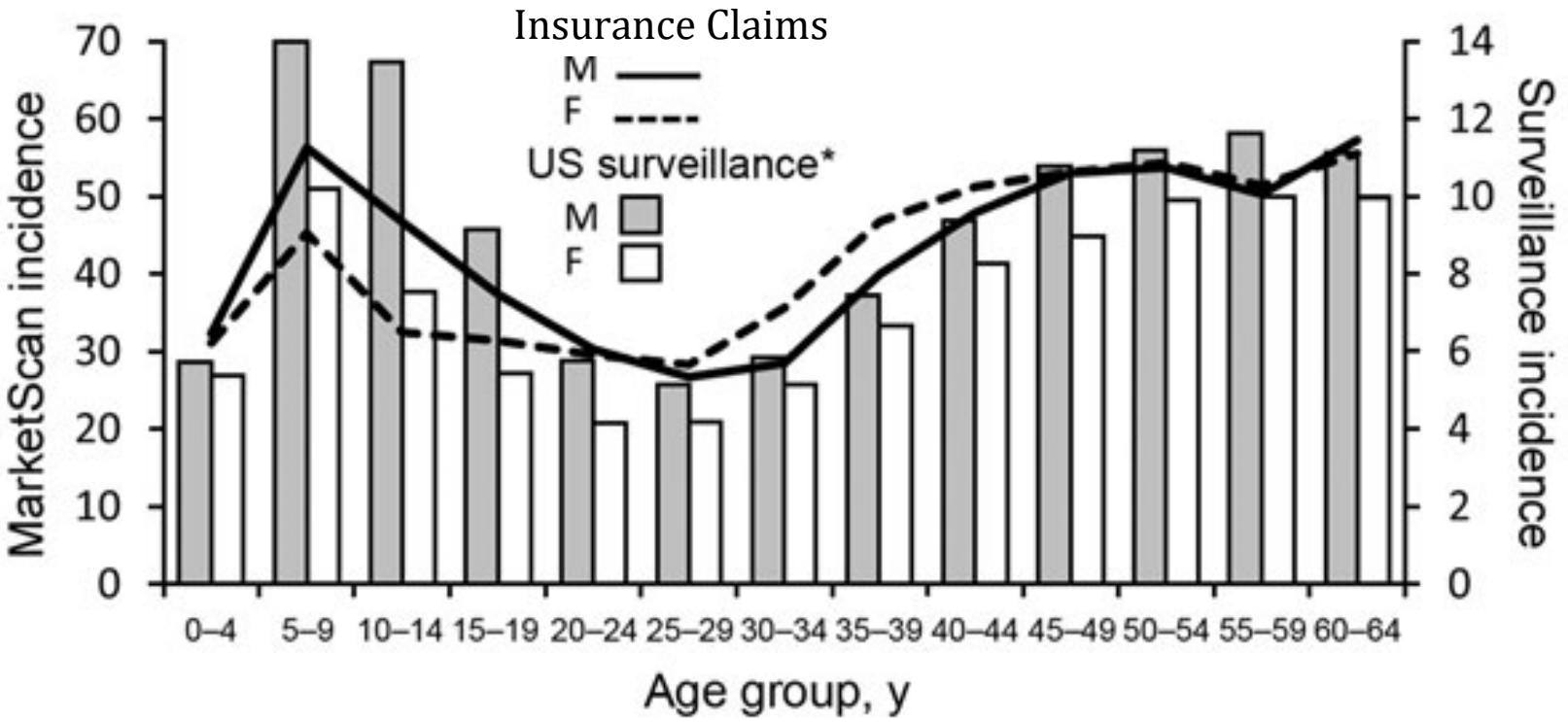
Lyme Disease

Reported cases, per 100,000 population, United States and territories, 1996



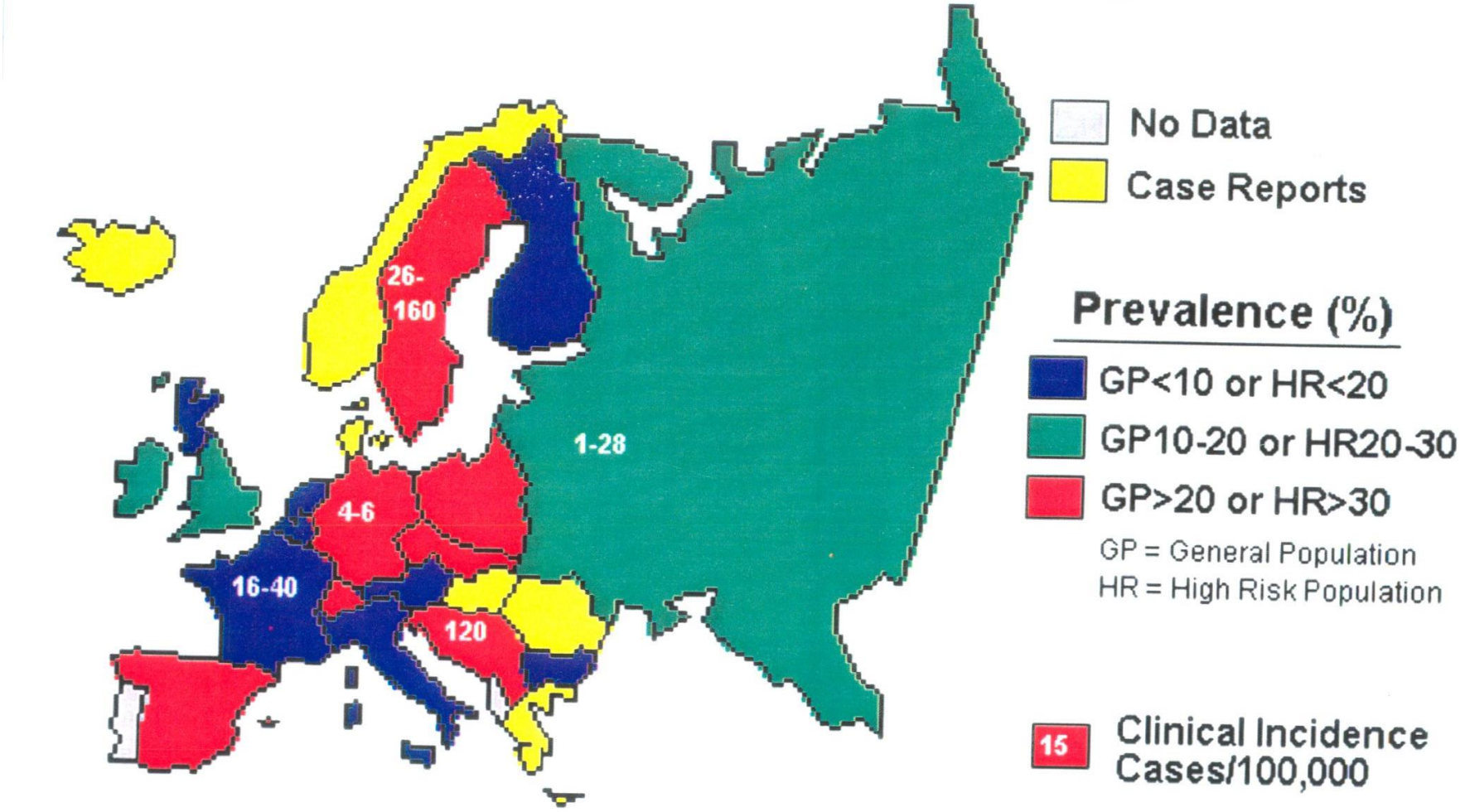
In 1996, a total of 45 states and the District of Columbia reported 16,455 cases to CDC. This was the highest number reported since national surveillance began in 1982.

Age Distribution of Lyme in the US



Comparison of trends in the age and sex distribution of persons with Lyme disease in MarketScan with US surveillance, 2005–2010. Incidence is per 100,000 persons. Age distribution of persons with Lyme disease in MarketScan did not differ from those reported through US surveillance (male patients: χ^2 test, p = 0.57; female patients: χ^2 test, p = 0.43). *US 2010 Census population estimates were used as the denominator for surveillance incidence calculations.

Lyme Disease in Europe: Current State of Knowledge



Borrelia Strains in U.S. and Europe

US	Europe
burgdorferii	burgdorferii (ST1)
mayoni	afzelii (ST2)
	garinii (ST3,5,6)
	bavariensis (ST4)

We Should Have a Lyme Disease Vaccine Because:

- Infection is prevalent in the US (300,000 per year) and in Europe (200,000 per year)
- Vaccination with OspA was proven to work in the 1990s
- Other preventive measures have not been shown to work on a public health scale

Anti-OspA Protective Response

Step 1	Step 2	Step 3	Step 4
Vaccine, when injected, elicits high levels of anti-OspA antibodies	Tick attaches to vaccinated human and begins blood meal (24- to 48-hour attachment needed to transmit *B. burgdorferi)*	Anti-OspA antibodies from vaccinee enter tick	Antibodies kill *B. burgdorferi* in midgut, preventing transmission to human host

Lymerix Efficacy in the Phase III Trial

Disease type	Efficacy, %	
	Year 1 (2 doses)	Year 2 (3 doses)
Symptomatic	49	76
Asymptomatic	83	100
Data from Steere et al, NEJM, 1998	57	80

NOTE. Data are from [9].

OspA antibodies neutralize Borrelia in the tick

Pediatric Response to Lymerix

Age	GMT	Titer ≥ 1400 E.U./ml
4-16 y	29,650	100%
15-18	20,722	100%

Sikand et al, Pediatrics, 2001

Overview of Lyme Vaccine History

- **LYMErix** was released in December 1998
  Permissive recommendation for use of vaccine in persons 15-70 years of age who lived or worked in *B. burgdorferi*-infected woody and grassy areas.

- It was voluntarily withdrawn by GSK in February 2002.

- First time in the modern era that an FDA-licensed vaccine in the US was withdrawn because of low public demand and class-action lawsuits.

Mistakes That Were Made with Lymerix

By GSK:

- Advertising directly to public, not physicians
- Launching pediatric study too late
- Not engaging patient groups

By CDC:

- Assigning vaccine recommendations to Fort Collins people
- Making weak recommendations: "should be considered"

By Others:

- Weak support by opinion leaders
- Opposition by patient groups
- Class-action lawsuit

Safety of OspA Vaccines

- In a hamster model, vaccination followed by infection led to arthritis; however, in human trials, this did not occur.
- Infection in vaccinated dogs or humans does not lead to arthritis.
- FDA Panel concluded no evidence for association between vaccine and arthritis.
- Later, FDA retrospective review of all safety data concluded no safety signal.

(Lathrop et al, Vaccine 2002)

Veterinary Vaccines

Vaccine	Company/ country	Species	Antigen	Adjuvant	Abbreviation
Merilym	Merial, Germany	B. burgdorferi s.s.	Lysate	Yes	V1-Bbss-lys-adj
LymeVax	Fort Dodge, USA	B. burgdorferi s.s.	Lysate	Yes	V2-Bbss-lys-adj
ProLyme	Intervet,USA	B. burgdorferi s.s.	rOspA	Yes	V3-Bbss-rOspA-adj
Recombitch Lyme	Merial, USA	B. burgdorferi s.s.	rOspA	No	V4-Bbss-rOspA
Biocan B	Bioveta Czech Rep.	B. afzilii B. garini	Lysate	Yes	V5-BgBa-lys-adj

In US, over 4 million doses annually

Borrelia burgdorferi peptidoglycan is a persistent antigen in patients with Lyme arthritis

Brandon L. Jutras, Robert B. Lochhead, Zachary A. Kloos, Jacob Biboy, Klemen Strle, Carmen J. Booth, Sander K. Govers, Joe Gray, Peter Schumann, Waldemar Vollmer, Linda K. Bockenstedt, Allen C. Steere, and Christine Jacobs-Wagner

PNAS first published June 17, 2019 https://doi-org.proxy.library.upenn.edu/10.1073/pnas.1904170116

A protein from Lyme disease persists in infected patients even after antibiotic treatment, inducing cytokines that could induce chronic arthritis.

THIS MEANS THAT ANTIBIOTICS DO NOT NECESSARILY PREVENT CHRONIC ARTHRITIS, AND A VACCINE IS THE ONLY WAY TO PREVENT CHRONIC LYME ARTHRITIS!

LA-2 *Borrelia* Antigens Needed in a Vaccine

ST	Strain
1	burgdorferii
2	afzelii
3	garinii
4	bavariensis
5	garinii
6	garinii

The Way Forward for a New Vaccine

- Definition of Correlate of Protection
- Tests of adjuvants to prolong antibody
- Early studies in children
- Incorporation of Lyme vaccine in VFC

VLA15

Lyme disease increasingly common in the US and Europe

There is a prospect for a new (or old) vaccine against it

Lyme disease
(Lyme borreliosis)

- Tickborne disease (Vector-Ixodes ticks)
- Caused by *Borrelia burgdorferi s.l.* 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 symptoms[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

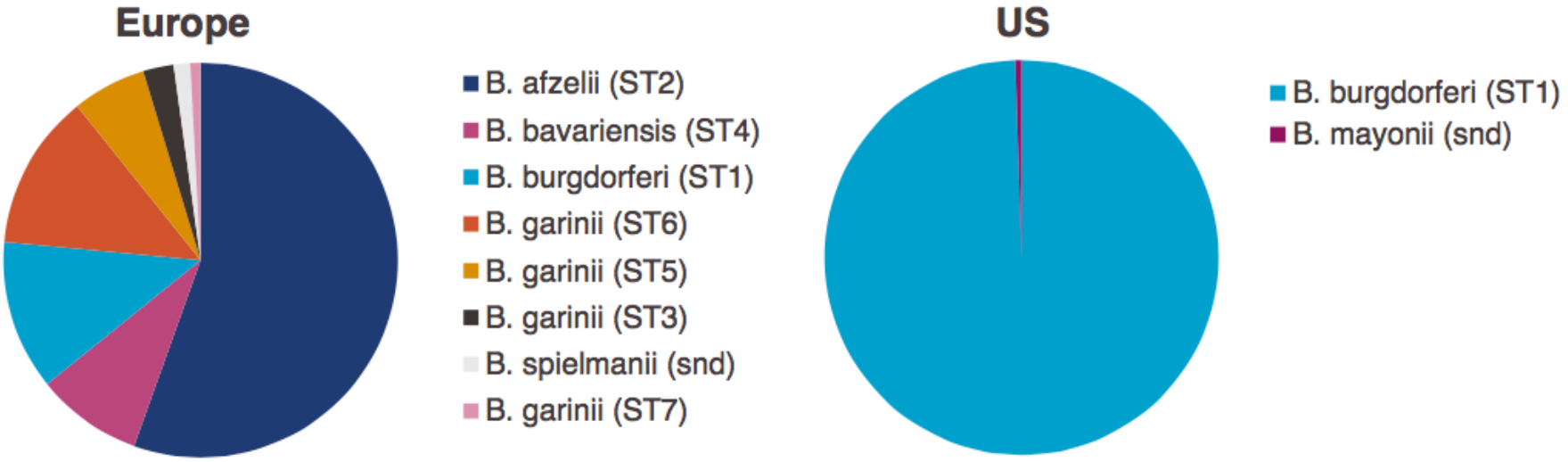
  Treatment: antibiotics (doxycycline, amoxicillin, or cefuroxime axetil)

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

Lyme disease – Epidemiology

Prevalent Strains in the US & Europe

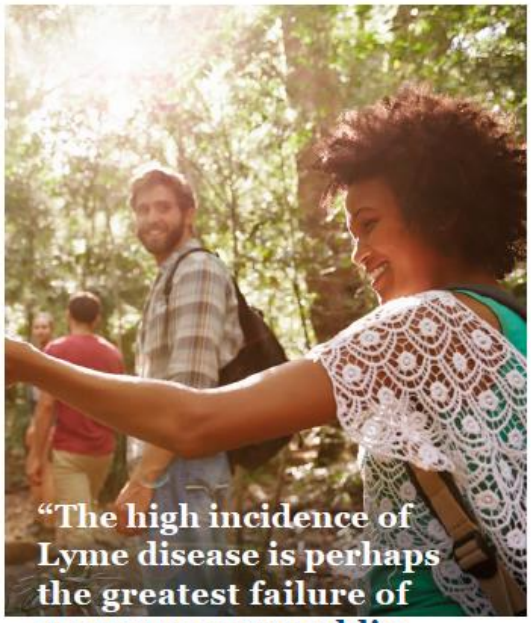
- **Analysis of US CDC statistics** and 595 European* (16 countries) LB-patient isolates**
  - US: LB is caused almost exclusively by *B. burgdorferi* s.s. (ST1)
    - The novel species *B. mayonii* rarely causes LB in US*** (prevalence and incidence to be watched)
  - Europe: *B. afzelii* (ST2) is the most common causative agent of LB
    - *Borrelia* belonging to OspA ST1 to ST6 are responsible for almost all European LB cases



* Data from German National Reference Centre for *Borrelia* at the Bavarian Health and Food Safety Authority (Germany) and Baxter have been summarized.
** Centers for Disease Control and Prevention. *** Pritt et al., Lancet. Infect. Dis. 2016. Snd; Serotype not determined

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

History of Lyme disease vaccines

Vaccination with OspA has been proven effective in the past

Efficacy of two OspA (ST-1) based vaccines in the 1990s:

- LYMErix (licensed in 1998, withdrawn from market in 2002): Vaccine efficacy (symptomatic LD) [1]: 49% in 1st year, 76% in 2nd year
- ImuLyme: Vaccine efficacy (symptomatic LD) [2] : 68% in 1st year, 92% in 2nd year

Postulate that OspA vaccines might induce antibiotic-refractory Lyme arthritis due to molecular mimicry of OspA and human LFA-1* epitope was disproven for LYMErix

- Postulate withdrawn in 2011 [3]
  - FDA Panel concluded no evidence for association between vaccine and arthritis
  - No difference of arthritis incidence seen in vaccinated subjects versus unvaccinated subjects in a post-licensure VAERS study (after 1.4 million distributed doses) and a Phase 4 safety study
    (2,568 vaccinated subjects vs 7,497 control subjects)
  - Later, FDA retrospective review of all safety data concluded no safety signal

Mechanism of action of OspA based vaccines well understood

* Leucocyte Function.associated Antigen ;
1 N Engl J Med. 1998 Jul 23;339(4):209-15; **2** Sigal LH et al N Engl J Med. 1998 Jul 23;339(4):216-22; **3** A.C. Steere et al. CID 2011:52 (Suppl 3) S259 / Lathrop et al, Vaccine 2002

Anti-OspA protective response with Lyme disease vaccines

Mode of Action

Step 1	Step 2	Step 3	Step 4
Vaccine, when injected, elicits high levels of anti-OspA antibodies	Tick attaches to vaccinated human and begins blood meal (24- to 48-hour attachment needed to transmit *B. burgdorferi)*	Anti-OspA antibodies from vaccinee enter tick	Antibodies kill *B. burgdorferi* in midgut, preventing transmission to human host

The Lyme Disease Vaccine Project (VLA15)

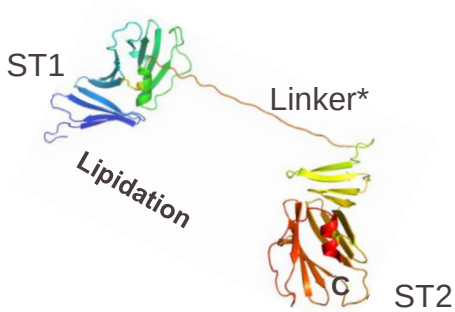
VLA15 – Design

Product based on three engineered proteins

Full-length OspA

Truncated stabilized OspA monomer

Stabilized OspA monomers representing 6 serotypes joined with a linker to 3 fusion proteins



ST1-ST2

ST4-ST3

ST5-ST6

* linked with a 21 amino acid linker derived from two N-terminal loops of OspA-ST1 (aa 65-74, aa 42-53)

Focus on C-terminal region of OspA

- Epitope LA-2 (OspA-ST1) correlates with protective immunity after vaccination[2]
- Truncated OspA monomers are stabilized through introduction of disulfide bonds
- T-cell epitope mimicking hLFA-1 sequence replaced by respective region from ST2[1]

3 fusion proteins targeting major OspA-serotypes[1]

- 3 fusion proteins target the most relevant *Borrelia* OspA serotypes (ST1- ST6) in Europe and US
- 3 proteins reduce industrialization complexity
- Lipidation and Alum-adjuvantation

1 Comstedt et al. 2014, PLoS One 9:e113294; Comstedt et al. 2015, Vaccine 33:5982-8 **2** Golde et al. Inf. Imm 1997

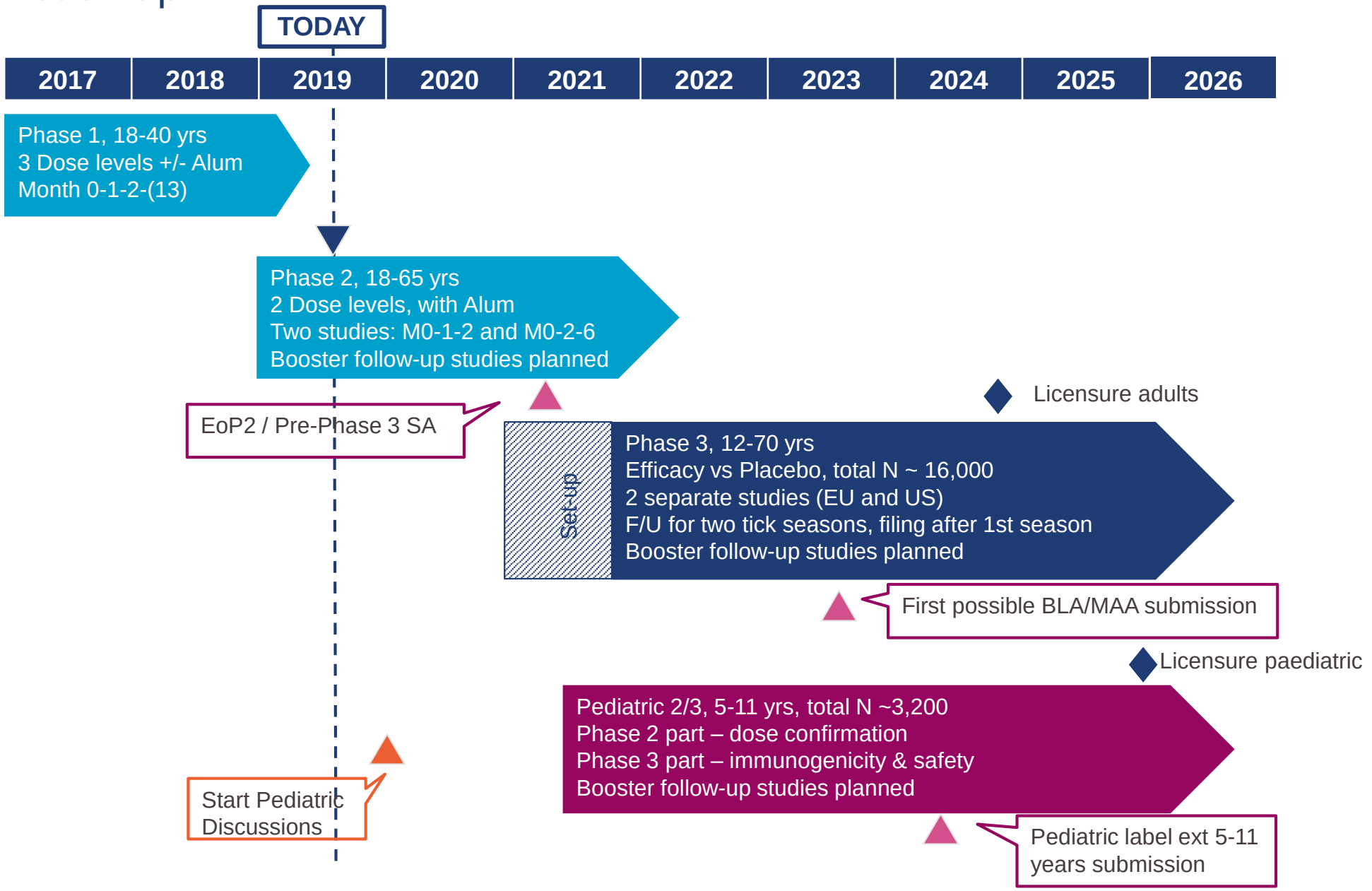
Valneva's Lyme disease vaccine candidate (VLA15)

Target Product Profile

Indications	▪ **Prophylactic active immunization against Lyme disease in individuals ≥ 2 years of age in US and Europe**
Dose and Administration	▪ Route of administration: Intramuscular injection ▪ Recommended dose: Best dose of 3 fusion proteins (ST 1/2, 4/3, 5/6) with Alum ▪ Dosage schedule: Month 0-1-2 (Booster M12) or alternative schedule Month 0-2-6 (Booster M18), further booster after 3-5 years (3 years for elderly)(tbc)
Dosage Form	▪ Single dose syringe (2-8°C)
Contraindications	▪ Hypersensitivity to any component of the vaccine
Adverse Reactions	▪ Comparable to intramuscularly injected Alum adjuvanted lipoproteins
Target Population/ Target Groups	▪ Individuals at risk who live in endemic areas ▪ People at risk with prior history of Lyme disease, since infection with *Borrelia* may not confer protective immunity ▪ People who plan to travel to endemic areas to engage in outdoor activities (e.g., hiking)
Efficacy	▪ Most KOLs see > 70% efficacy as acceptable

VLA15 Clinical Development Route To Potential US & EU license

Roadmap



VLA 15 – Key Regulatory Agency Feed-back

Some take-aways…

"The company´s concept to use OspA fusion proteins for a vaccine against Lyme borreliosis is in principle supported since all six described OspA serotypes are incorporated and provisions to ensure the drug substance´s stability, epitope accessibility and immunogenicity were made."

„We agree that efficacy data from the proposed phase 3 studies based on a clinical disease endpoint can be used to support US licensure of your investigational vaccine in adults. You have stated that a multivalent vaccine may be of benefit to US residents traveling to Europe. Please note that based on the indication you are seeking, we recommend that you recommend efficacy against serotypes 2-6. Your planned European phase 3 trial cold provide substantial data supporting the effectiveness for serotypes not prevalent in the US. Therefore, we recommend that such a trial be conducted under IND with our consultation in its design."

„The conduct of two pivotal studies, one in Europe and one in the USA, is endorsed. It is not required that a study in Europe should be powered to formally assess species-specific and/or OspA-type efficacy, since it is acknowledged that even the conduct of a separate pivotal study in European countries may not provide sufficient numbers of cases for these sub-analyses. Nevertheless , the conduct of two studies as proposed will allow for a larger total number of cases relevant to Lyme borreliosis in Europe to be collected and, hence, an estimate of vaccine efficacy that can be used to assess the benefit-risk relationship".

"Inclusion of adolescents in Phase 3 could be accepted since it is expected that the safety and immunogenicity data obtained in adults will be applicable to subjects aged from 12 years.

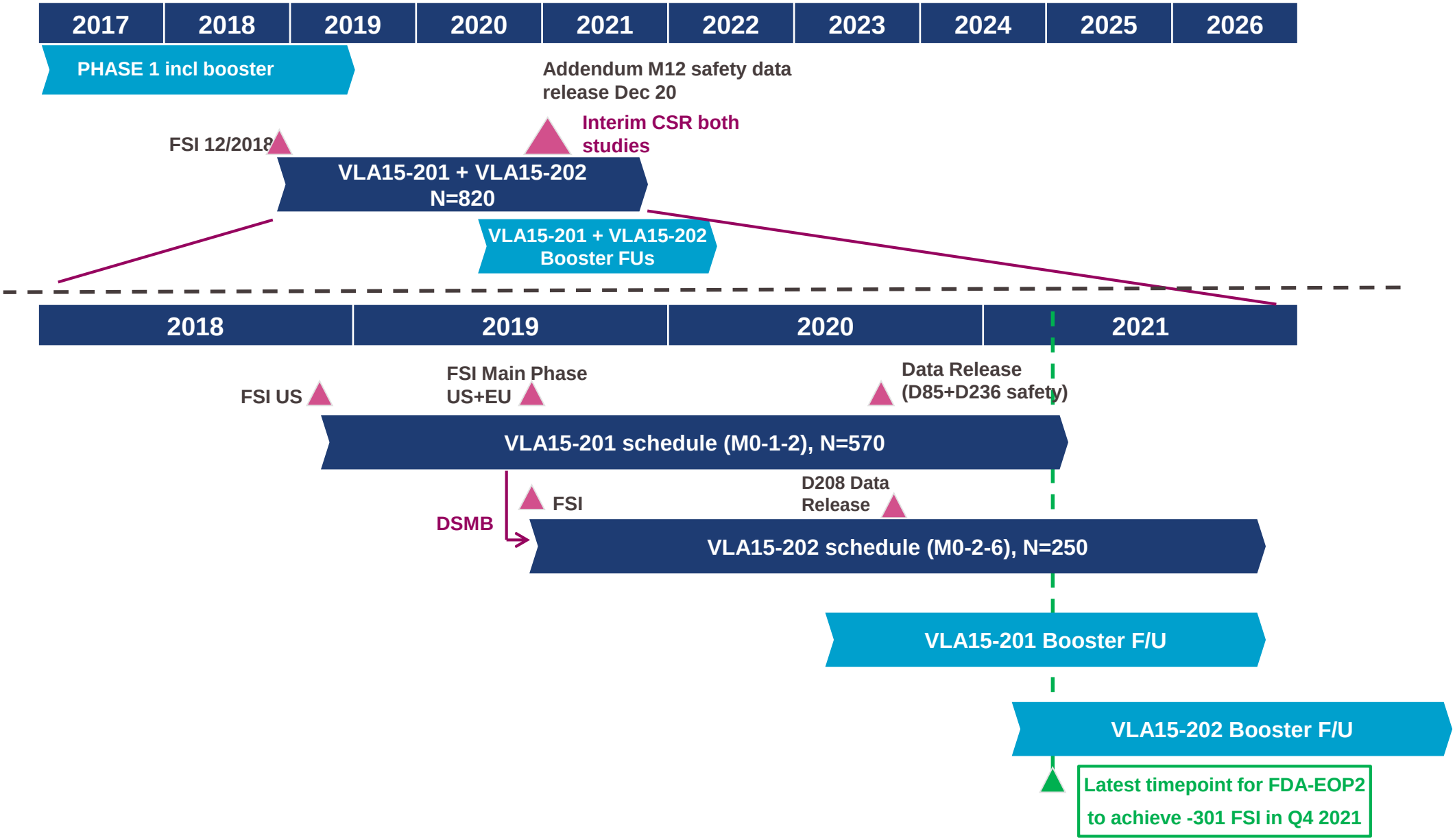
„The agency agrees that the current clinical development plan is acceptable"

"The CHMP agrees that paediatric development in children older than 5 years could commence after availability of Phase II safety and immunogenicity data from adults and in parallel with Phase III."

"The proposed strategy to initiate paediatric development of the vaccine after availability of Phase III efficacy data in adults was agreed … a combined Phase II/Phase III study for the paediatric population would also be acceptable."

Phase 1 and 2 Data & Outline

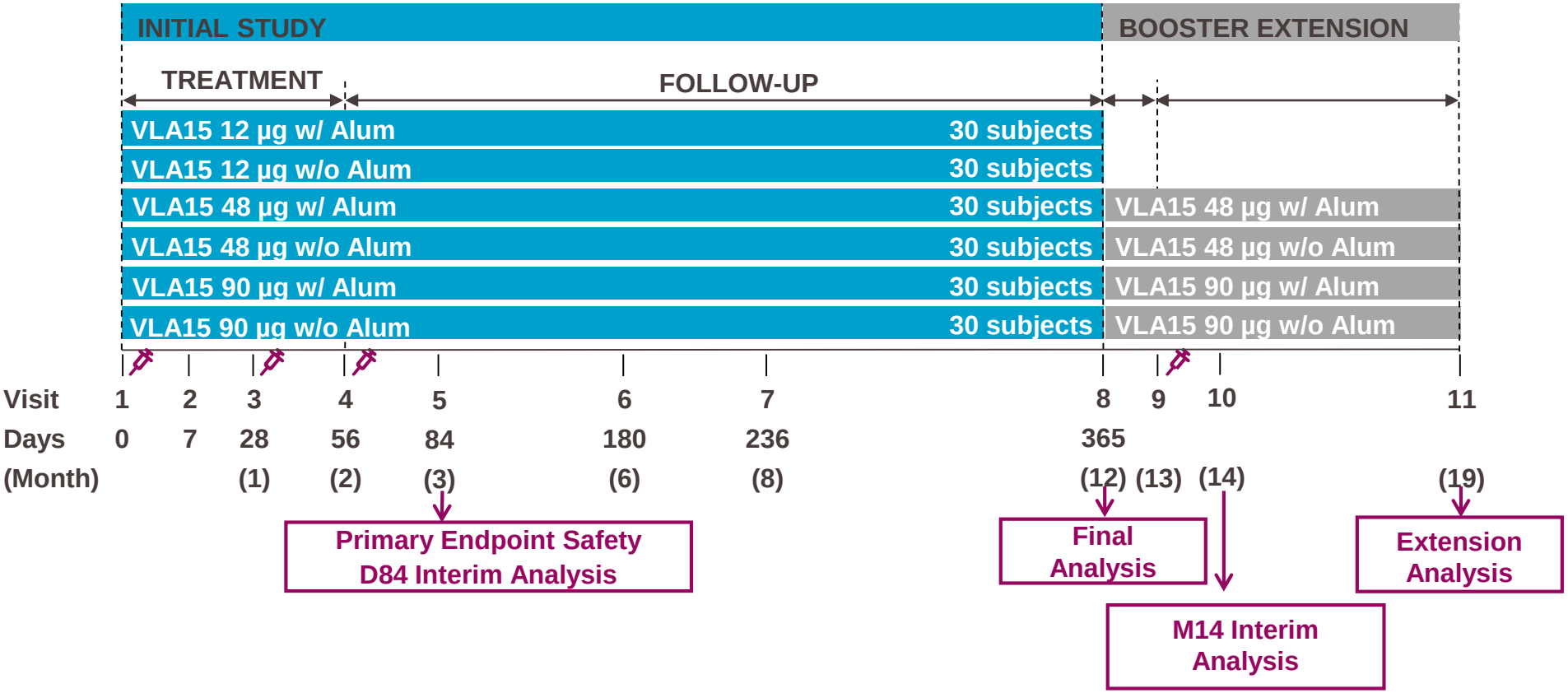
VLA15 Clinical Development Phase 1/2
Roadmap



VLA15-101 Phase 1 Study

Observer-blind, partially randomized, dose escalation study

+ Study Population: ~180 healthy volunteers aged 18 to <40 years
+ 1 site in Belgium (145 subjects), 2 sites in the US (34 subjects)
+ Immunization route: I.M. in non-dominant arm
+ Booster administered at Month 12-15 to subgroup of 64 subjects



Phase 1 study (VLA15-101) – Safety

Favorable safety profile and no associated safety concerns

No associated safety concerns:

- No serious adverse event considered related to VLA15 immunization
- No cases of arthritis or rheumatoid arthritis

Very few severe, related AEs:

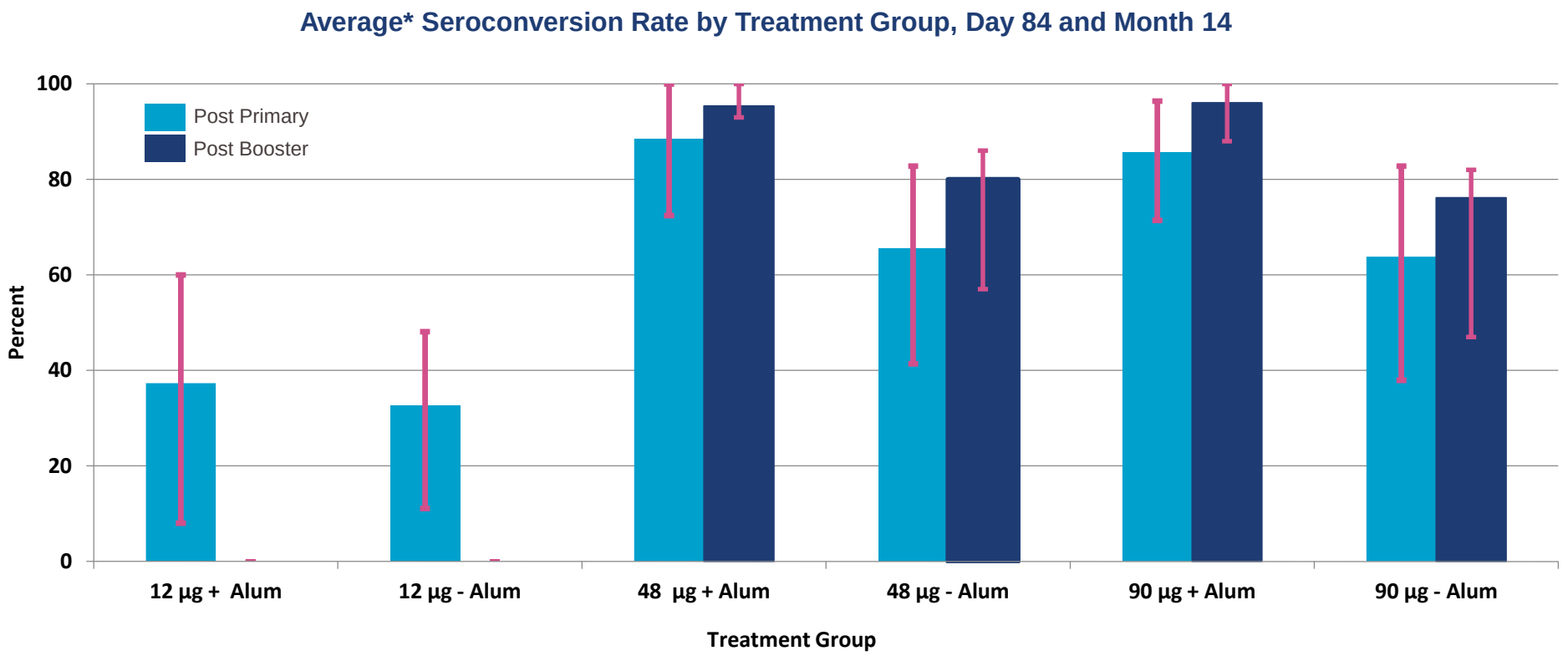
- Total of 8 subjects with severe, related AEs, from different treatment groups
- All were solicited AEs (i.e., predefined, volunteer-reported, by default considered related to vaccination)
- Study investigators considered AEs as related in 4 subjects:
  - 2 Subjects with severe local pain/tenderness
    - Both not medically attended, one treated with a single Paracetamol dose
  - 1 Subject with nausea, not medically attended, no treatment
  - 1 Subject with headache, not medically attended, treated with a single Paracetamol dose

- Severe arthralgia and myalgia seen in one subject, considered unrelated to vaccination by study investigator, following an ultramarathon 100 km walk

Phase 1 study (VLA15-101) – Immunogenicity

SCR for Highest Adjuvanted Dose Group between 71.4% (ST1) and 96.4% (ST2), Substantial Booster Effect

Seroconversion Rates (SCR) After Primary Series and Booster Dose

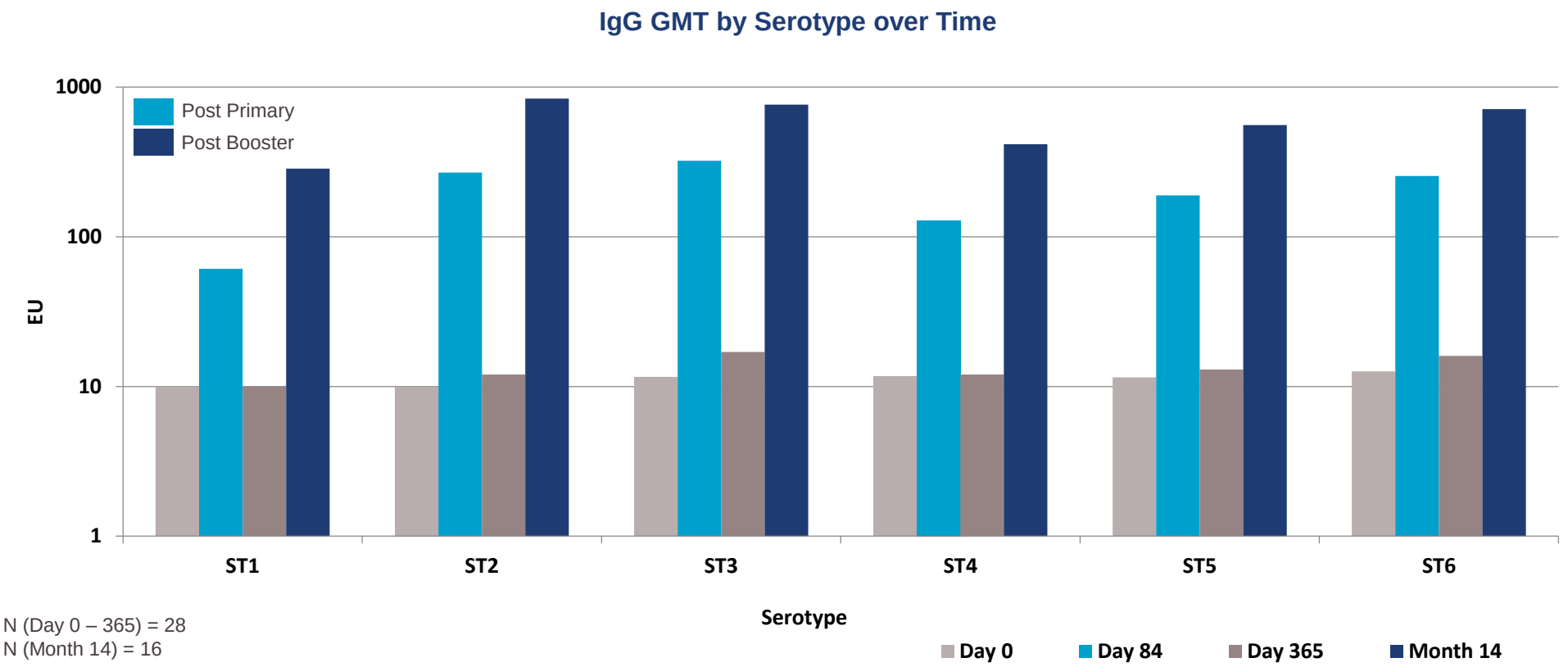


*Average = Arithmetic Mean of SCRs against individual Serotypes 1-6 (Rate of subjects with ≥4-fold increase in OspA-specific IgG)
** Error Bars represent highest / lowest individual Serotype SCR for treatment group

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

Phase 1 Study (VLA15-101) – Key Study Conclusions

Encouraging results fully supporting further development

- VLA15 generally safe and well tolerated, no associated safety concerns
- VLA15 was substantially more immunogenic in adjuvanted dose groups as compared to respective non-adjuvanted groups in same dose levels
- VLA15 showed encouraging immunogenicity with the 90 µg w/ Alum group inducing SCRs against individual OspA serotypes ranging between 71.4% for ST1 and 96.4% for ST2 on Day 84
- No significant dose response between 48µg and 90µg. Day 56 data indicate better kinetics of immune response at higher dose levels
- A substantial booster effect of VLA15 on GMT and SCR levels from 28 days after completed primary immunization was found in all groups, superiority of adjuvanted formulations was confirmed after booster

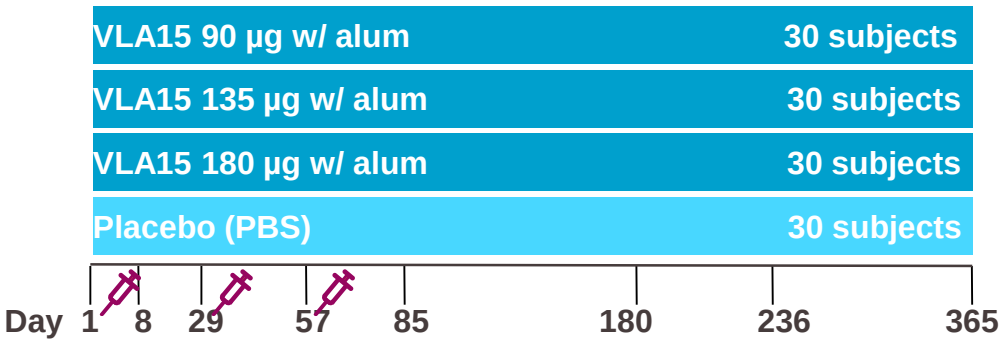
As circulating antibody levels are of utmost importance for OspA-based vaccines, further dose increase and alternative schedules are introduced in Phase 2, aiming to induce an earlier, higher and more durable immune response

Design Phase 2 Clinical Study VLA15-201

Dose Increase and Dose Confirmation

ONGOING

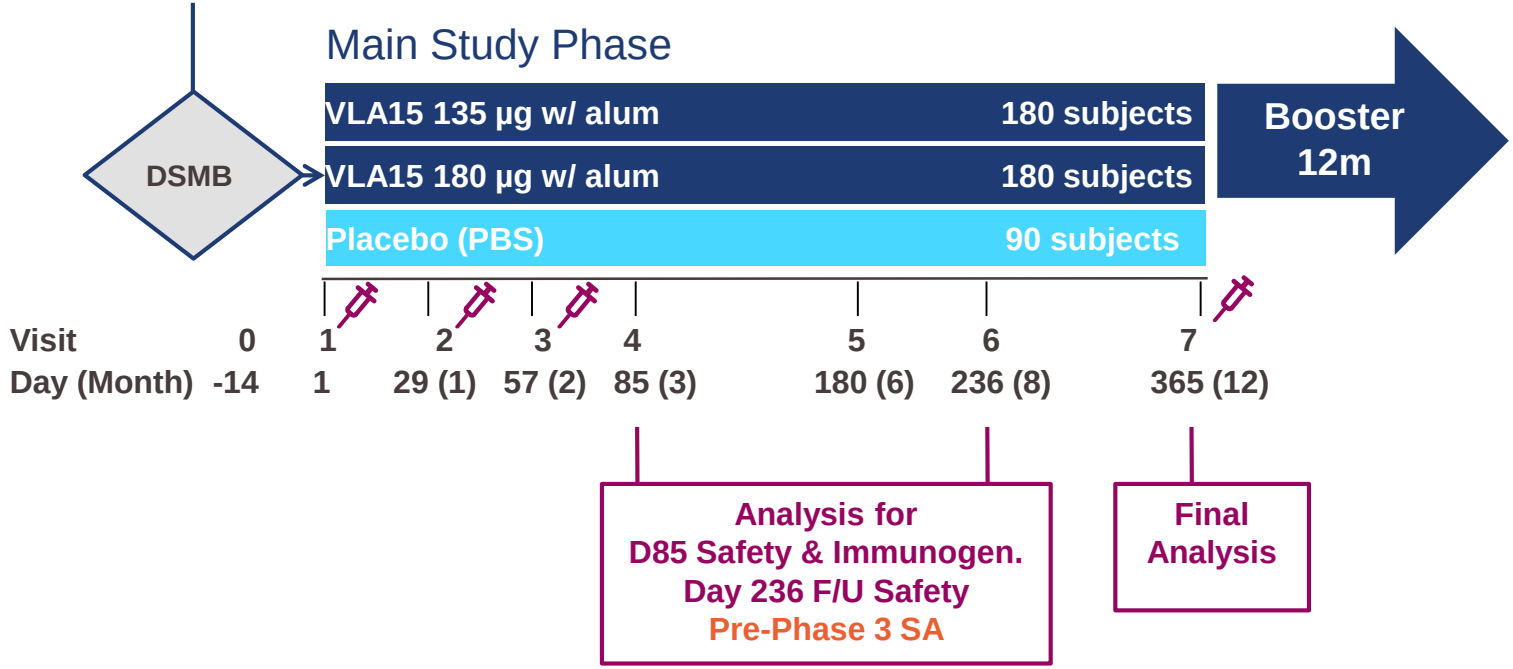
Run-in Phase



- Study population: Subjects aged 18-65 years, B.B. s.l. seronegative & seropositive (VlsE ELISA)
- Ratio 18-49 yrs to 50-65 years, 2:1
- Study conduct & sites: endemic regions in US and Europe; Run-in Phase in US only, Ratio US:EU 1:1

- Serological testing for EoP2 Package:
  - ELISA: Days 1 and 85, all subjects
  - SBA: Subset of Study

Main Study Phase



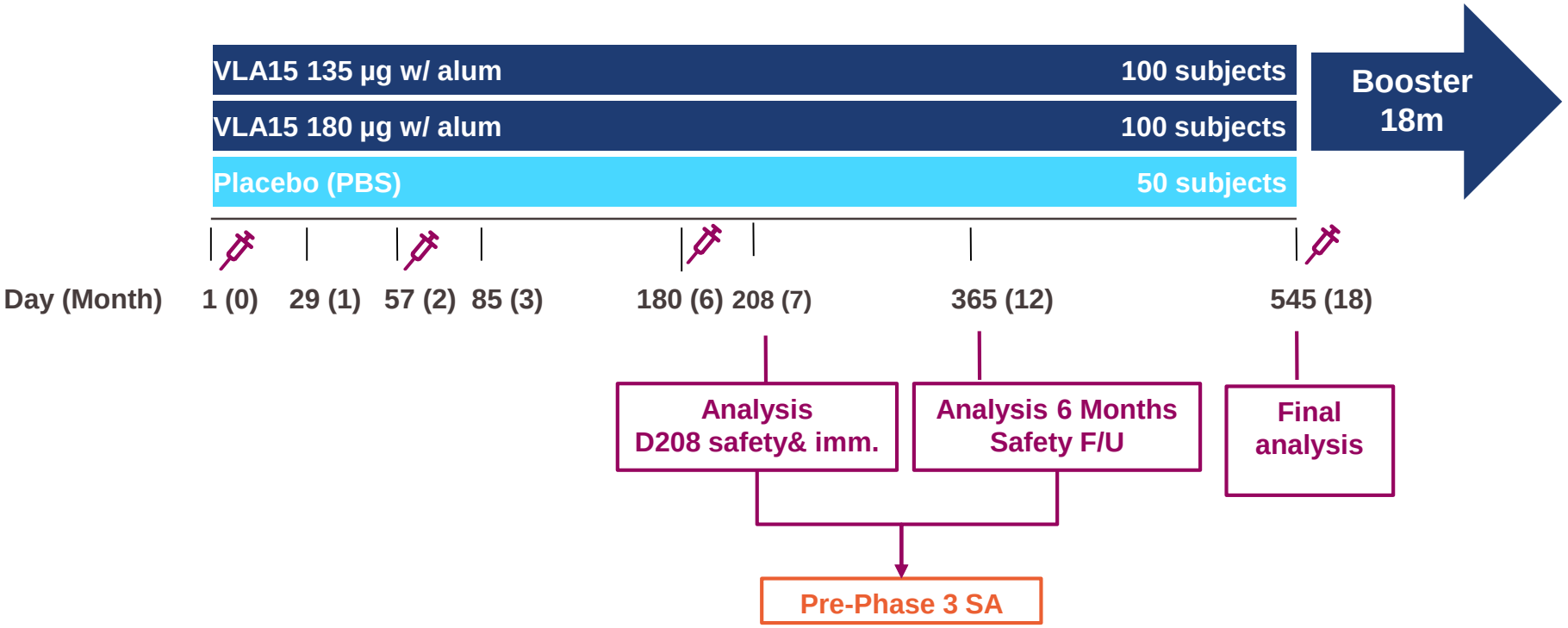
Design Phase 2 Clinical Study VLA15-202

Impact of Alternative Schedule

ONGOING

- Study population: Subjects aged 18-65 years, B.B. s.l. seronegative & seropositive (VlsE ELISA)
- Ratio 18-49 yrs to 50-65 years, 2:1
- Study conduct & sites: endemic regions in US

- Serological testing for EoP2 Package:
  - ELISA: Days 1, 85, 208 for all subjects
  - SBA: Subset of Study



Phase 3 Outline &
First Market Access considerations

Lyme vaccine candidate (VLA15)

First 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 mid 2020
- Booster studies with additional 12 months follow-up

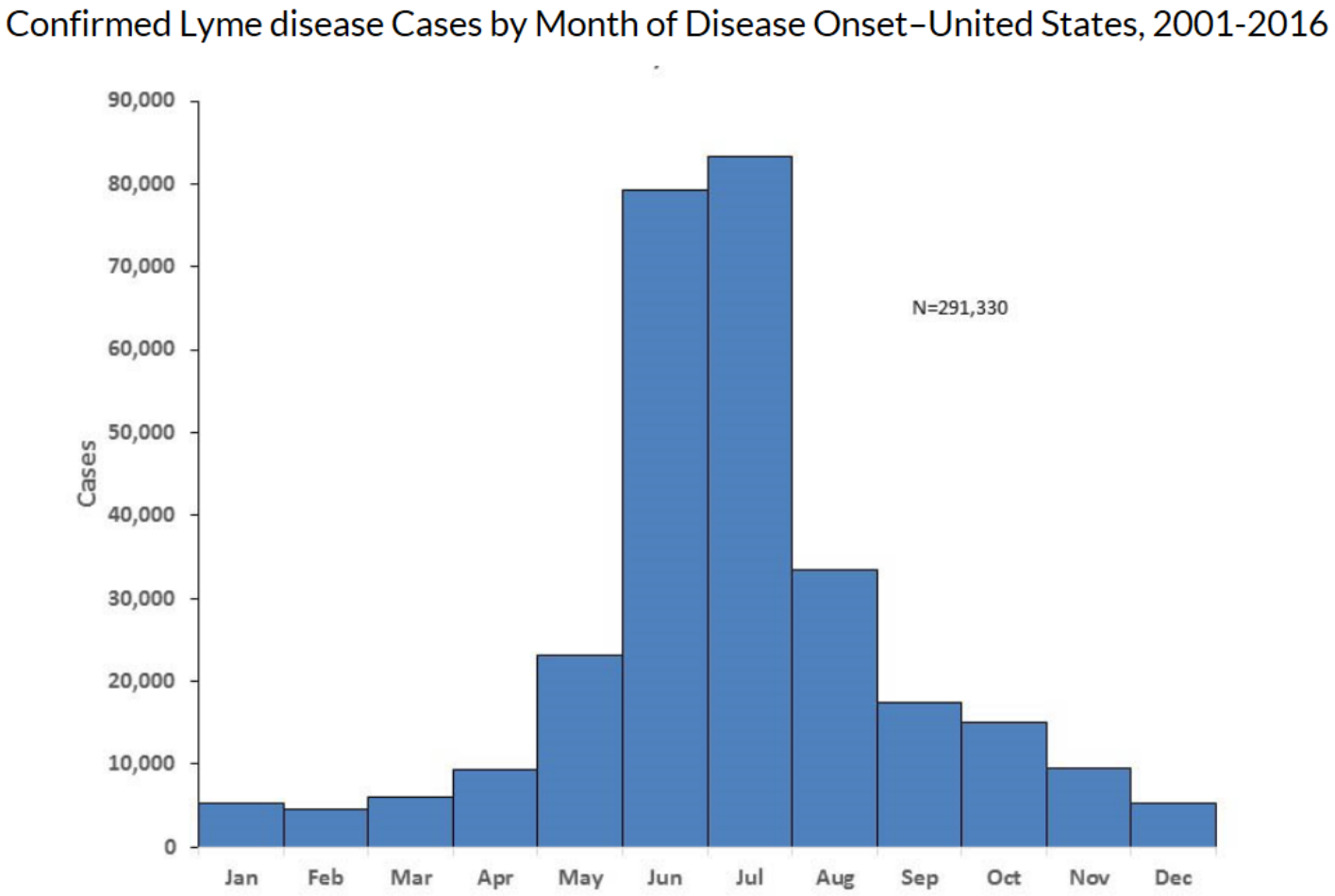
End-of-Phase 2 Meeting / Pre-Phase 3 Scientific Advice

- Targeted in Q1 2021

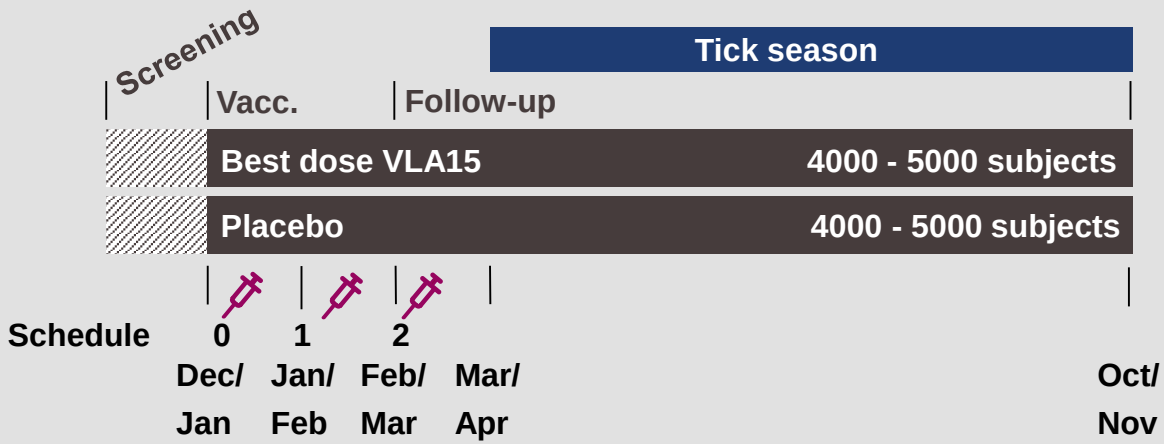
Phase 3 could be initiated 2021/2022

- Large-scale efficacy study needed: two separate trials for US and EU
- Study start in Q4 2021, in time for 2022 tick season
- Efficacy followed for two tick seasons, target BLA/MAA filing after 1st season
- Phase 3 might include adolescents (12 yrs+) in addition to adults
- Pediatric (5 - <12 years) data in children at point of licensure
- We expect a Phase 3 duration of approximately three years

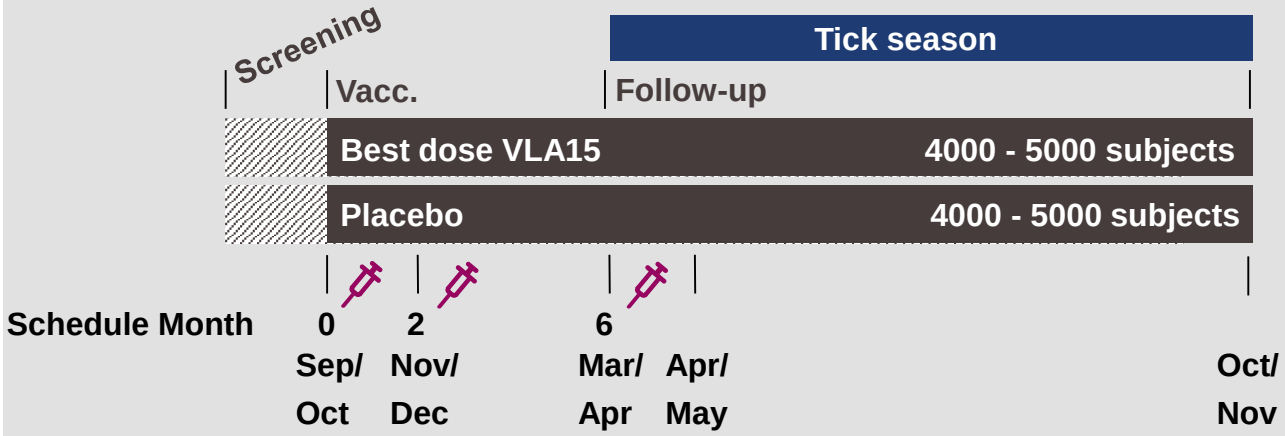
Seasonality of Lyme Disease Cases



Phase 3 Clinical Study VLA15-301 / VLA15-302
Execution considerations



- Full protection by **mid April** at the latest (Start of tick season – avoidance to see breakthrough cases due to incomplete schedule)
- 3 dose vaccination schedule **(M 0-1-2),** starting December
- 1 season observation time for BLA submission



- Full protection by **end of May** at the latest (Avoidance to start immunizations in August and risk breakthrough cases after 1 immunization)
- 3 dose vaccination schedule **(M 0-2-6),** starting September
- 1 season observation time for BLA submission

Market access considerations
Focus on handling scientific misconceptions

Engagement with and education of the Lyme disease community crucial to gaining their acceptance of VLA15

- Emphasize the ability of VLA15 to prevent (chronic manifestations of) Lyme disease
- Generate and communicate robust safety data to alleviate side effect concerns
- Provide safety and efficacy data in individuals who had Lyme disease
- Emphasize the accuracy of laboratory tests in diagnosing Lyme disease

Market access considerations

VLA15 is expected to be recommended for at risk populations in the majority of markets

VLA15 recommendations are expected to cover at risk areas and populations

- Experts expect VLA15 to be recommended for high risk individuals in endemic areas
- Expected vaccination rates may reach from 15-50%, subject also influenced by national vaccination campaigns. We estimate US endemic of up to 25%.
- Reimbursement is expected

Should aim to avoid key pitfalls of previous Lymerix vaccine by:

- Robust safety data
- Engage with ACIP[2]
- Engage with Lyme disease patient organizations to alleviate all safety concerns

North America and EU revenue potential of ~USD 1bn[1]

1 Company's position, supported by L.E.K. interviews, research and analysis; **2** Advisory Committtee on Immunization Practices

Market access considerations

The disease burden for Lyme disease in the US is estimated at $0.7bn-$1.3bn annually

- A 2015 study based on large insurance patient databases estimated the total direct medical costs attributable to LD and Post-Treatment Lyme Disease Syndrome (PTLDS) at $0.7bn-$1.3bn annually (Adrion et al. 2015)
  - The mean total costs per individual with Lyme disease were ~$3k annually greater than those of the control group
  - The range of total cost estimates arises from a range of total Lyme disease incidence estimates of 240k-244k annually, spanning L.E.K.'s estimate of ~330k annual cases in the US

The CDC estimates costs of diagnostic testing for Lyme disease to be ~USD $490m annually (Hinckley et al. (2014)).

- Zhang et al. (2006) published a utilization study and estimated the national economic burden from a societal perspective at $203m annually based on reported Lyme disease cases only (~24k cases annually), so is likely a significant underestimate
  - Assuming an incidence of 300k cases annually, this would instead equate to a total annual cost burden of ~$2.5bn
- Health-economic assessments for LYMErix (inflated to 2017) estimated $3k-$12k for treatment

*Published and inflated to 2017; Source: Meltzer et al. 1999; Shadick et al. 2001; Hsia et al. 2002; Mac et al. 2019: Hinckley et al. 2014; Zhang et al. 2006; Adrion et al. 2015 L.E.K. secondary research and analysis

CHIKUNGUNYA

STANLEY A. PLOTKIN, MD
Professor Emeritus
Wistar Institute
University of Pennsylvania

Should We Vaccinate Against Chikungunya?

Chikungunya

An RNA arbovirus

ORF codes for 4 NS proteins, 5 structural C, E1, E2, E3, 6K

E1 mutation at 226 valine to alanine. Increased infection of *Aedes Albopictus*

Replicates in mosquito midgut, goes to salivary glands

Replicates in fibroblasts of humans and animals

Chikungunya

271K reported cases in 2016

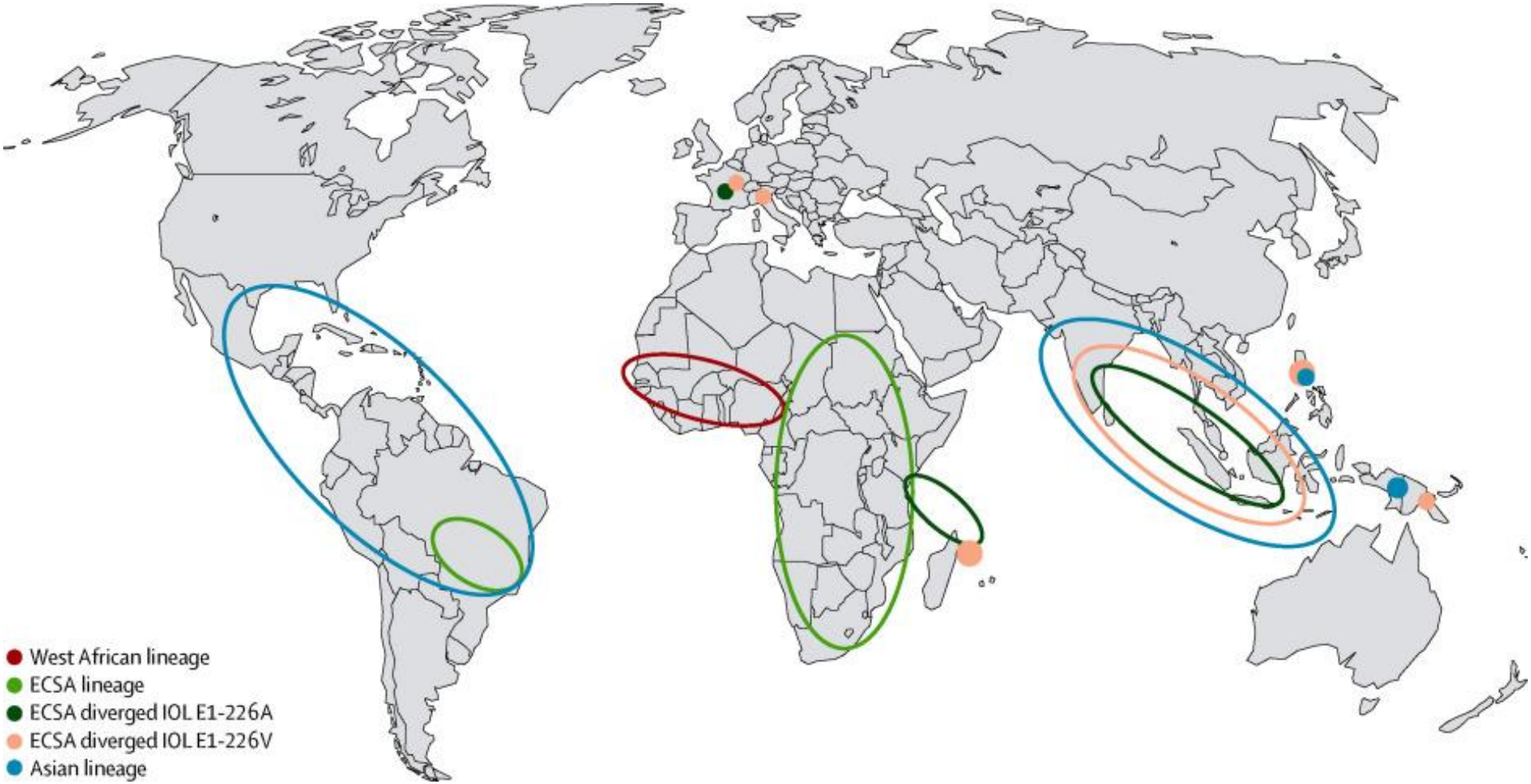
Can be transmitted via mosquito bite, blood transfusion, vertically in near-term deliveries (cesarean doesn't help)

Causes fever, maculopapular or petechial rash due to cytokines, IL1, IL6 TNF alpha

May involve eyes, heart, brain

IgG works as prophylaxis and therapy, but some think low Nt Ab may enhance disease

Figure 1. Distribution of chikungunya virus The figure shows the spread and divergence of the East Central South African (ECSA) lineage to the Indian Ocean islands (IOLs) and Asia,9; 69 ; 70 the spread of the Asian lineage to the Americas in 2013,82 and the sp...



Burt et al, *Lancet Infect Dis* 2017

Global Spread of Chikungunya

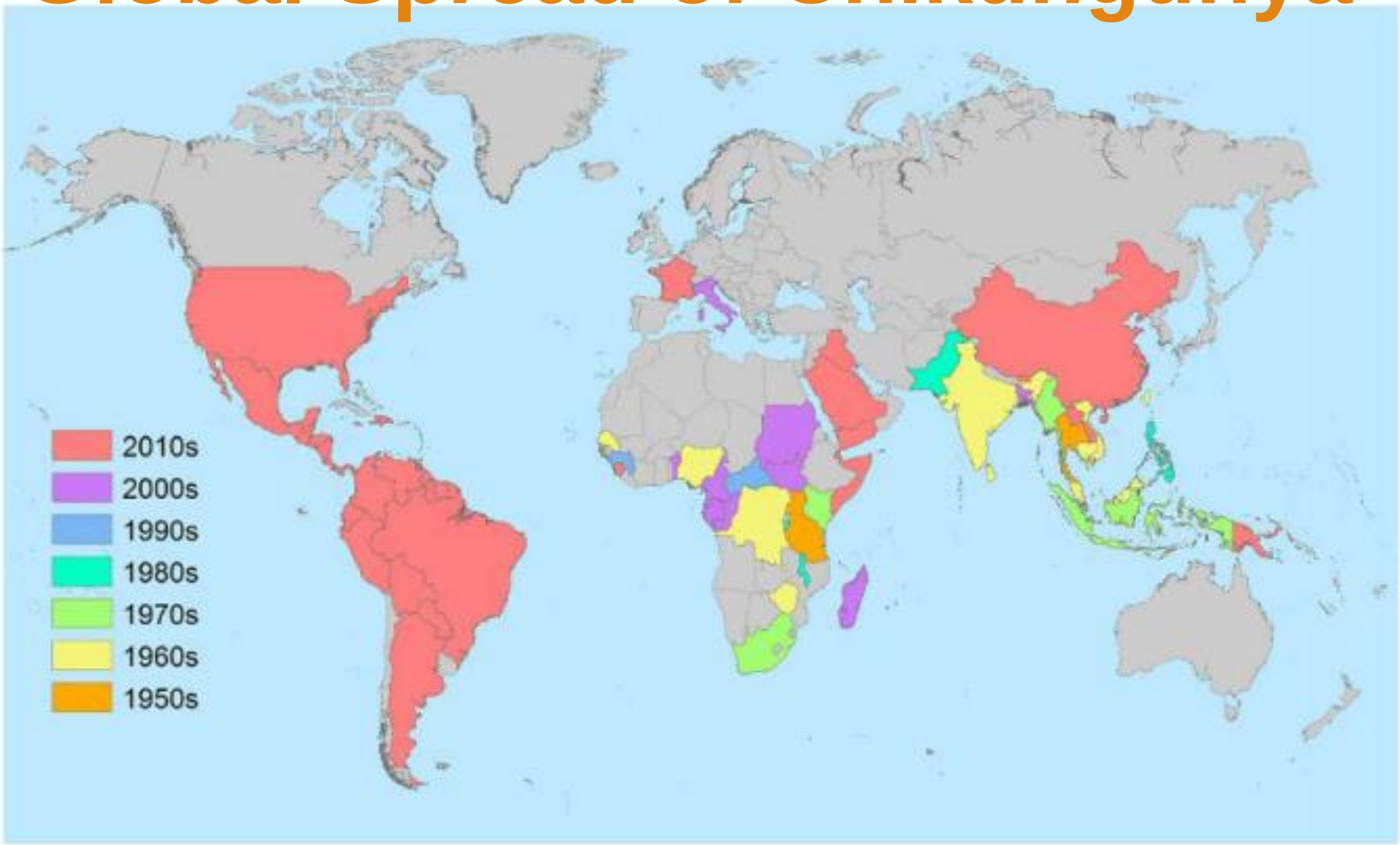


FIG 1 Global distribution of CHIKV. Country colors correspond to the decade of the first reported identification of the local transmission of CHIKV by either serological, molecular, or virological detection methods. (Image created by Nicole Lindsey.)

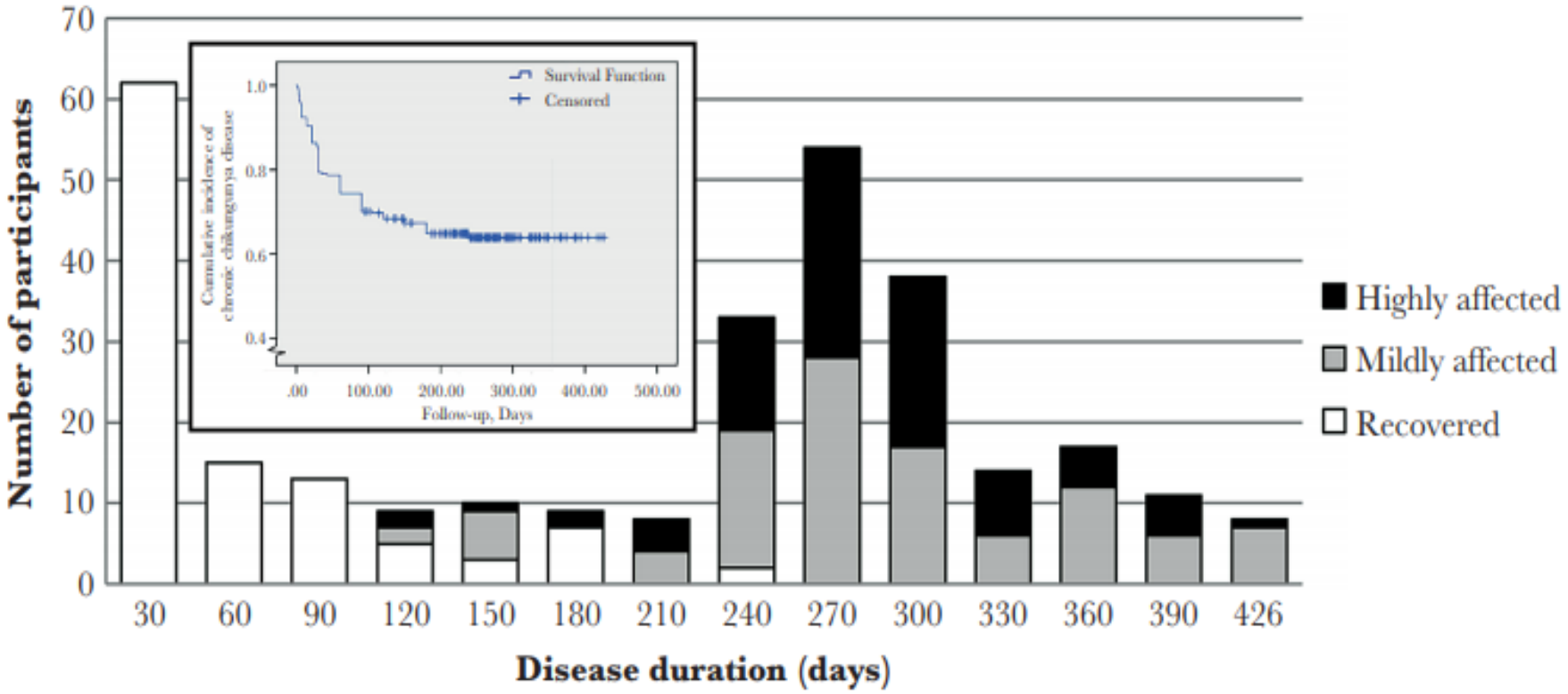
Powers, A., *Clinical Microbiology Review* 2017

Sequelae of Chikungunya

Persistent Arthralgia	
Réunion	83% at 32 months
Mexico	42% 46% at 10 months
Curacao	64% at 100 days
Phillipines	32-95% at 3 years

High viral load predicts poor prognosis

Duration of Chikungunya Symptoms



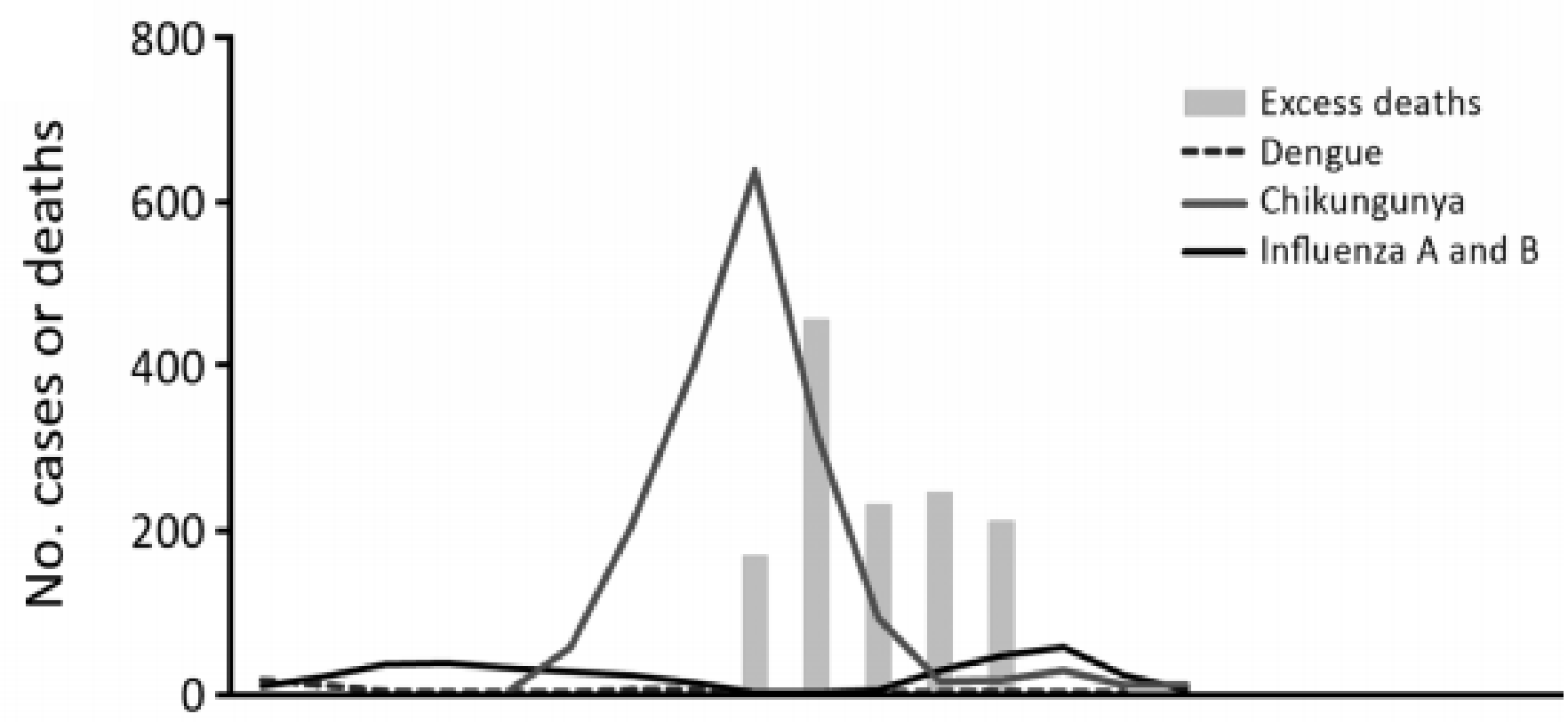
Elsinga et al, *JID* 2017

Evasion of Antibody in Chronic Cases

Pathogenic Chikungunya Virus Evades B Cell Responses to Establish Persistence

David W. Hawman,[1] Julie M. Fox,[2] Alison W. Ashbrook,[3,4,9] Nicholas A. May,[1] Kristin M.S. Schroeder,[1] Raul M. Torres,[1] James E. Crowe, Jr.,[3,5] Terence S. Dermody,[3,4,5,10] Michael S. Diamond,[2,6,7,8] and Thomas E. Morrison[1,*]

Expected and observed monthly deaths in Puerto Rico, 2014–2015. Excess number of monthly deaths and number of chikungunya, dengue, and influenza A and B cases diagnosed



Freitas, et al *Emerging Infectious Diseases* Dec 2018

Prevalence of persistent arthralgia and impaired physical functionality among residents in a study of persistent arthralgia after a Chikungunya virus outbreak, US Virgin Islands, December 2014 - February 2016*

Variable	Prevalence difference (95% CI)
Persistent arthralgia	
6 month analysis*	0.32 (0.24–0.40)
12 month analysis*	0.19 (0.11–0.28)
Difficulty performing daily activities	
Walking	0.11 (0.03–0.18)
Climbing stairs	0.12 (0.05–0.19)
Lifting heavy objects	0.04 (–0.02–0.11)
Getting in and out of cars	0.09 (0.03–0.14)
Opening jars	0.15 (0.07–0.23)

* **Adjusted for age group, sex, and self-reported history of arthritis**

Curacao = 64% disability at 400 d.

Feldstein et al, *Emerging Inf Dis* 2017

Correlates of Protection Against Chikungunya

Passive antibodies have been shown to protect in animal models

Induction of neutralizing antibodies has been protective and even therapeutic

lg G3 antibodies associated with neutralization

T cell responses may be responsible for symptoms

Types of Chikungunya Vaccines in Development

Live Attenuated	Subunit
Vectored: Measles Alphavirus VSV MVA Adenovirus Vaccinia	Inactivated, whole DNA RNA RNA Replicon
VLPs	

Response to Chikungunya VLP Vaccine

Neutralization IC titre$_{50}$ (strain OPY1)

	10 µg group (n=5)	20 µg group (n=10)	40 µg group (n=10)
0*	50	51	52
4*	188	236	346
8	2688	1775	7246
20*	650	510	1485
22	NA	NA	NA
24	8745	4525	5390
44	940	717	1385

*Boosts

Chang et al, *LANCET* 2014

VLA1553

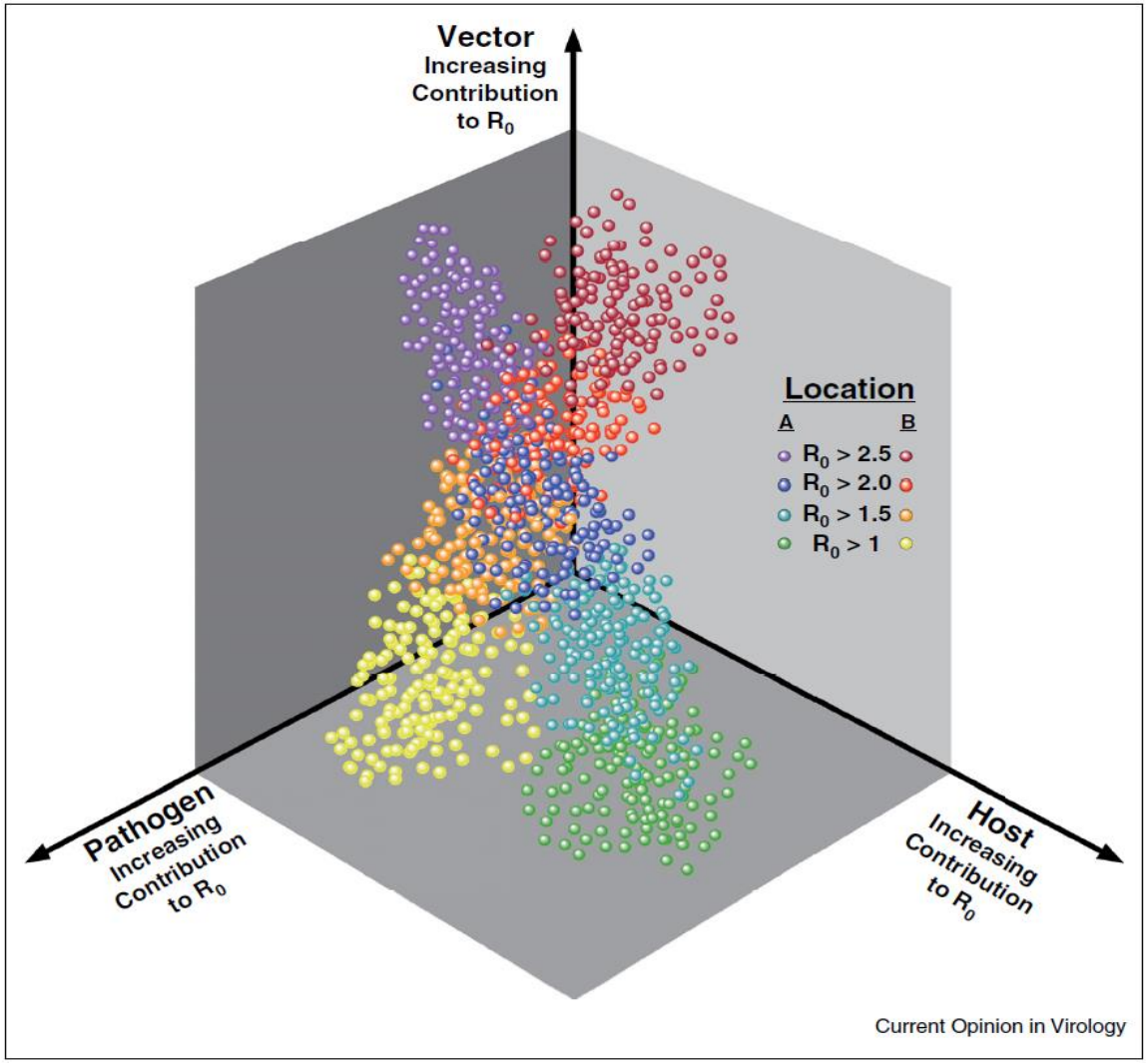
Dr. WOLFGANG BENDER, MD, PhD,
MPH, MHA, DTMP,
CHIEF MEDICAL OFFICER

Arbovirus outbreaks difficult to predict
Preparedness strategy options needed

Ecological Effects on Arbovirus-Mosquito Cycles of Transmission

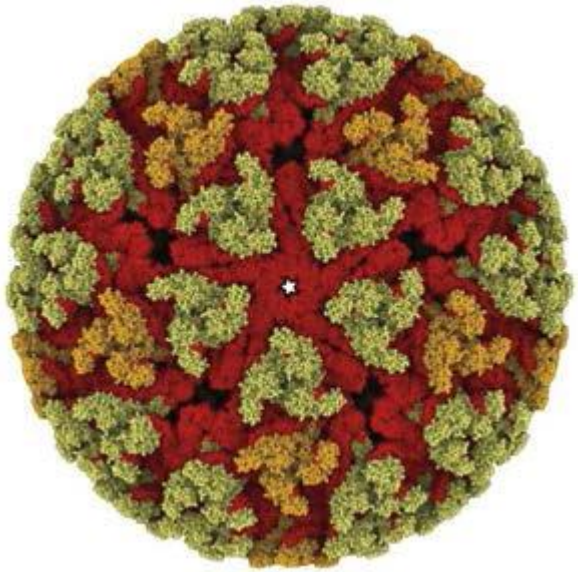
Will AI and quantum-tech bring break-through in forecasting?

Factors e.g. Bayesian networks - R_0



Tabachnik 2016

Chikungunya Virus



- **Single stranded RNA virus**
- **Family *Togaviridae* - Genus *Alphavirus***
- **Antigenically related to other polyarthritis causing alphaviruses**
  e.g. Mayaro-, Semliki Forest-, O'nyong-nyong- and Ross River viruses

Picture: Weaver and Lecuit 2015

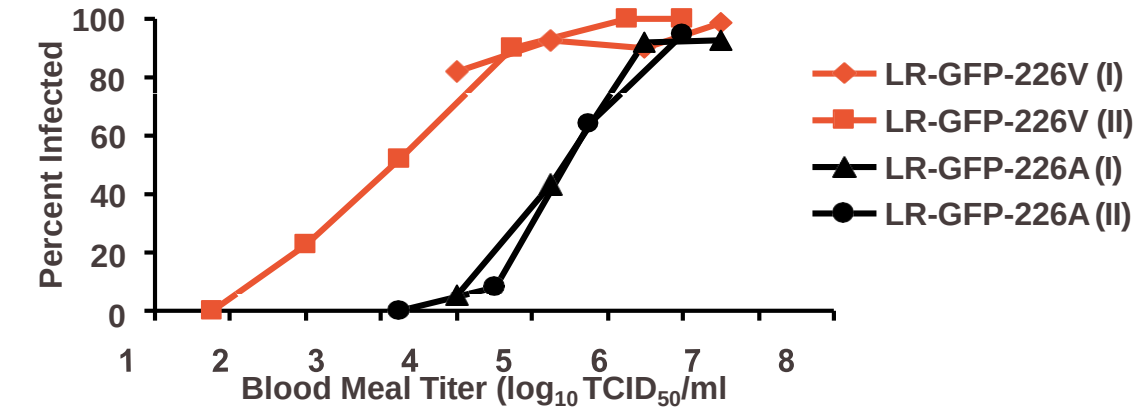
Chikungunya Virus Vectors

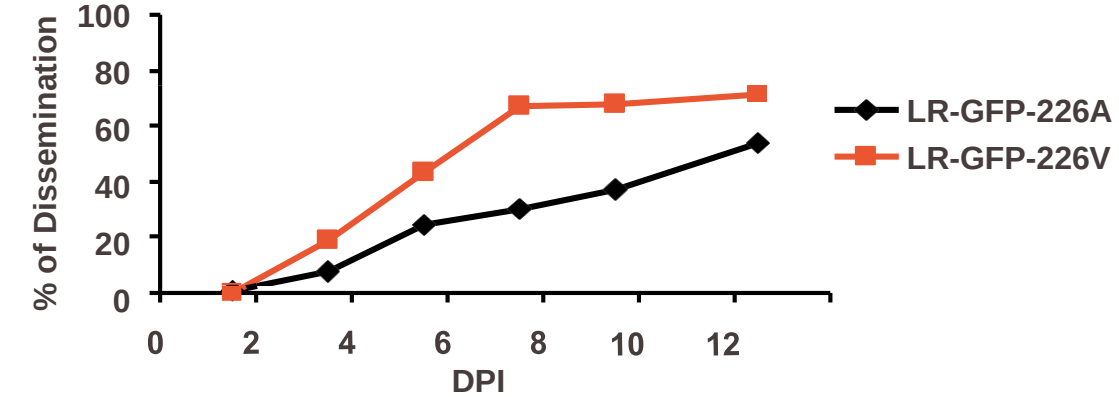
Aedes aegypti

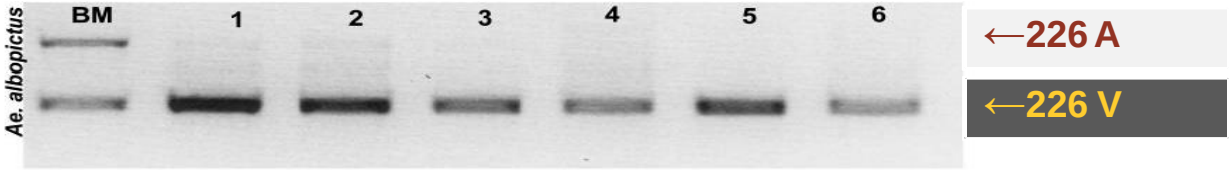
Aedes albopictus

Virus – Vector Interplay: Pathogen Mutation with Impact

Examples: Viral Envelope E1 Mutation → Ae. albopictus Transmission ↑↑↑ of IOL CHIKV; Ae. aegypti E1:K211E and E2:V264A







E1-A226V mutation

- Viral fusion to endosomal membranes
- Increased midgut cell infectivity by 50-100 fold
- Increased viral dissemination to salivary glands
- Increased viral transmission to mice

Tsetsarkin K et al 2007; Berry et al 2019

Chikungunya: Vector Prevalence and Disease Outbreaks

Global warming → increased vector prevalence, longer transmission season

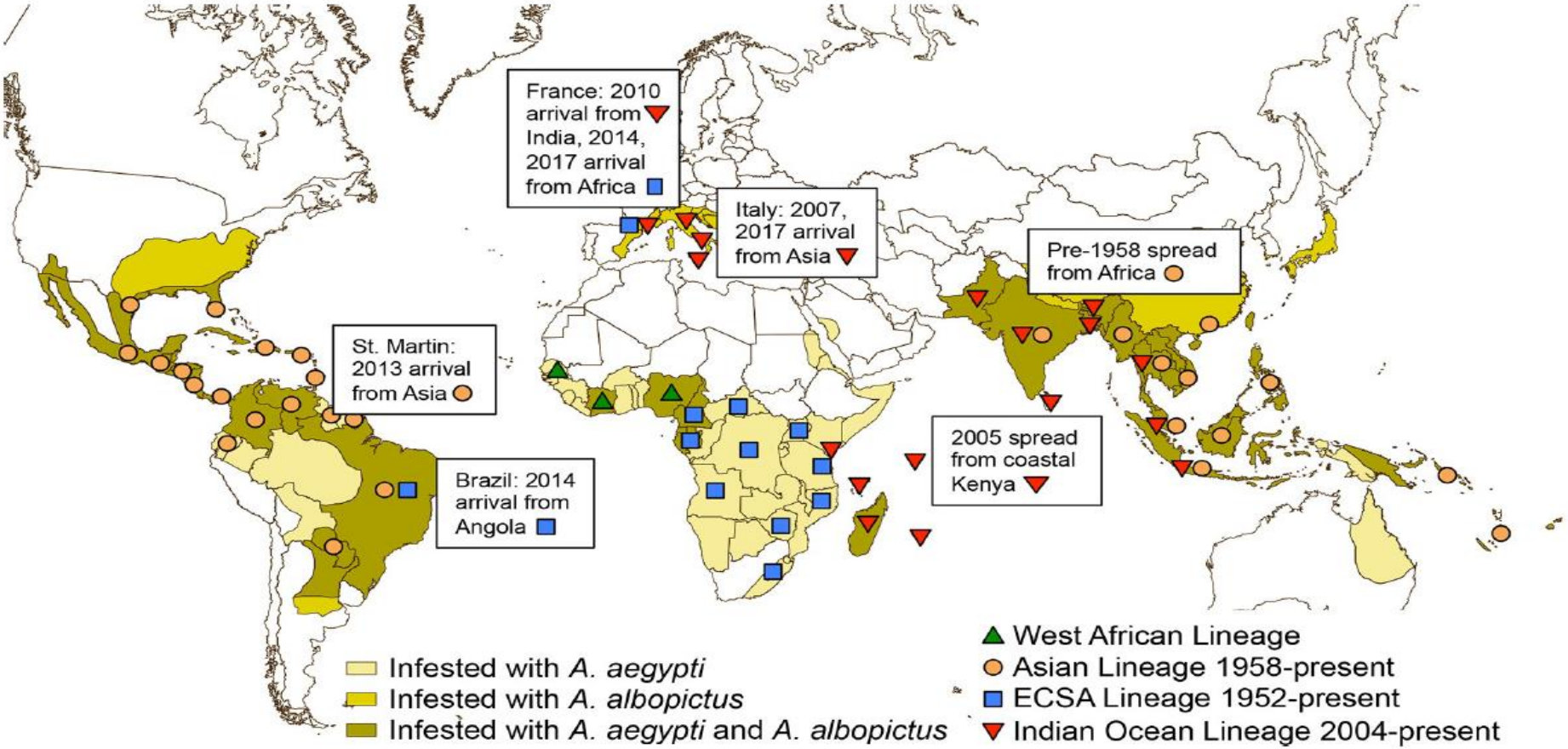


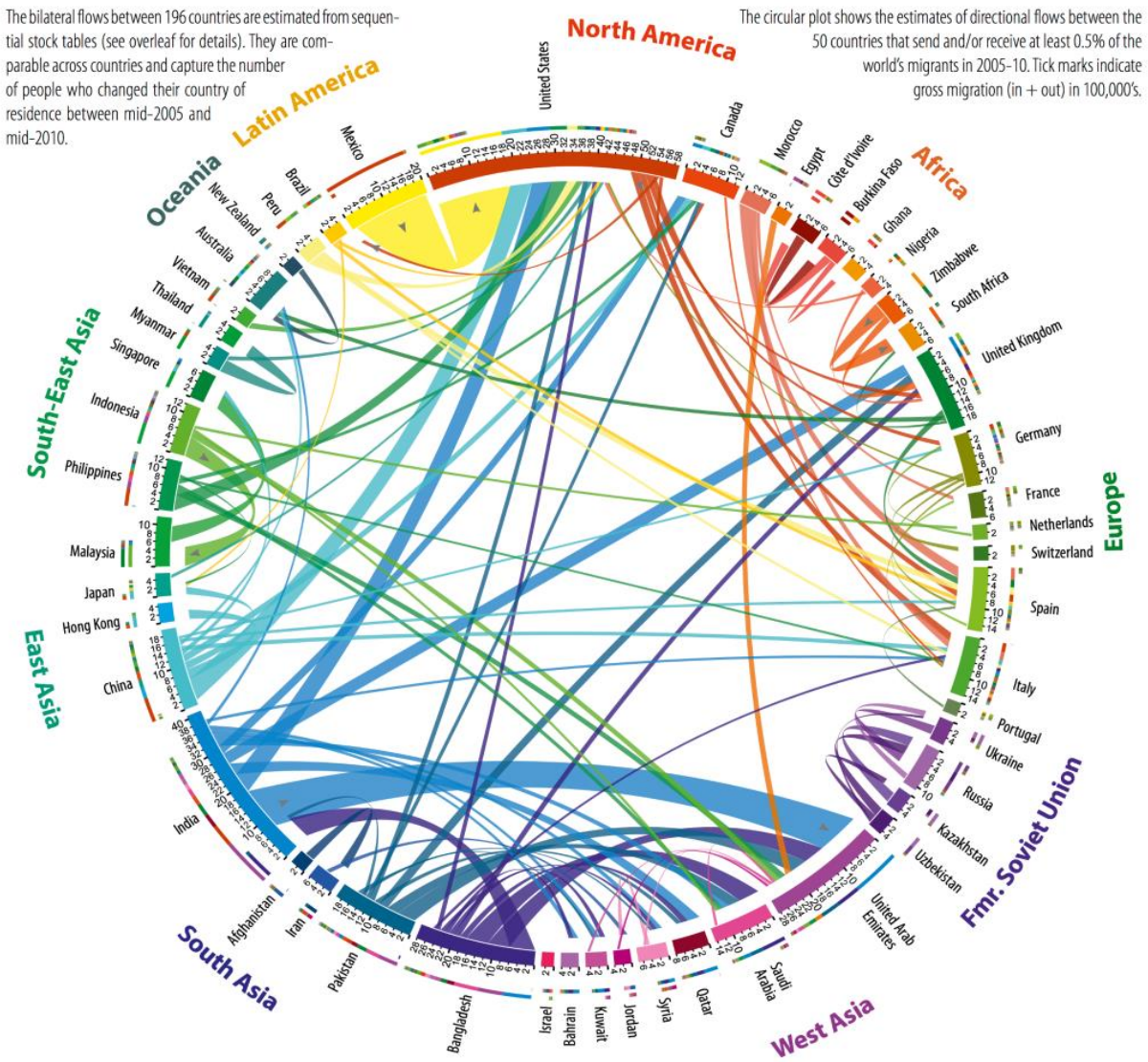
Fig 1. World map with countries where autochthonous (locally initiated) chains of CHIKV transmission have been identified. Data from World Health Organization (http://www.who.int/emergencies/diseases/chikungunya/en/) and Pan American Health Organization (https://www.paho.org/hq/index.php?option=com_topics&view=article&id=343&Itemid=40931&lang=en).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

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

Rezza & Weaver 2019

Human Migration and Visiting Friends & Relatives (VFR) Add Risk

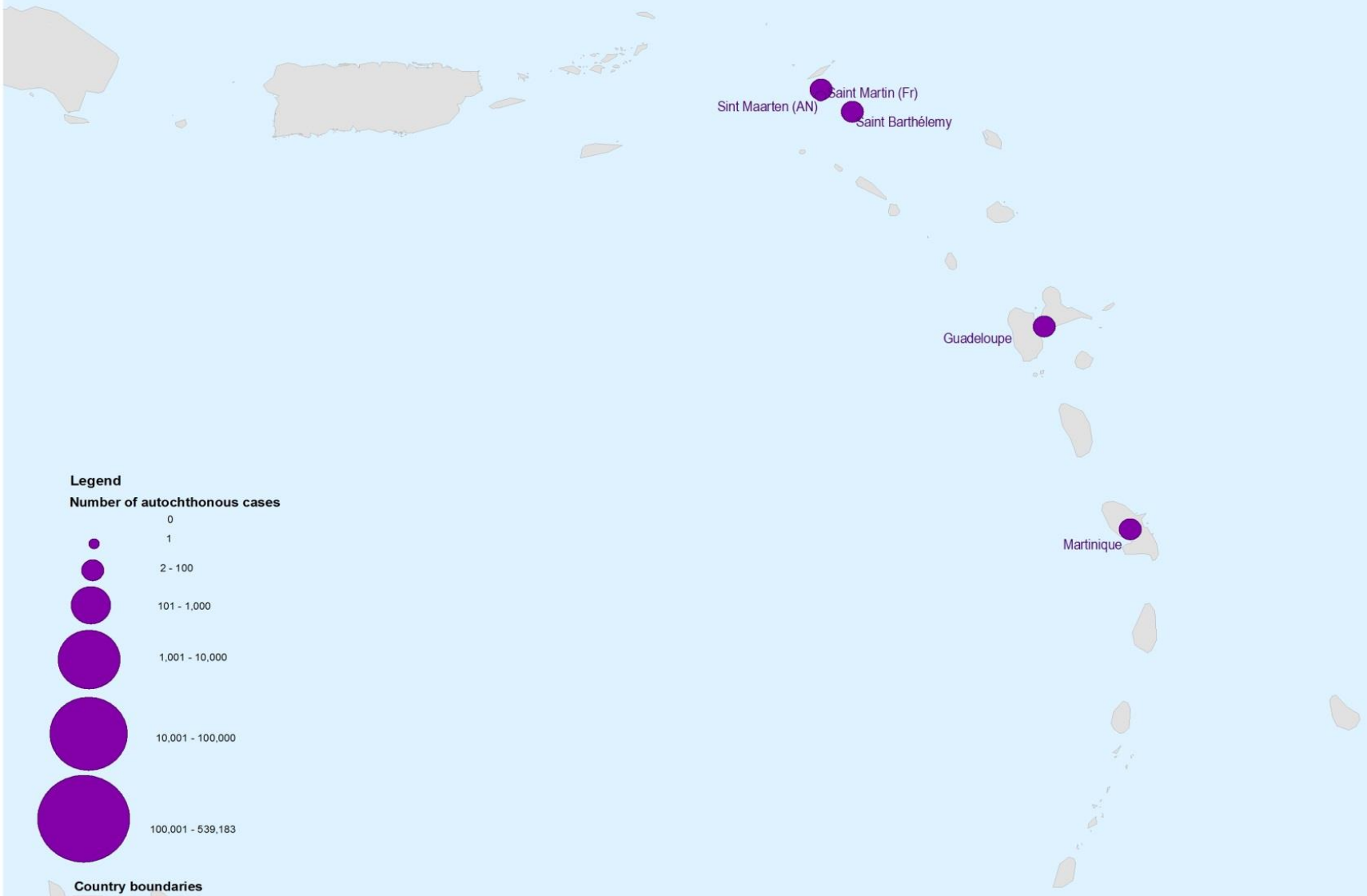
…on top of other travellers (business, tourists), military



Murphy et al 2014

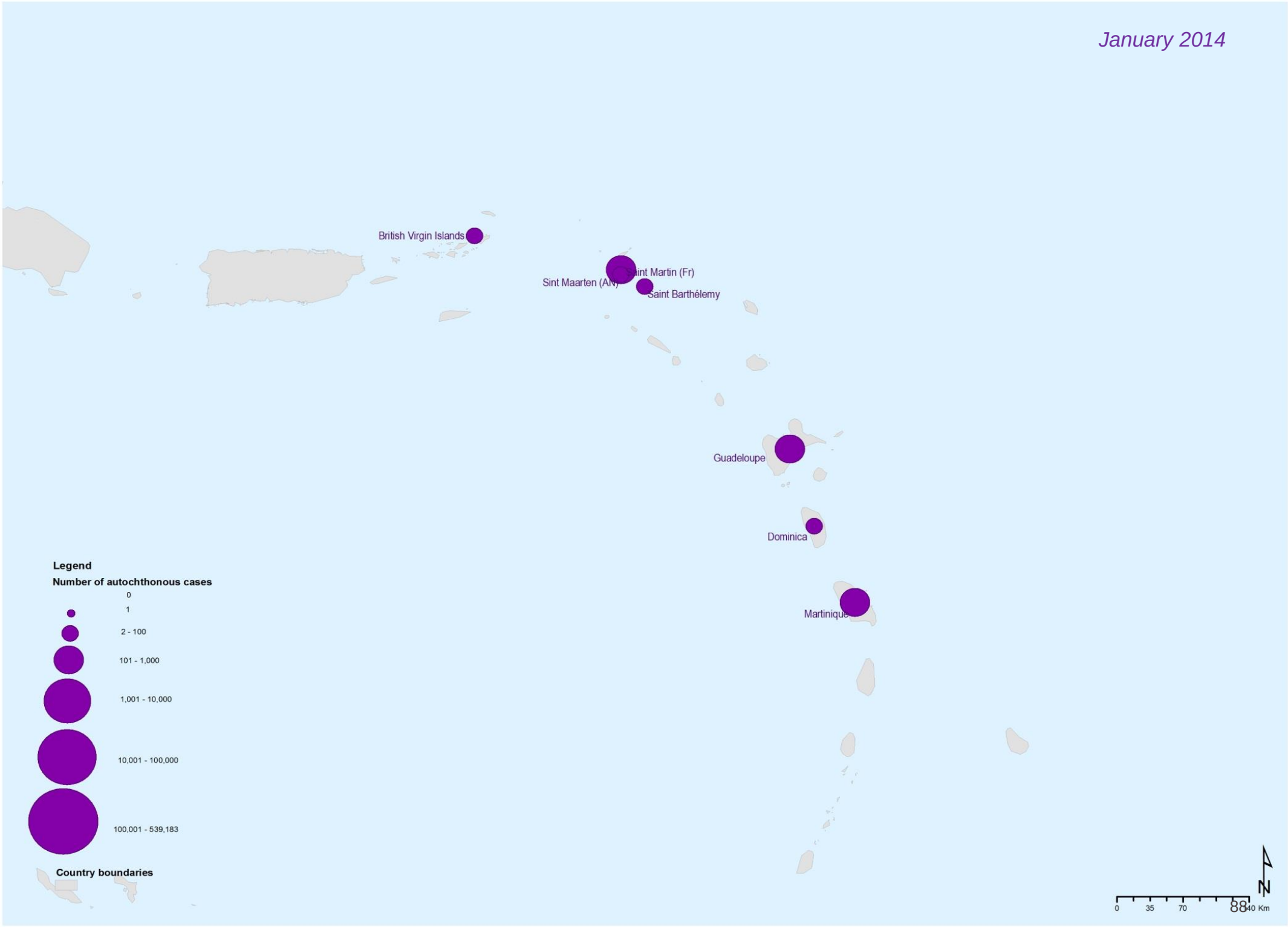
Often Overwhelming Speed of Outbreaks:

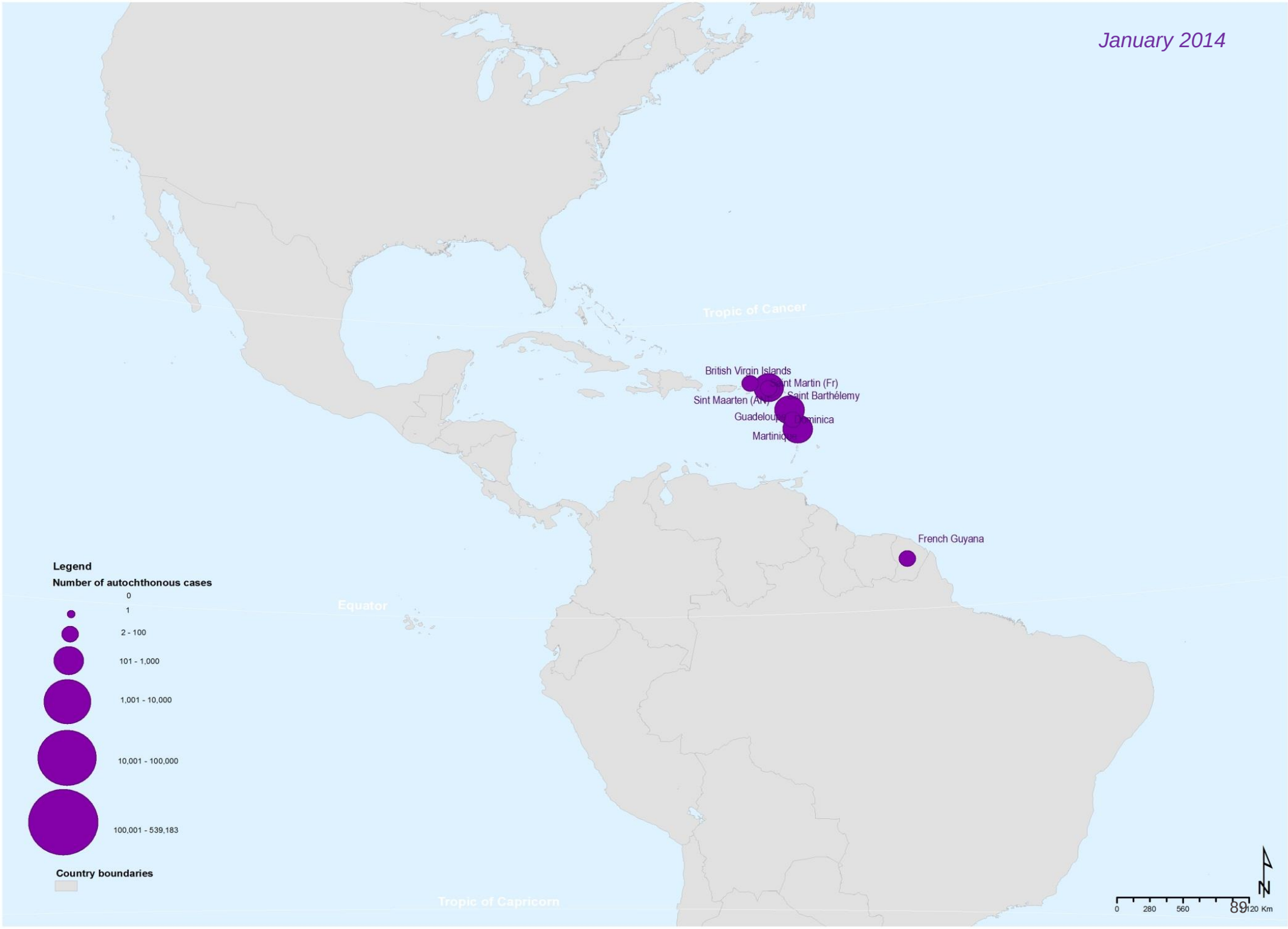
Example: 1 Year of Chickungunya 2014 (1 slide = 1 month)

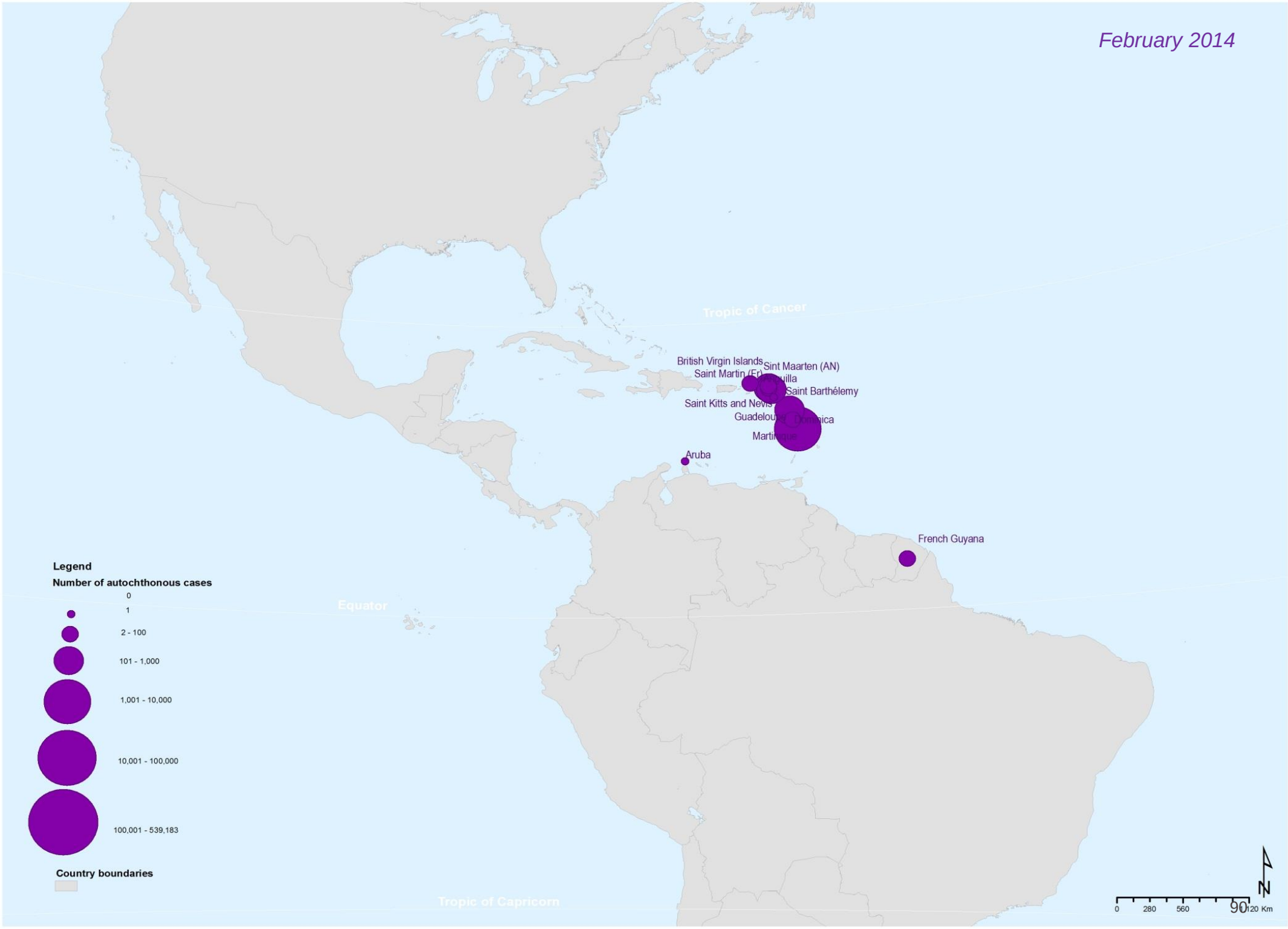


Simon 2016

January 2014




January 2014
Tropic of Cancer
British Virgin Islands
Saint Martin (Fr)
Sint Maarten (Dutch)
Saint Barthélemy
Guadeloupe
Dominica
Martinique
French Guyana
Equator
Tropic of Capricorn
Legend
Number of autochthonous cases
0
1
2 - 100
101 - 1,000
1,001 - 10,000
10,001 - 100,000
100,001 - 539,183
Country boundaries
0
280
560
1120 Km
N


February 2014
Tropic of Cancer
British Virgin Islands
Sint Maarten (AN)
Saint Martin (Fr)
Anguilla
Saint Barthélemy
Saint Kitts and Nevis
Guadeloupe
Dominica
Martinique
Aruba
French Guyana
Equator
Tropic of Capricorn
Legend
Number of autochthonous cases
0
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2 - 100
101 - 1,000
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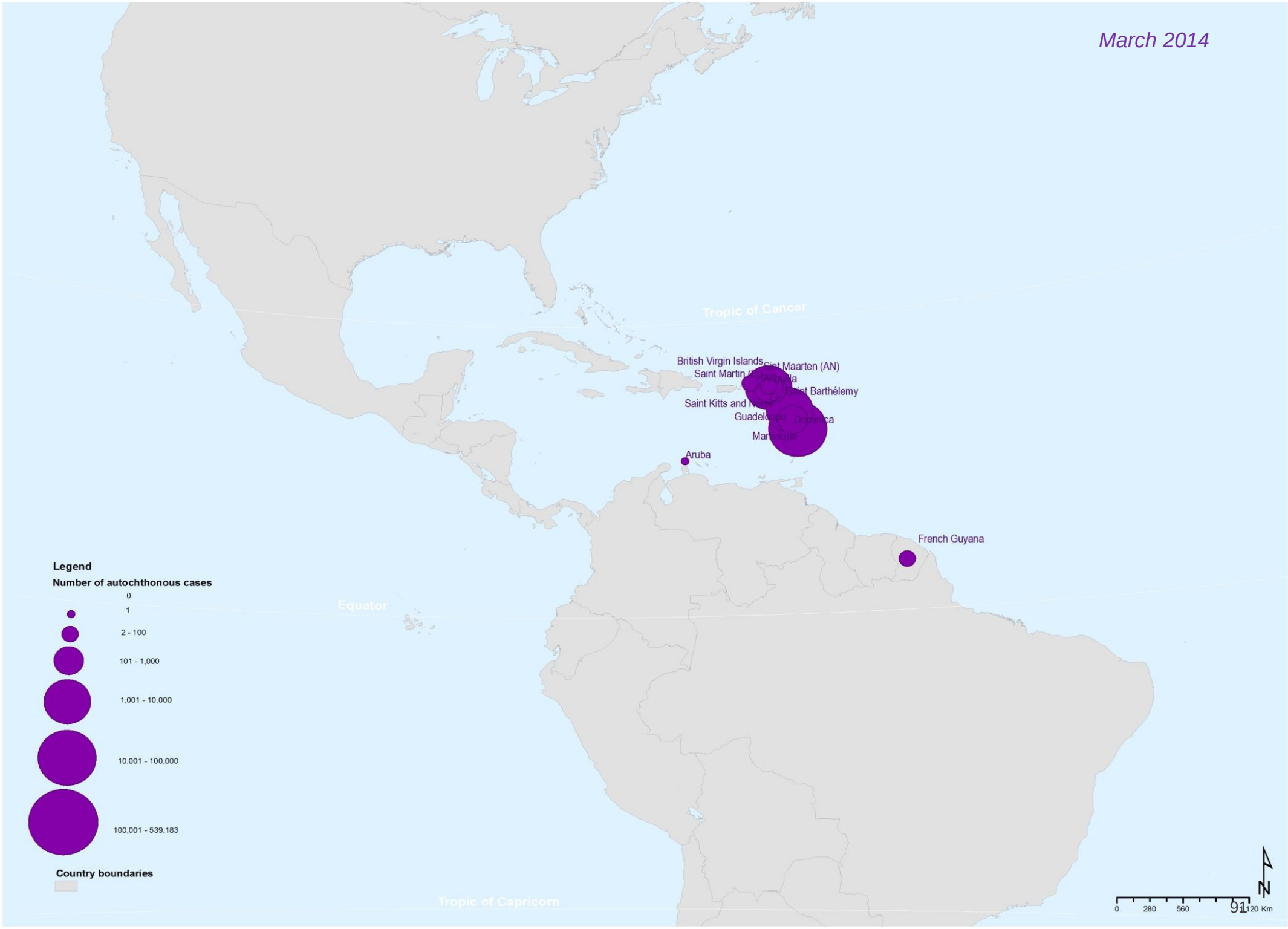
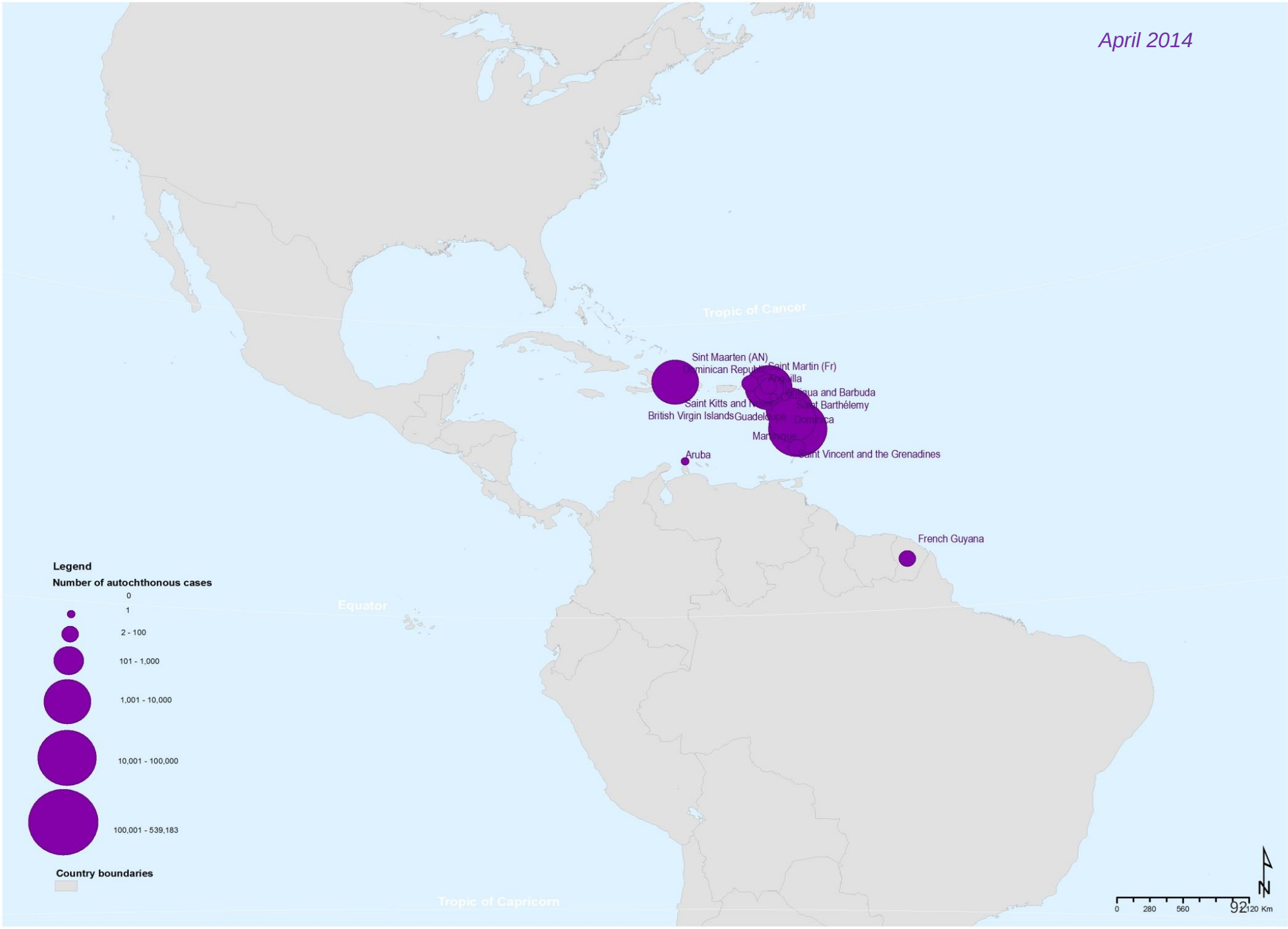
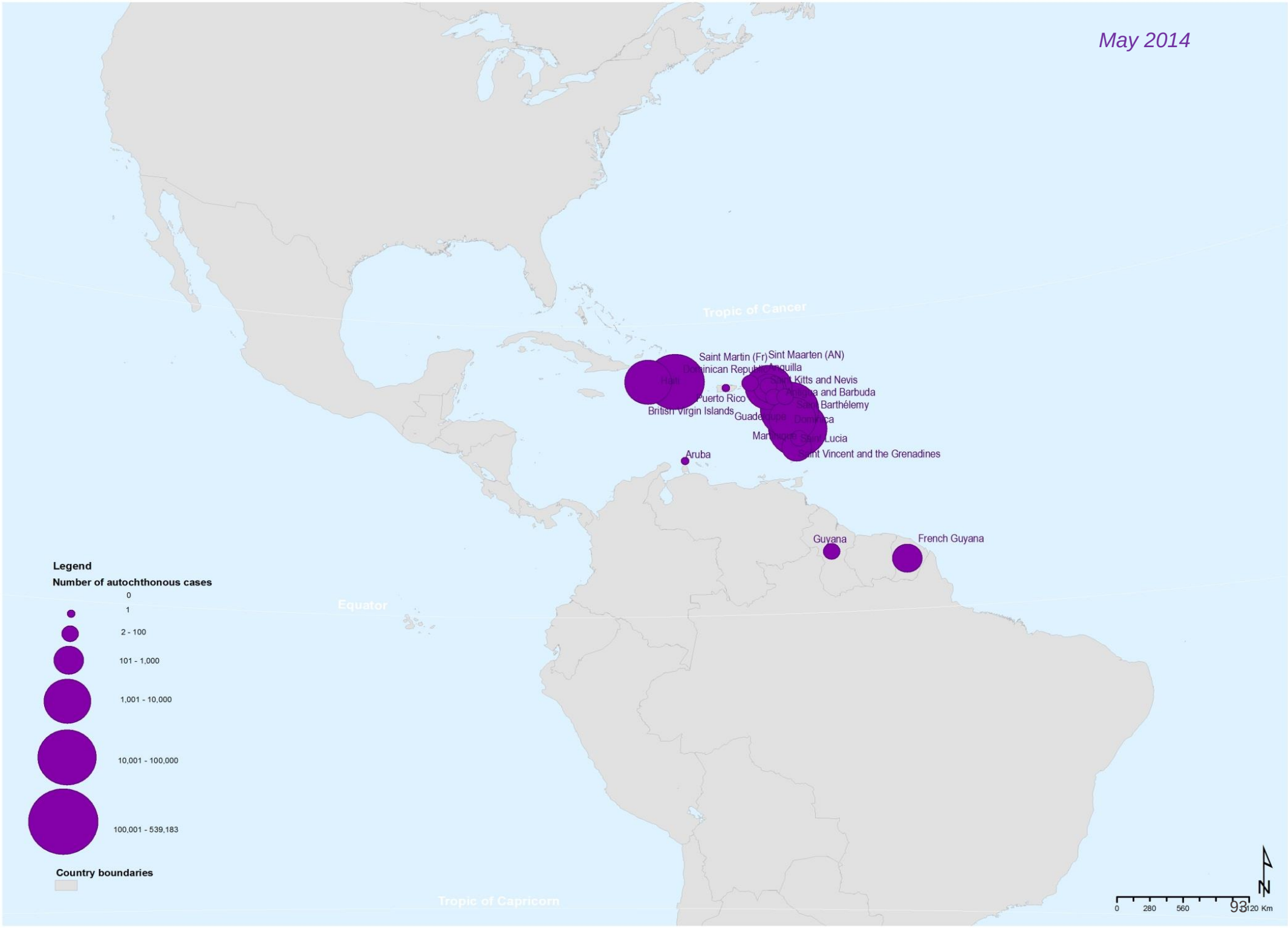
100,001 - 539,183
Country boundaries
0
280
560
1120 Km
N


March 2014
Tropic of Cancer
British Virgin Islands
Saint Martin
Sint Maarten (AN)
Anguilla
Saint Barthélemy
Saint Kitts and Nevis
Guadeloupe
Dominica
Martinique
Aruba
French Guyana
Equator
Tropic of Capricorn
Legend
Number of autochthonous cases
0
1
2 - 100
101 - 1,000
1,001 - 10,000
10,001 - 100,000
100,001 - 539,183
Country boundaries
0
280
560
1120 Km
N


April 2014
Tropic of Cancer
Equator
Tropic of Capricorn
Sint Maarten (AN)
Saint Martin (Fr)
Antigua and Barbuda
Saint Barthélemy
British Virgin Islands
Aruba
French Guyana
Legend
Number of autochthonous cases
0
1
2 - 100
101 - 1,000
1,001 - 10,000
10,001 - 100,000
100,001 - 539,183
Country boundaries
0
280
560
1,120 Km
N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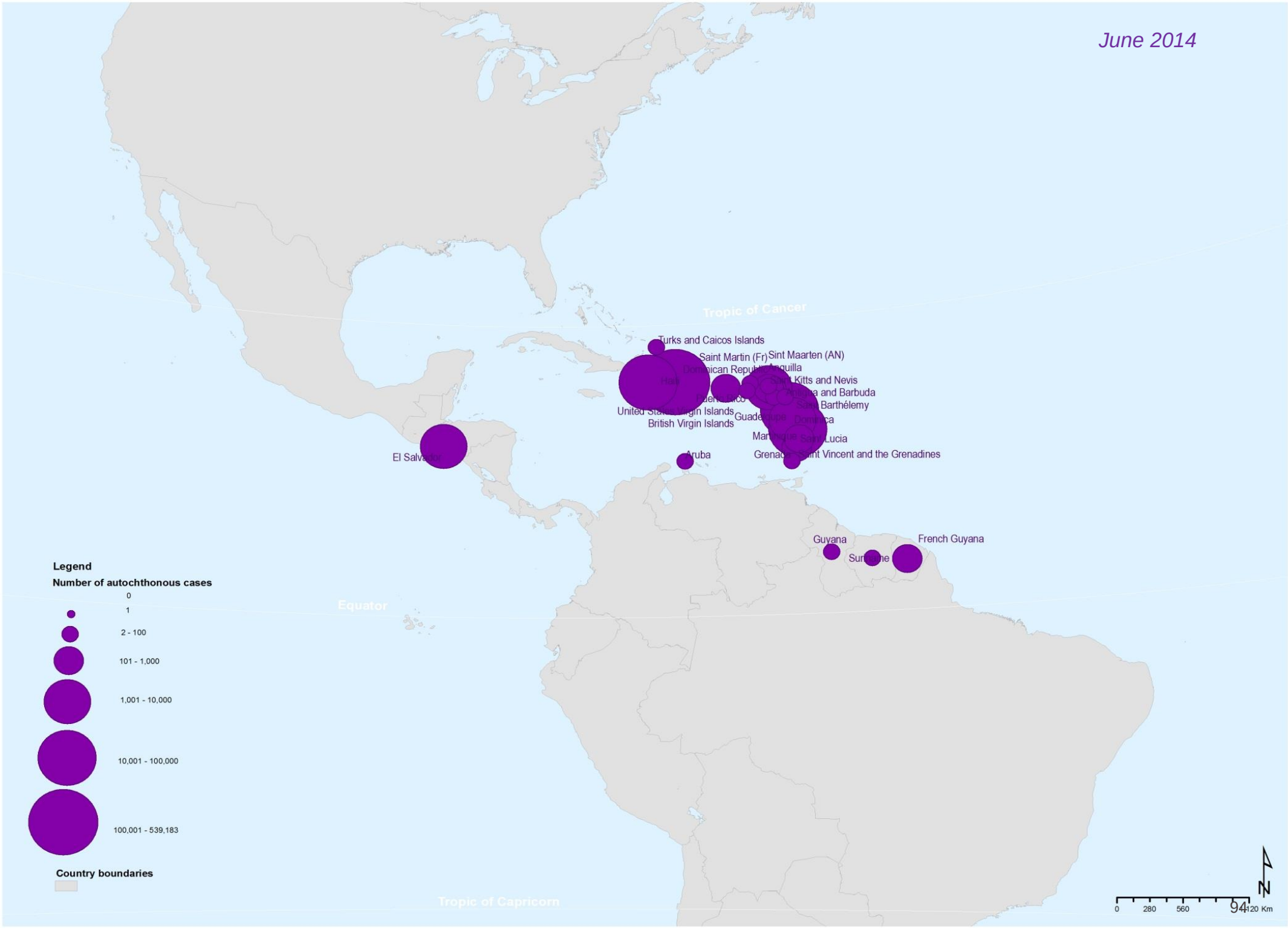
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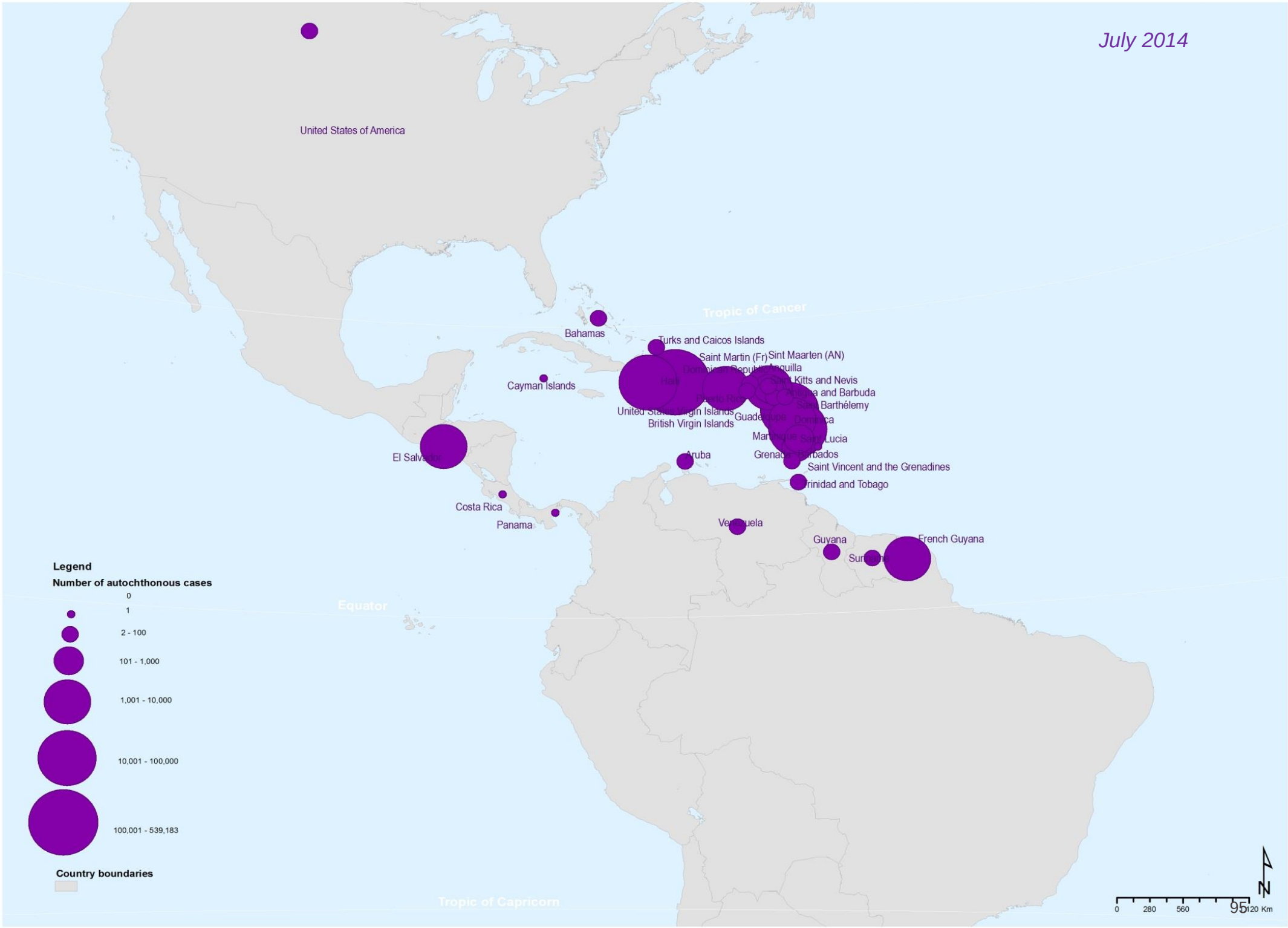
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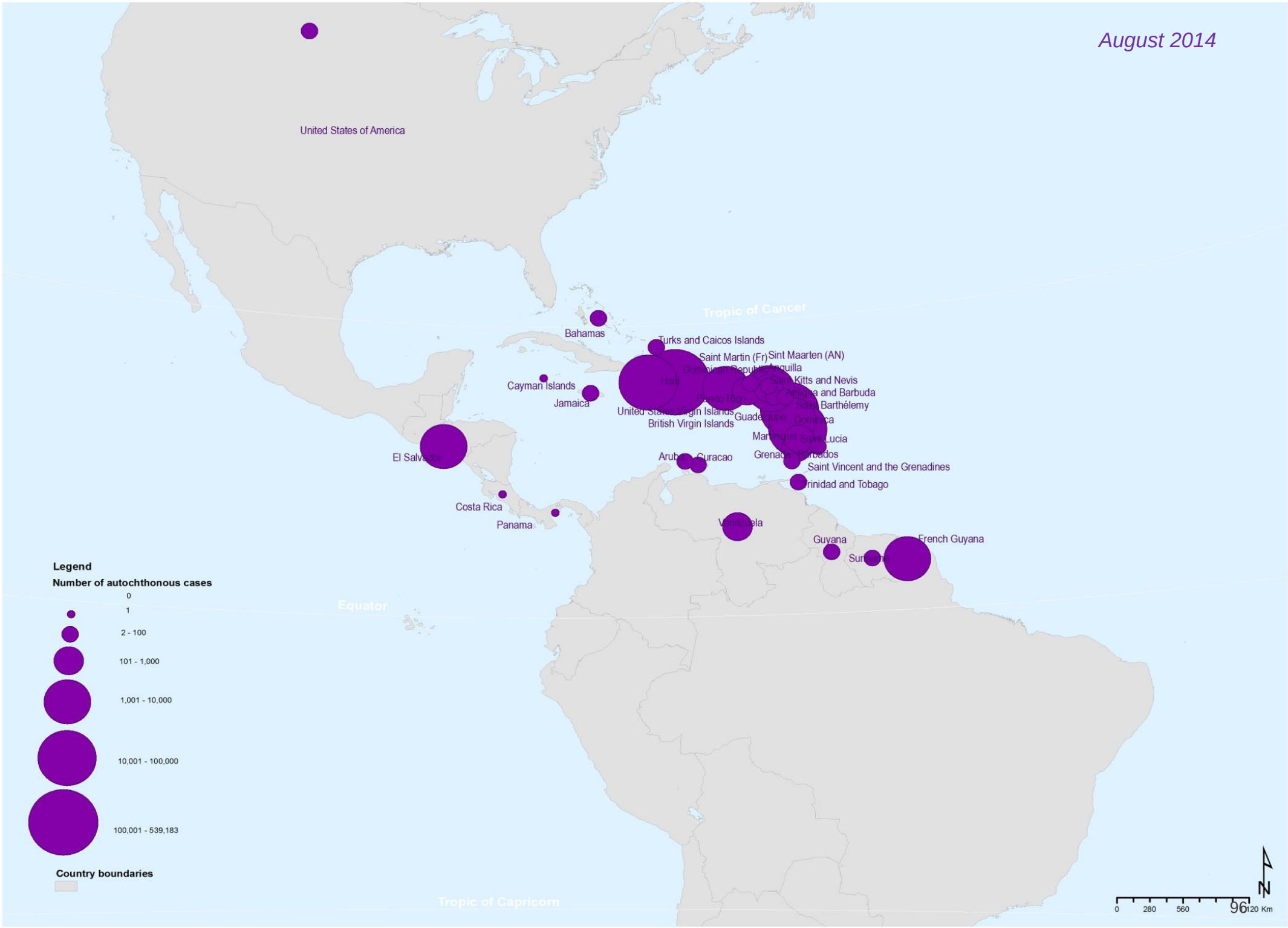
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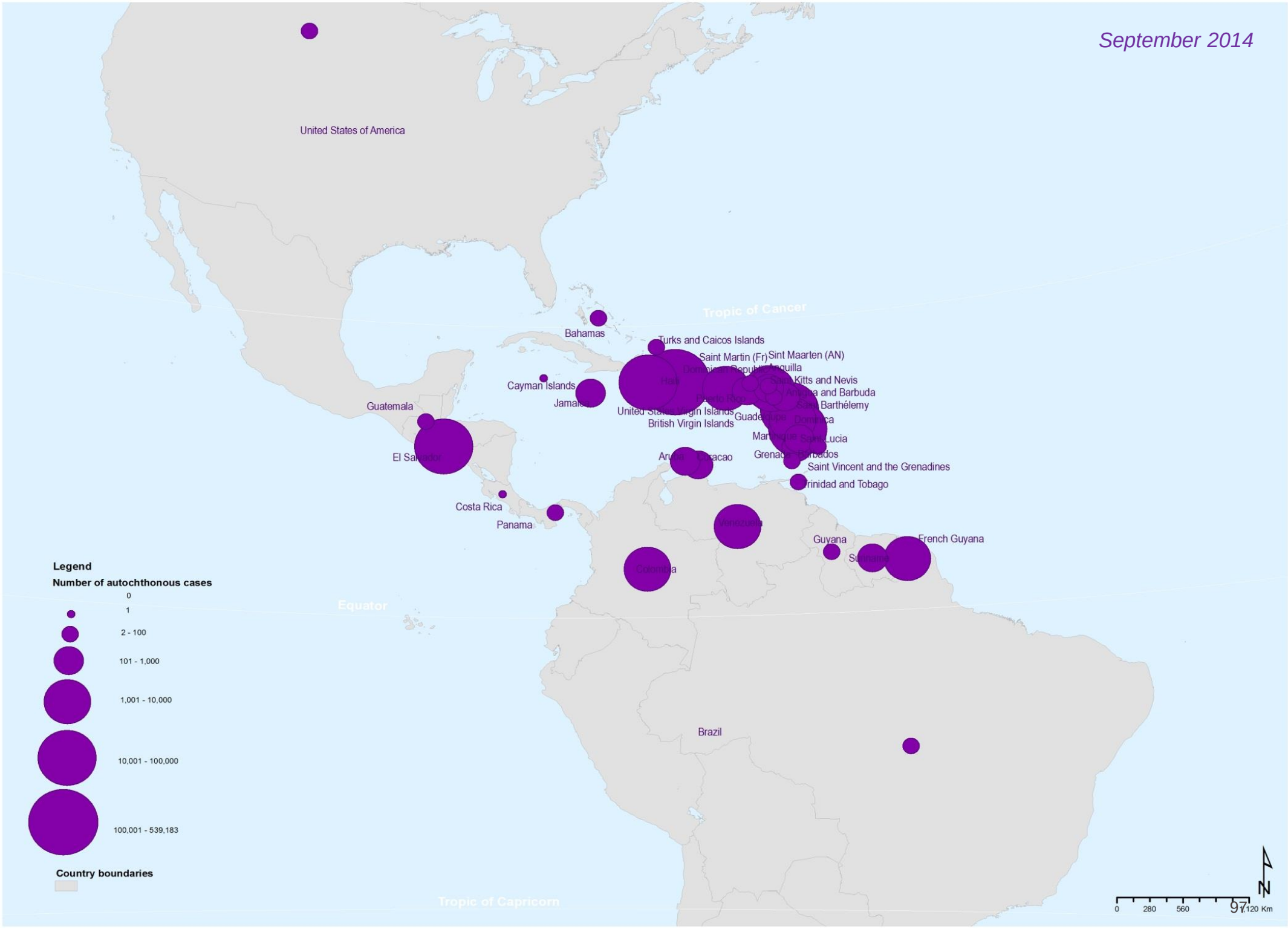
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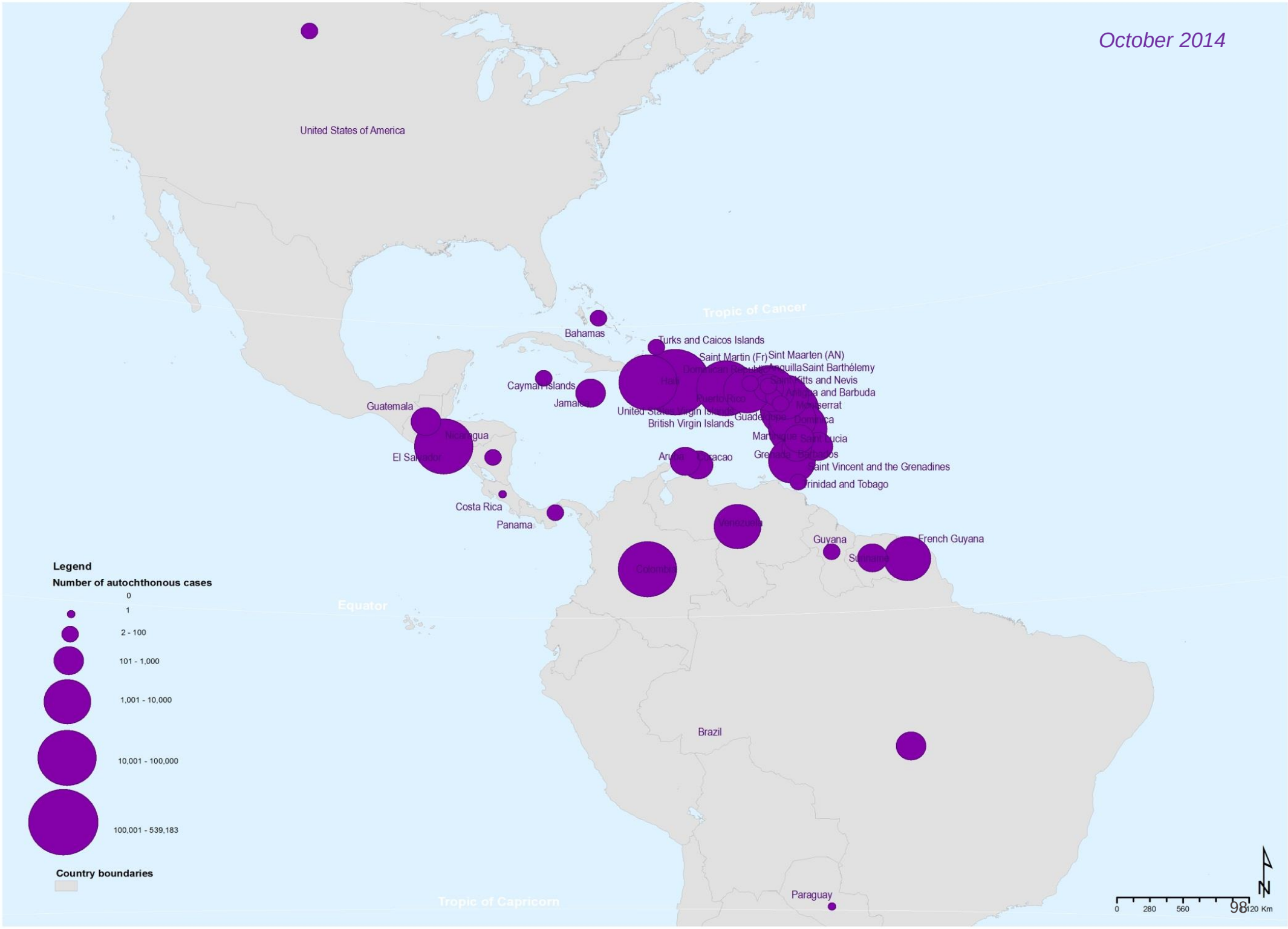
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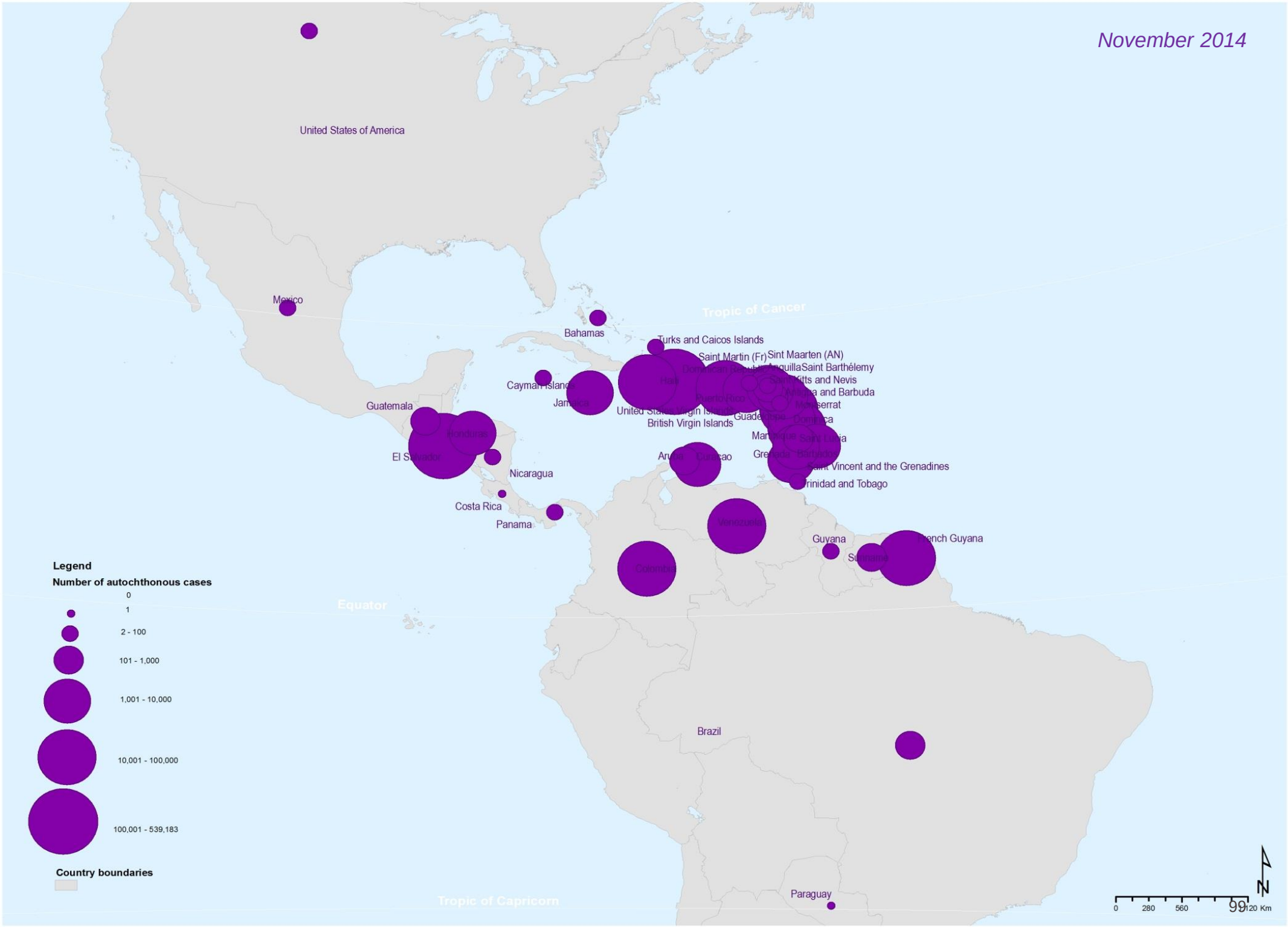
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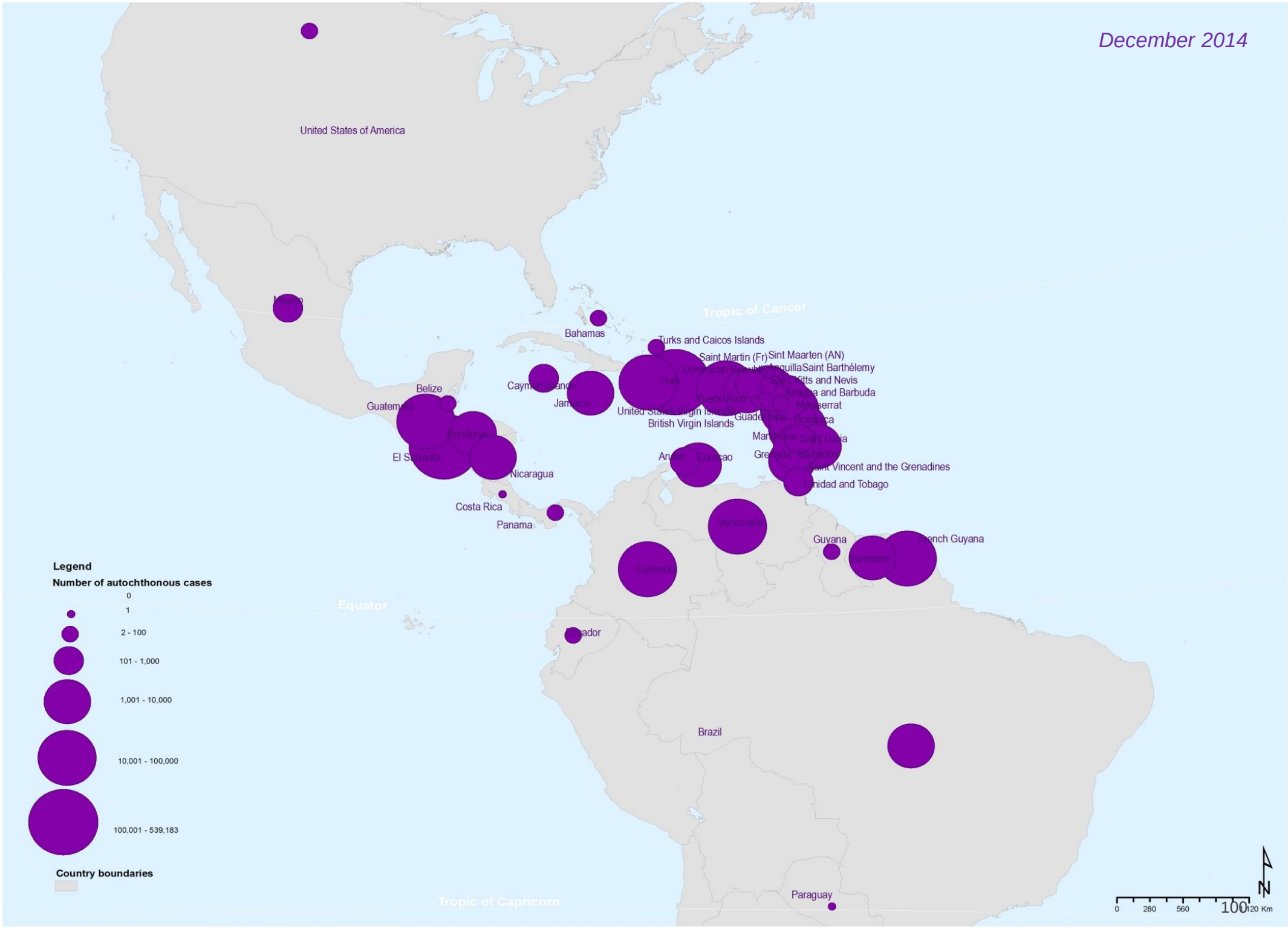
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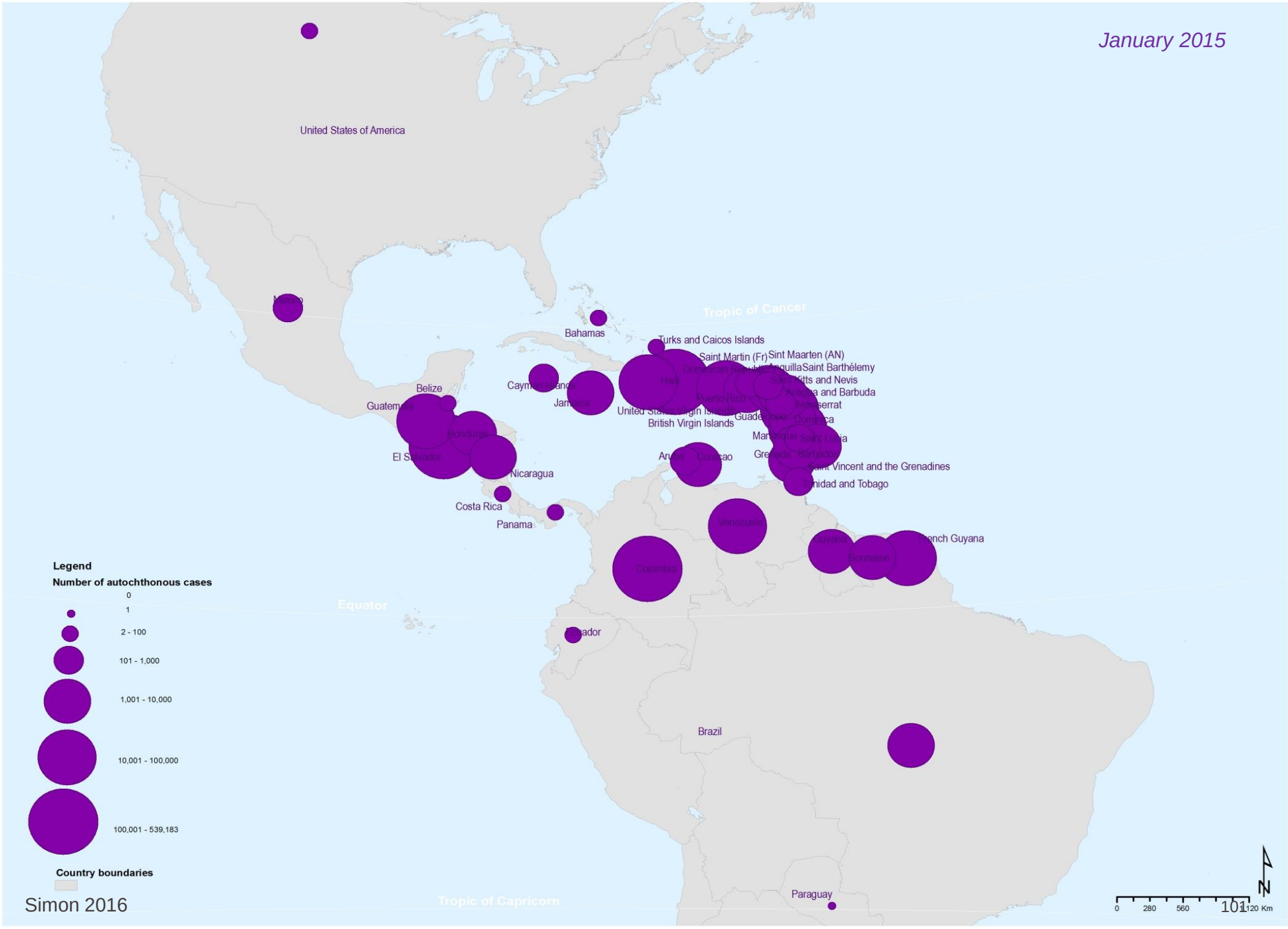
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Simon 2016

The Chikungunya Virus Vaccine Project

Valneva's Chikungunya Vaccine Candidate VLA1553

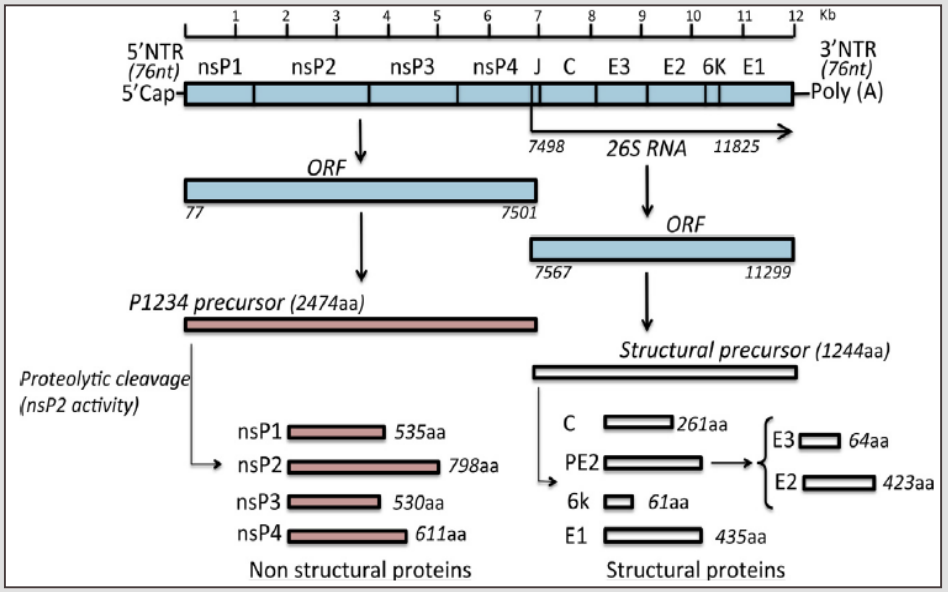
Attenuation Principle

CHIKV Δ5nsP3 (VLA1553) vaccine is based on ECS African strain of Indian Ocean lineage with cross-protective immunity against Asian isolate which is now rapidly spreading across the Americas.

- **60 amino acids deletion in gene encoding nsP3**
- No change of deletion detectable after up to 20 passages on Vero cells
- Slightly reduced plaque size as compared to CHIKV clone LR2006-OPY1
- Reduced replication (1.2×10^7 pfu/mL) as compared to CHIKV clone LR2006-OPY1 (4.4×10^8 pfu/mL)

Vaccine construct

CHIKV genome



Hallengärd et al. 2013

VLA1553 Target Product Profile

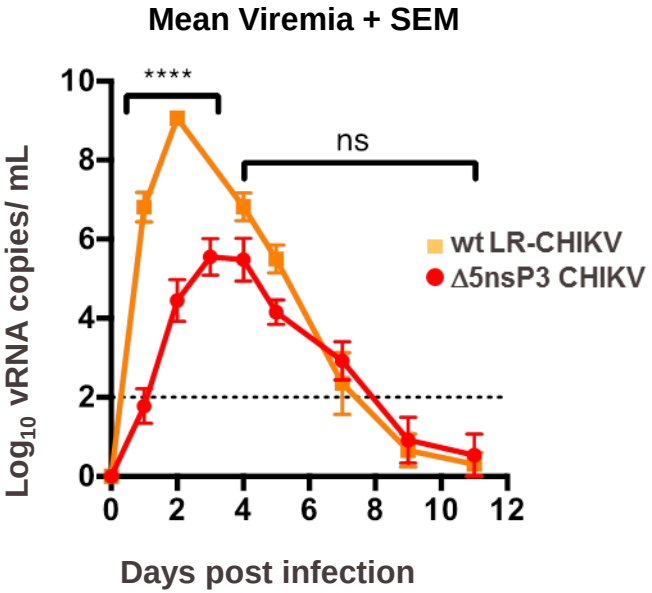
Chikungunya Vaccine Candidate Target Product Profile

Key Value Proposition	Single-dose, live-attenuated Chikungunya virus vaccine
Indication	Prophylactic active immunization against Chikungunya virus in individuals ≥ 1 year of age, including › Travelers to endemic or outbreak regions (e.g. HCPs, military, others) › Populations exposed to an outbreak situation (reactive emergency use) › Individuals living in endemic regions as routine/endemic use
Dose and Administration	› Route of administration: intramuscular or subcutaneous › Recommended dose: Single dose of 10^4 $TCID_{50}$/dose (or lower) live-attenuated Chikungunya virus › Dosage schedule: single-dose
Formulation	Lyophilized; 24-month stability at +2 to +8°C
Co-Administration	Co-administration with relevant traveler/military vaccines (e.g. DENV, Yellow Fever, Twinrix, JEV) and routine immunization vaccines
Desired Immune Response	› Neutralizing antibody response (useable as correlate of protection) › Protective against various Chikungunya outbreak phylo-groups and strains › Duration of protection: long lasting immunity, at least 5 years studied
Measures of Efficacy	› >95% (optimum) of vaccinated population show a protective antibody titer › 100% seroconversion rate for neutralizing antibodies at Day 14
Target Population / Target Groups	› Travelers, military personnel, HCPs › Individuals at risk who live in endemic regions
Safety	› Similar to licensed vaccines for active immunization in adults & children › Fever rate ≤ 20% › Suitable for malnourished populations

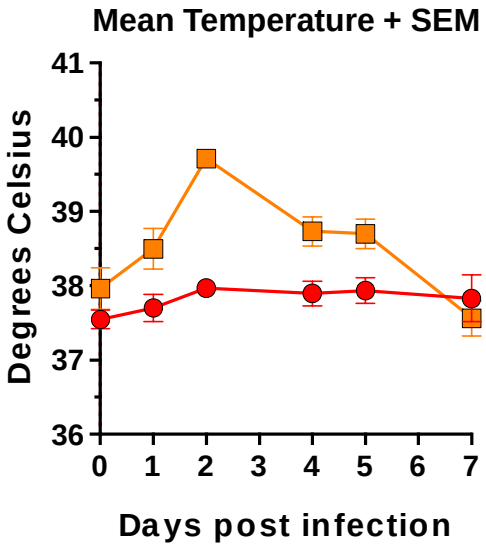
VLA1553 - Chikungunya Vaccine Candidate

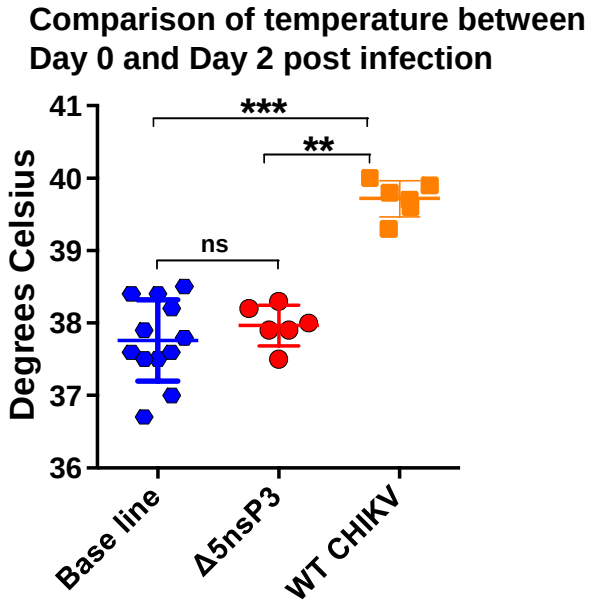
Non-Clinical Studies in Non Human Primates – Safety

- Viremia 3-4 logs lower than compared to wild type LR-CHIKV infection
- Delayed onset of viremia by 1-2 days compared to wild type LR-CHIKV infection
- No significant fever (rectal) after vaccination
- No fever (rectal) in vaccinated NHPs after wild type LR-CHIKV challenge
- No clinical signs of infection - edema, erythema, joint swelling, hunching, fur ruffling, rash (data not shown)



***** P < 0.0001; 2 way ANOVA*
+ Bonferoni's multiple comparison





***: P < 0.01; ***: P < 0.001; Kruskal-Wallis followed by Mann & Whitney rank test*

Source: Roques et al. 2016

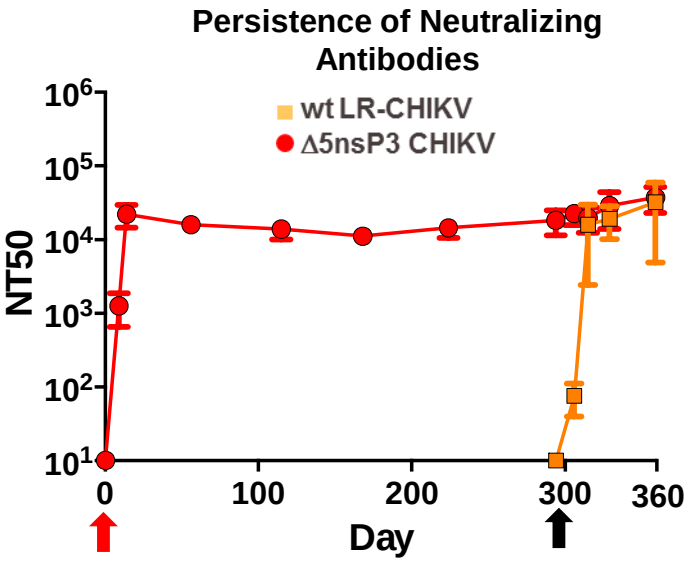
VLA1553 - Chikungunya Vaccine Candidate

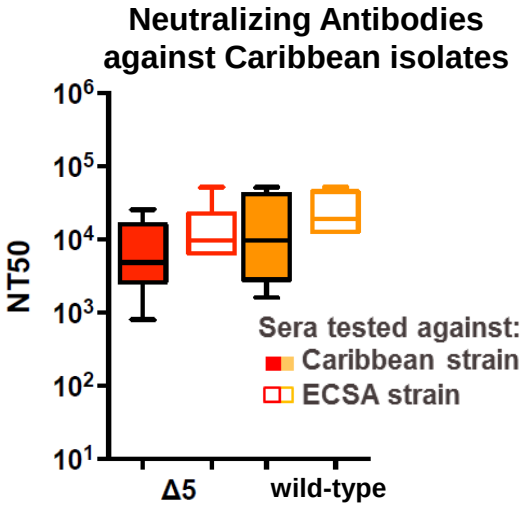
Non-Clinical Studies in Non Human Primates – Immunogenicity/Efficacy

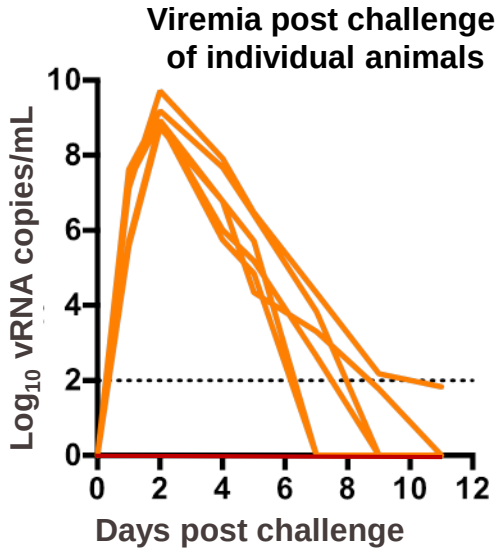
Neutralizing antibodies* against CHIKV in sera of cynomolgus macaques

Single immunization of 1 x 10^5 pfu VLA1553 s.c.

Challenge with app. 1 x 10^4 pfu (100 AID_{50}) wild type LR-CHIKV i.v.







- Strong and long-lasting immune response induced after single-shot in NHPs
- No anamnestic response observed after challenge with wild type LR-CHIKV
- Cross-neutralizing antibodies against Caribbean CHIKV strain induced
- No viremia at any time point observed in vaccinated NHPs upon challenge with high dose of wild type LR-CHIKV (100 AID_{50})

Source: Roques et al. 2016; * Neutralization titers measured by Luciferase assay.

VLA1553 – Chikungunya Vaccine Candidate
Summary pre-clinic: Safety and immunogenicity

- VLA1553 has a 60 aa deletion in nsP3 causing the attenuation which is stable and does not revert back when passaged 20 times on Vero cells
- A single shot of VLA1553 was highly immunogenic and induced a strong and long lasting neutralizing antibody response
- VLA1553 caused no clinical manifestations typically associated with wild type CHIKV infections in the NHP model
- VLA1553 showed delayed and strongly reduced viremia as compared to wild type CHIK infection
- VLA1553 is highly immunogenic and sufficiently attenuated to warrant clinical testing

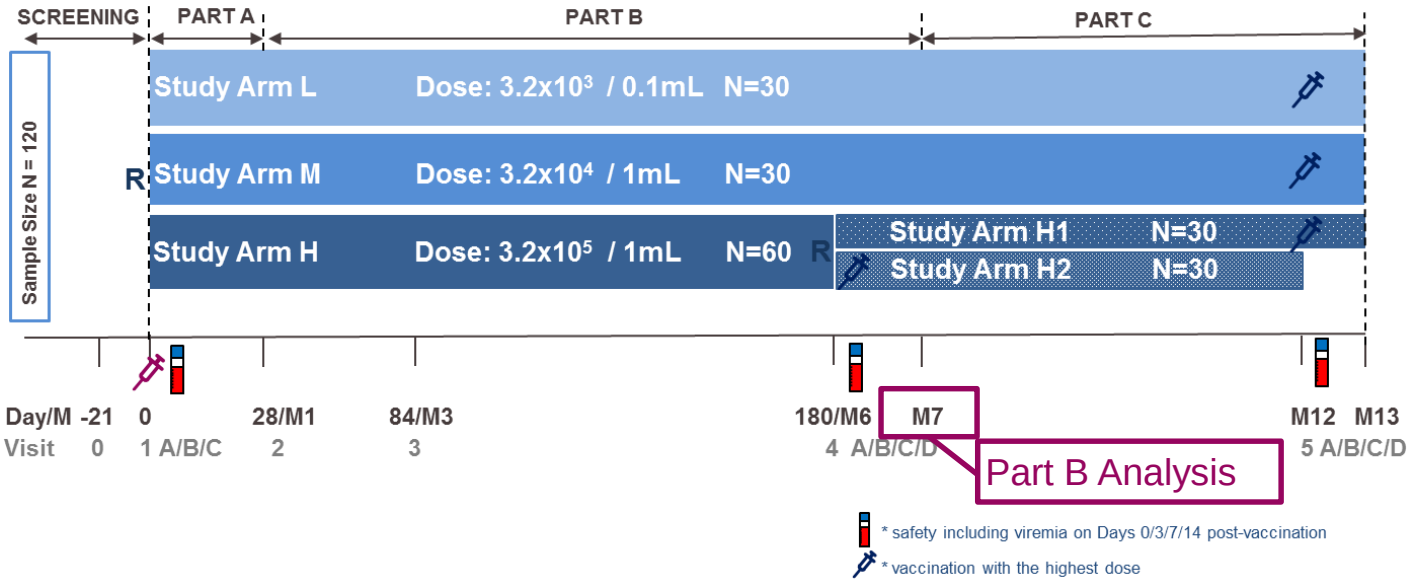
VLA1553 early development code = Δ5nsP3

Safety Phase 1

Valneva's Single Shot Chikungunya Vaccine Candidate

Phase 1 Study: VLA1553-101

- Observer-blinded, randomized, multicenter, dose escalation study
- Study Population: 120 healthy volunteers aged 18 to 45 years
- Dosage: $3.2x10^3$ $TCID_{50}$ (0.1ml), $3.2x10^4$ $TCID_{50}$ (1ml), $3.2x10^5$ $TCID_{50}$ (1ml)
- Immunization route: i.m.



Part B Analysis: safety and immunogenicity data up to Month 7 – unblinded at a group level
Final Part C Analysis expected Q1/2020

Re-vaccination at Month 6 (and12) with highest dose: Homologous viral challenge

VLA1553-101: Summary Safety Outcomes

No AE of Special Interest (AESI), one unrelated SAE in all dose groups

Solicited Local AEs:

- Few solicited local AEs were reported by 3.2%, 6.7% and 6.8% of subjects in Groups L, M and H, respectively; all mild.
- The most common solicited local AE was tenderness (5.1%, Group H).

Solicited Systemic AEs:

- Solicited systemic AEs were reported by 35.5%, 40.0% and 67.8% of subjects in Groups L, M and H, respectively (*p= 0.0040 and 0.0220 in pairwise comparisons to Group H*).
- Most solicited systemic AEs were mild or moderate.
- Fever was reported in 9.7%, 20.0% and 37.3% of subjects in Groups L, M and H, respectively, with a significant difference in pairwise comparison between Group L and H (*p= 0.0061)*.
- Muscle pain was reported in 3.2%, 13.3% and 30.5% of subjects in Groups L, M and H, respectively, with a significant difference in pairwise comparison between Group L and H (*p= 0.0022*).

Unsolicited AEs:

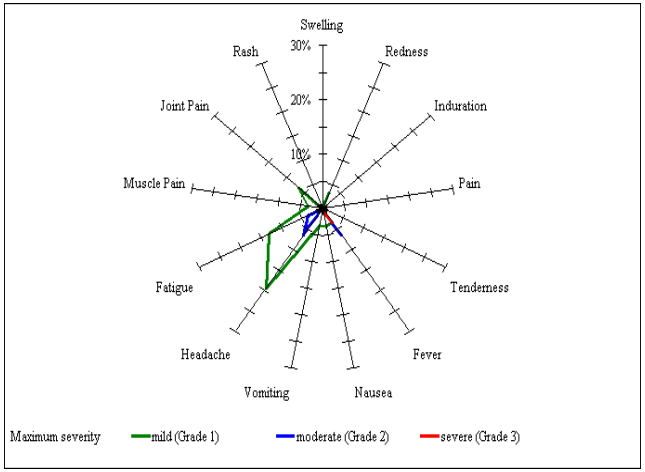
- Related unsolicited AEs were reported by 41.9%, 26.7% and 49.2% of subjects in Groups L, M and H, respectively, of those 9.7%, 3.3% and 3.4%, respectively, were reported as severe (6 cases).
- Severe unsolicited AEs were experienced by in Group L (1 case of back pain, 2 cases of neutropenia), in Group M (1 case of neutropenia) and in Group H (2 cases of lymphopenia). All without accompanying clinical signs or symptoms.

VLA1553-101: Higher Reactogenicity in High Dose Group

Subjects with solicited AEs after Single Vaccination by Maximum Severity

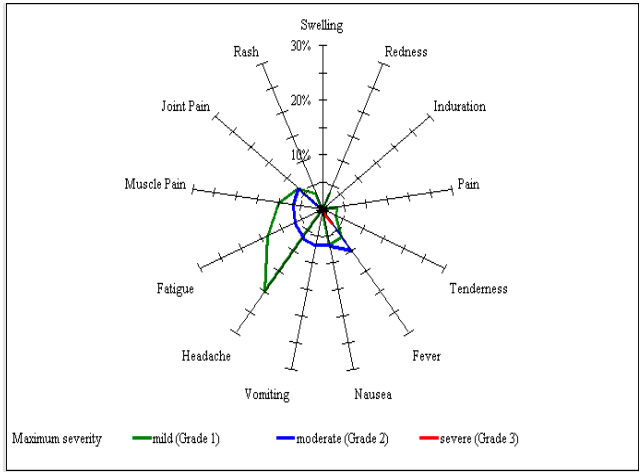
Low Dose

Low dose: 3.2*10^3 TCID$_{50}$



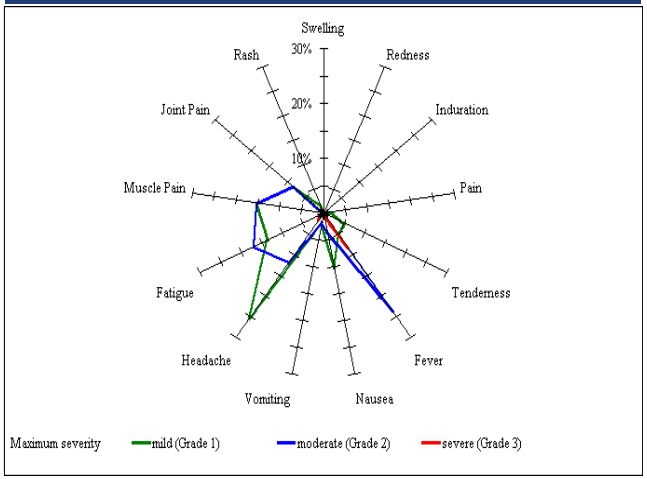
Medium Dose

Medium Dose: 3.2*10^4 TCID$_{50}$



High Dose

High Dose: 3.2*10^5 TCID$_{50}$



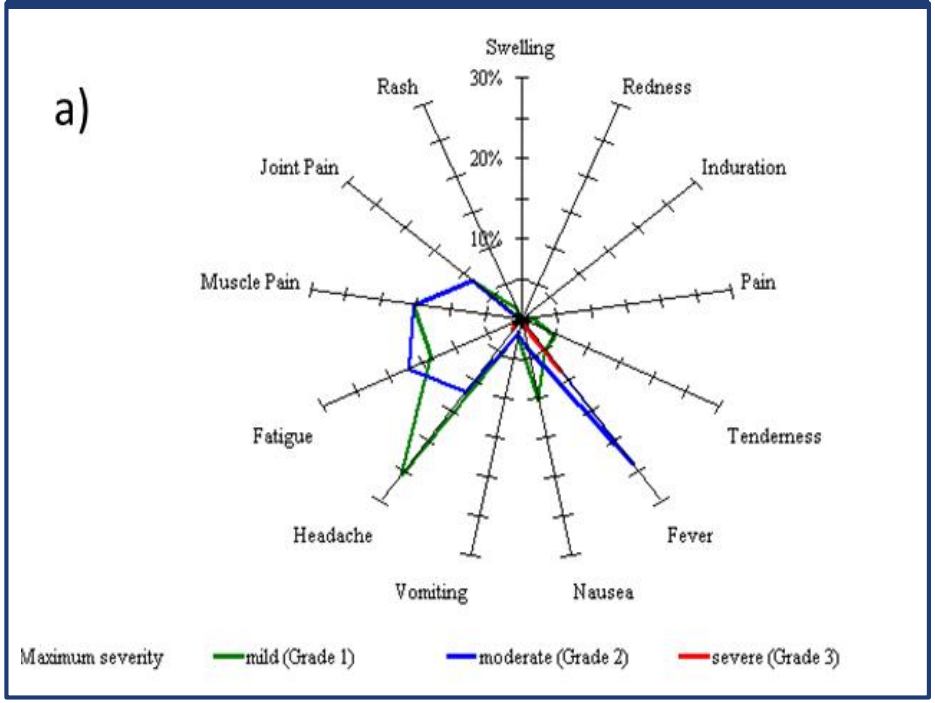
The low and medium dose of VLA1553 have a superior safety profile (including viremia) compared to the high dose group, which had a higher reactogenicity

No Adverse Events of Special Interest (AESIs) and one unrelated SAE were reported up to Month 7 in all dose groups

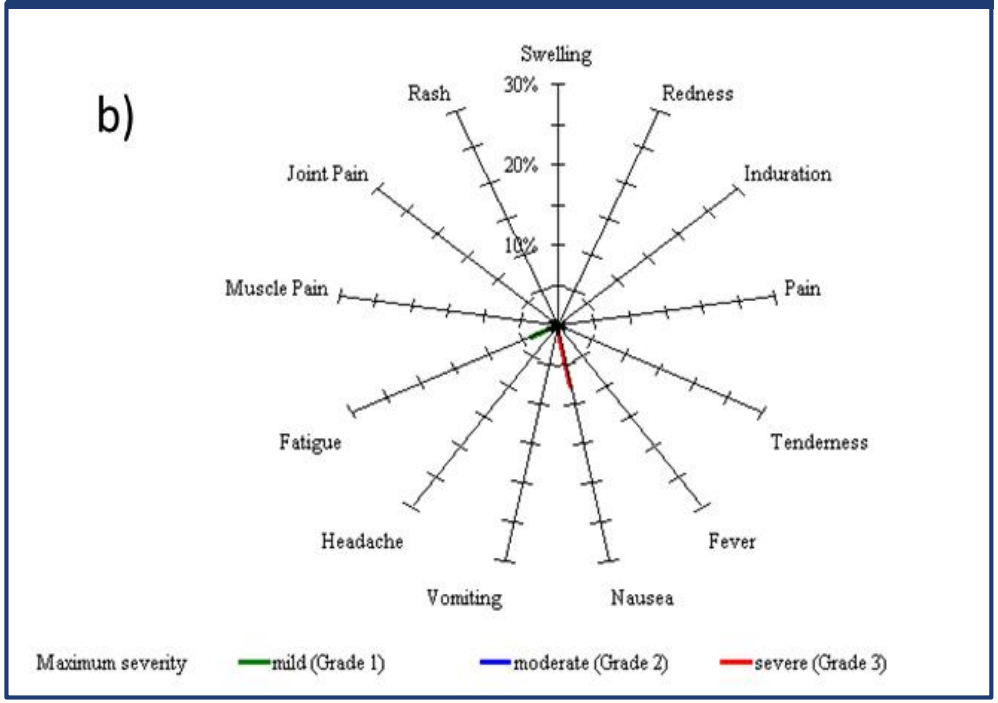
VLA1553-101: High Dose After Single- or Re-Vaccination

High Dose Vaccination Protects against Challenge-Induced AEs

Reactogenicity of High Dose After Single Vaccination



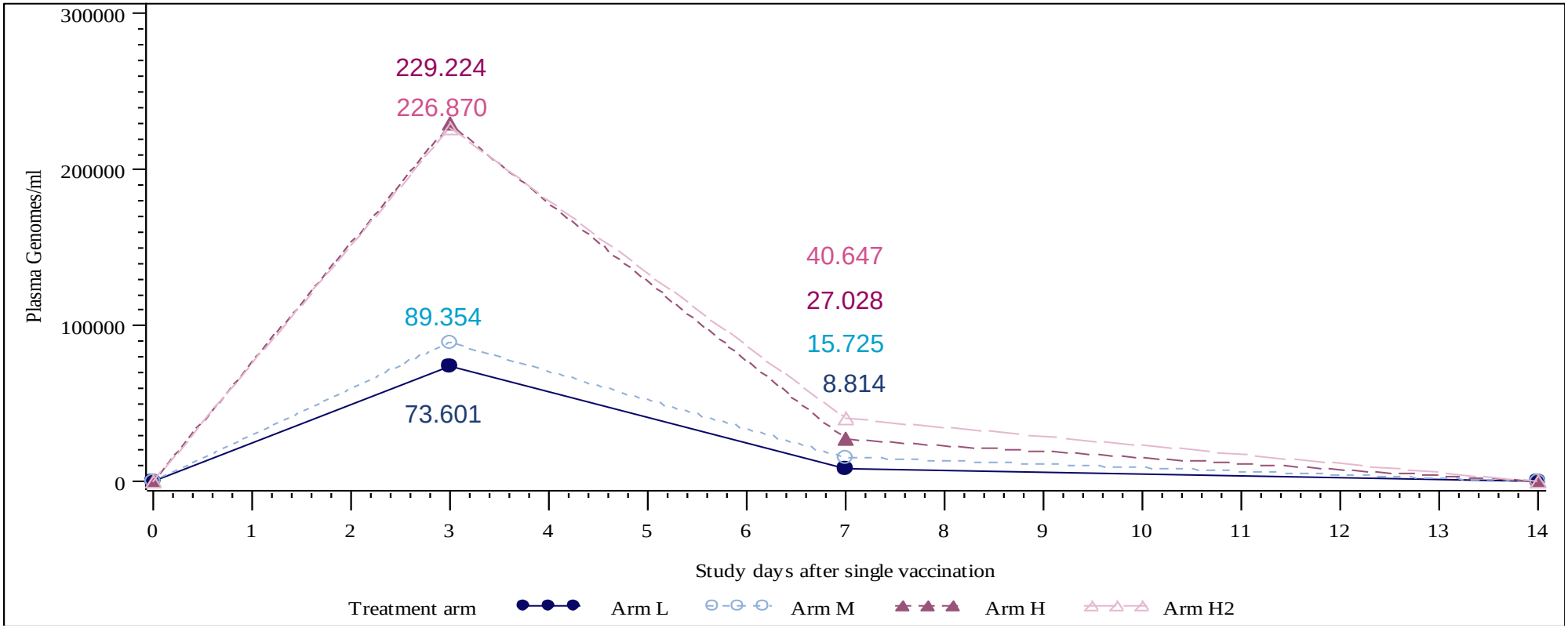
Reactogenicity of High Dose After Re-Vaccination (M6): Protection from AEs



High Dose: $3.2*10^5$ $TCID_{50}$

VLA1553-101

Plasma Viremia at Days 0, 3, 7, 14 after Single Dose



Numbers indicate 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.

No positive viremia result reported after re-vaccination!

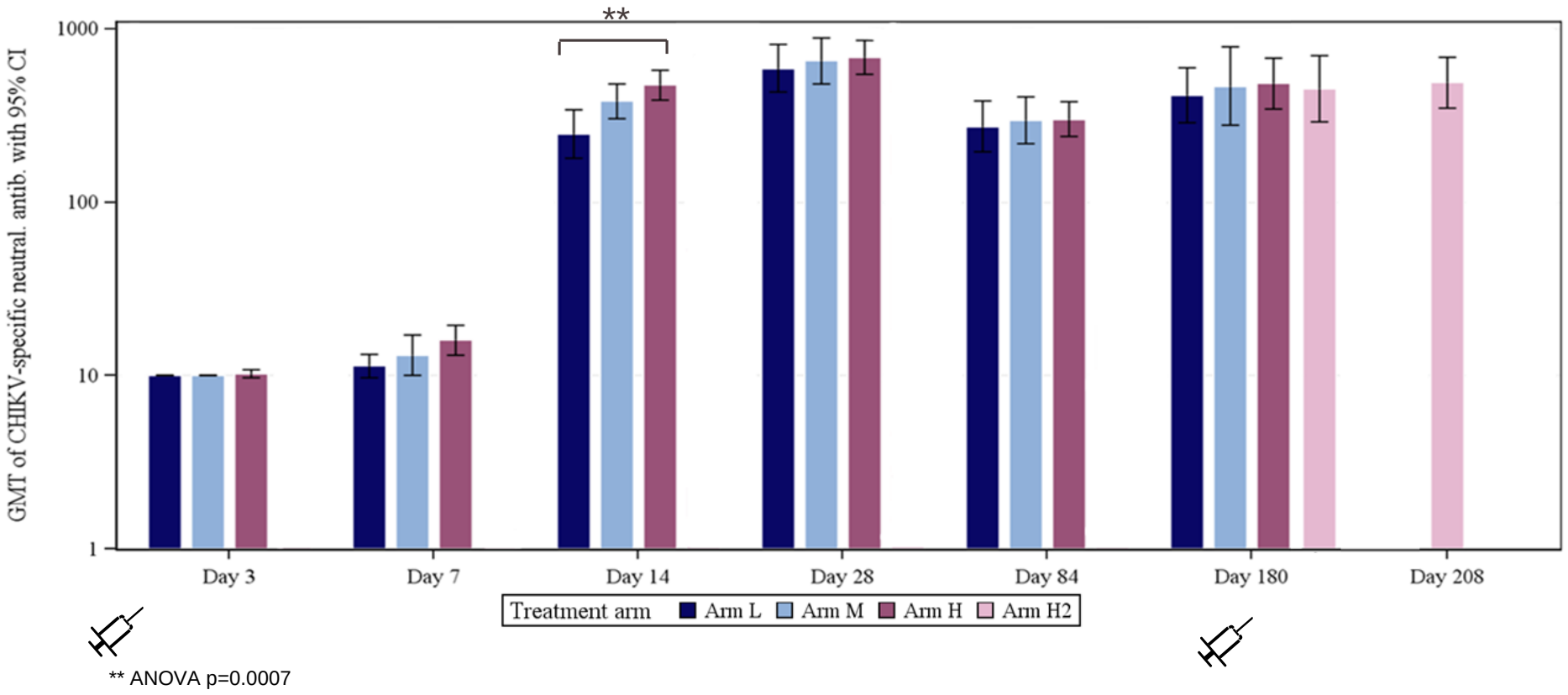
VLA1553-101 Phase 1
Conclusions - Safety

- VLA1553 was **generally safe and well-tolerated** in the low and medium dose group.
- The low and medium dose of VLA1553 have a **superior safety profile** (including viremia) compared to the high dose group.
- **No Adverse Events of Special Interest (AESIs)** and one unrelated SAE were reported up to Month 7.
- The local tolerability profile at all dose levels was considered excellent. Notable systemic adverse events included short-term fever, headache and muscle pain. Rates were lower in the low (significantly) and medium dose groups compared to the high dose group.
- **Early Proof of Efficacy**: Following re-vaccination (“intrinsic human viral challenge”) vaccinees were protected from vaccine induced viremia as indicated by the absence of positive viremia results in plasma and urine as well as associated adverse events.

Immunogenicity Phase 1

VLA1553-101: High GMTs in All Dose Groups Day 14

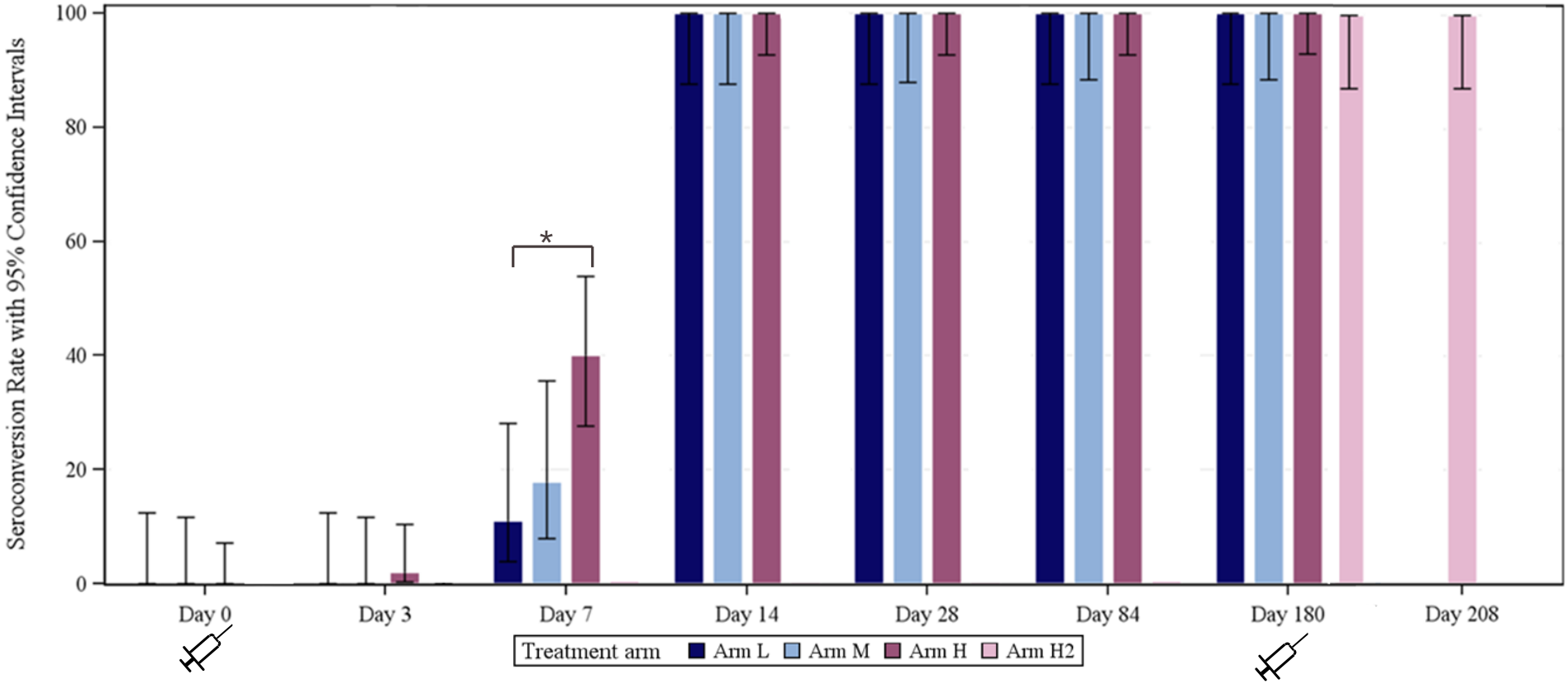
CHIKV-specific neutralizing antibodies (GMT) after Single Vaccination and Re-Vaccination



** ANOVA p=0.0007

VLA1553-101: 100% SCR Day 14

CHIKV-specific Seroconversion Rates after Single and Re-Vaccination



SCR defined as proportion of subjects achieving a CHIKV-specific neutralizing antibody titer of at least 20 (NT_{50} ≥20)

* Pairwise test p=0.0092

VLA1553-101 Phase 1
Summary and Conclusions - Immunogenicity

VLA1553 showed an **excellent immunogenicity** profile after a **single vaccination** in all dose groups.

- **100% seroconversion* was already achieved at Day 14** after a single vaccination in all dose groups and sustained at 100% until Month 6.
- > 96.3% of the subjects in all dose groups achieved an at least 16-fold increase in antibody titers at Day 28.
- Mean peak antibody titers at Day 28 ranged from 592.6 to 686.9 GMT from Groups L to H, respectively, with max. titers reaching 2560.
- **A single vaccination is sufficient to induce sustaining high titer neutralizing antibodies**, as demonstrated by the absence of an anamnestic response following re-vaccination and the development of sterilizing immunity characterized by a ≤ 4-fold increase (96.2% of subjects) in antibody titers as compared to pre-vaccination titers.

* Seroconversion defined as the proportion of subjects achieving a CHIKV-specific neutralizing antibody titer of NT_{50} ≥20

Overall Conclusions Phase 1

VLA1553-101 Phase 1
Overall Conclusions

- VLA1553 was well-tolerated in the low and medium dose groups and generally safe in all dose groups after a single vaccination. The low and medium dose of VLA1553 have a **superior safety profile** (including viremia) compared to the high dose group.
- VLA1553 showed an excellent immunogenicity profile in all dose groups after a single vaccination.
- 100% seroconversion* was achieved at Day 14 after a single vaccination in all dose groups and sustained at 100% until Month 6.
- The absence of an anamnestic response following re-vaccination demonstrates that a single vaccination of VLA1553 was sufficient to induce sustaining high titer neutralizing antibodies.
- Following re-vaccination (“intrinsic human viral challenge”) vaccinees are protected from vaccine induced viremia.

*Seroconversion defined as the proportion of subjects achieving a CHIKV-specific neutralizing antibody titer of NT_{50} ≥20

Next steps

VLA1553: Regulatory Pathway to Licensure

Approval of Chikungunya vaccine based on immunological correlate

Immune Correlate of Protection (ICOP)

- Good evidence from animals and humans that neutralizing antibodies provide protection against CHIKV[1].
- Robust IgM/IgG antibody responses following CHIKV infection in humans and animal models.
- Neutralizing antibodies primarily target E1/E2 structural proteins and are protective in passive transfer studies.
- Natural infection is believed to confer life-long immunity[2,3].
- Serological threshold associated with protection after natural infection:
- Presence of neutralizing antibodies against CHIKV of $PRNT_{80}$ ≥10 was associated with 100% protection from symptomatic CHIKV infection in a prospective human cohort study in the Philippines[4] (potential ICOP).

→ In order to establish a threshold titer for protection after vaccination with VLA1553, Valneva will conduct studies with NHPs using human sera from VLA1553-101.

[1]Gasque P et al 2015; [2]Galatas B et al.2016; [3]Nitatpattana N et al. 2014; [4]Yoon I-K. et al.2015

VLA1553: Further Development Considerations and Plans

Outline Accelerated Clinical Development *

FDA Fast track granted to VLA1553 development program

Phase 1 generated data for dose-selection

- 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

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

Aiming at accelerated approval procedure at FDA

VLA1553: Further Development Considerations and Plans

Outline Accelerated Clinical Development *

Pivotal Study Considerations

- Large double-blinded, controlled, multicenter safety and immunogenicity study in adults ≥18 yrs.
- N = ca. 4,000 subjects of either gender
- Including antibody persistence follow-up for one year

Lot-to-Lot Study Considerations

- To demonstrate lot-to-lot manufacturing consistency in adults aged 18 to 64 yrs.
- Randomized to three different manufacturing lots

Pediatric Development Plan

- Pediatric development plan (i.e. PIP and iPSP) for appropriate pediatric age group under development and subject to regulatory discussion

QUESTIONS & ANSWERS

CLOSING REMARKS

Thank you
Merci
Danke
Tack

valneva