



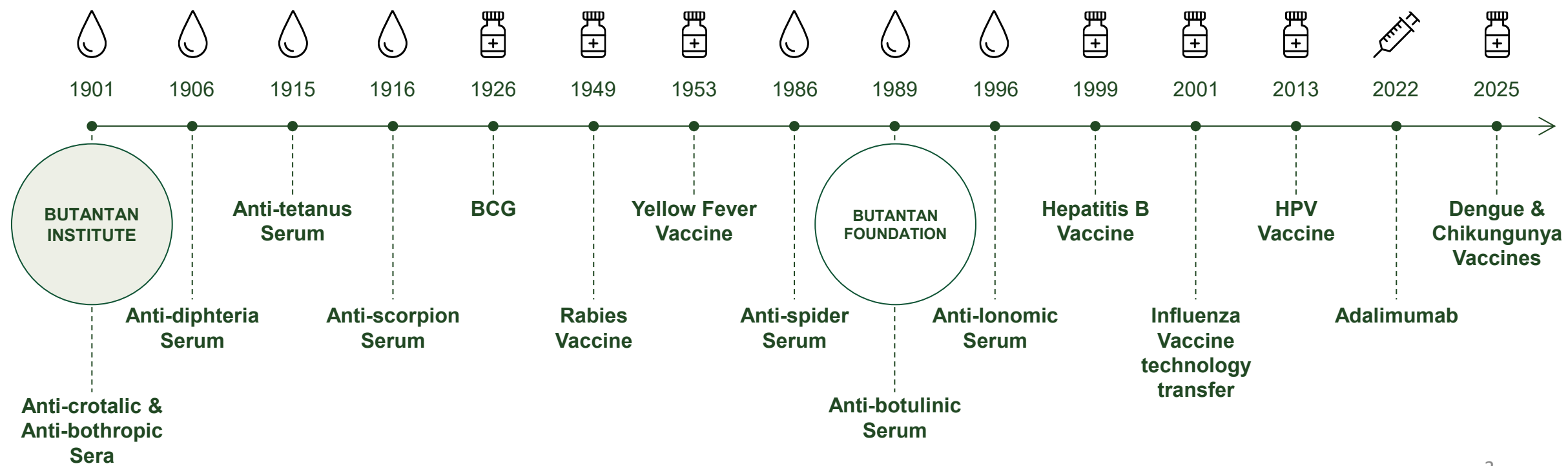
125
ANOS

Vaccine innovation and production

Butantan Science Goes Global

CENTENNIAL, NOT-FOR-PROFIT, STATE OF SÃO PAULO OWNED RESEARCH INSTITUTE

- BASIC RESEARCH
- APPLIED RESEARCH
- PRODUCT DEVELOPMENT
- CULTURE
- EDUCATION
- HEALTH SCIENCE ADVOCACY

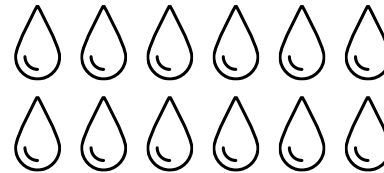


PORTFÓLIO ATUAL



10 VACCINES

Flu*, HPV*, DTP/DTPa*,
Hep A*, Hep B, Rabies, RSV*,
Covid-19 mRNA*,
Chikungunya, Dengue



12 ANTITOXINS E ANTIVENOMS

For snakes, spiders, scorpions,
caterpillars, bacterial toxins and
rabies virus



4 MONOCLONAL ANTIBODIES

Adalimumab*,
Natalizumab*,
Pembrolizumab*,
Bevacizumab*

*Transferência de tecnologia

Our current projects and capabilities for pandemic and emergency response





NEW QUALITY BUILDING

VACC.
BACT.
INFECTION

P41CG/FOR/SEA

PAM 2

HPV

CPF14

DTP

CAR

PAM

CPS

HEPATITIS B

INVENTORY

CPMV

FACILITIES

BIOBANCO

CPR – mRNA API
MANUFACTURING PLANT

INFLUENZA

PVD
DENGUE
PRODUCTION

PBI

NEW RESEARCH,
DEVELOPMENT
AND INNOVATION
BUILDING

Industrial Capacity

FUTURE FACILITIES

Bio Industrial Capacity

01

Influenza Vaccine Factory **140M doses**

2026 production of 70 million doses entirely supplied to Unified Health System (SUS)



02

CPMV Factory/BLS-3 Factory **100M doses**

Multipurpose cell-based vaccine production site, one of the few BSL-3 facilities in Brazil



03

Freeze-Dried Vaccine Production Site **1.6M Freeze-dried doses** **580M liquid doses**

Production of vaccines against dengue and chikungunya



04

Monoclonal Antibody Factory **Up to 2,000L stirred-tank bioreactor**

Treatment of cancer, autoimmune diseases and chronic degenerative diseases



Bioindustrial Capacity

05

Cold Storage Warehouse

Center for storage of all the finished products of Butantan



06

Multipurpose Form and Fill Facility

Two lines for formulation, fill and finishh, and secondary packaging



07

Administrative Center

Located at the former Arts Museum Paço das Artes, it now houses the headquarters of both Butantan Institute





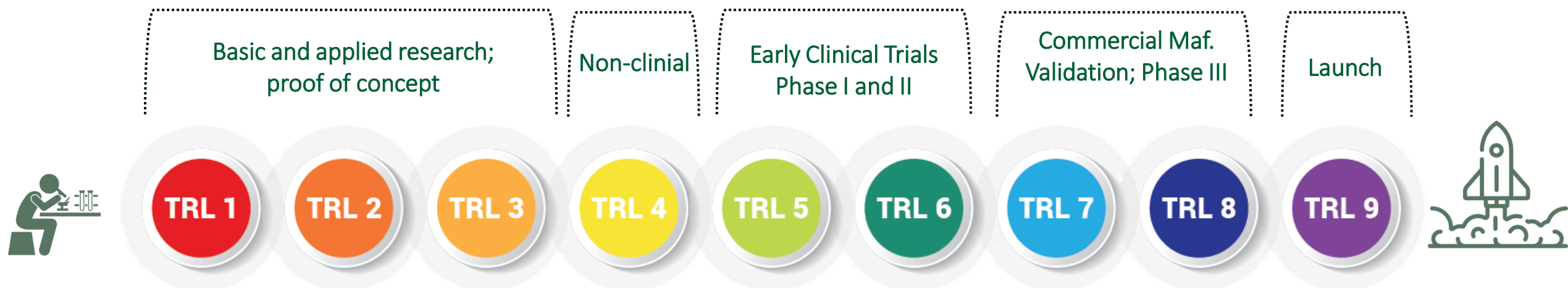
Our manufacturing platforms

Platforms	Current	2026-2030
VACCINES	EGG-BASED	EXPANDED EGG-BASED
	CELL-BASED	EXPANDED CELL-BASED
		mRNA PLATFORM
		SACCHAROMYCES
		PROKARYOTIC-BASED
SERA	12 TYPES	12 TYPES
MONOCLONAL ANTIBODIES	CELL-BASED	+ BIOSIMILARS AND INNOVATIVE TROPICAL DISEASES



Building the Technology Route at Butantan

TRL: Technology readiness level scale

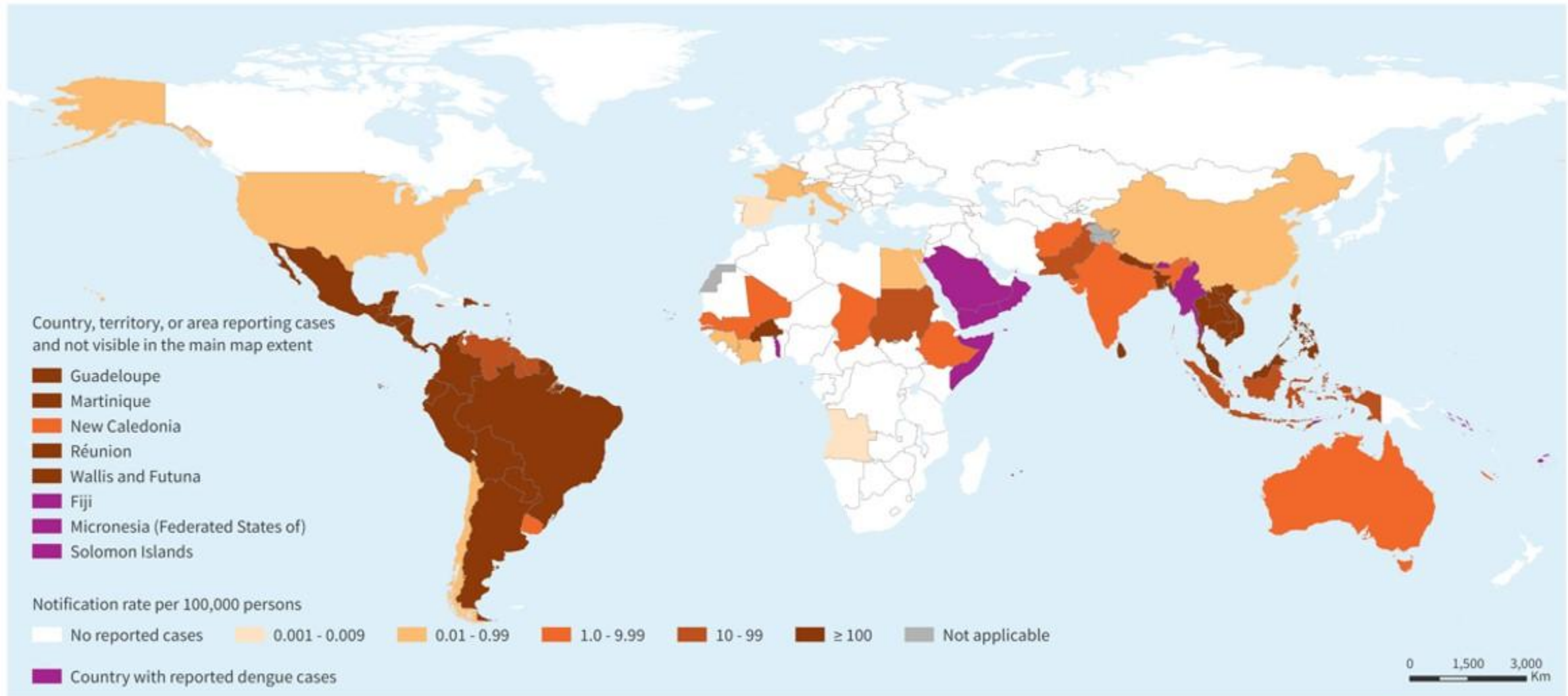


Center for Scientific Development (CDC)
 Center for Development and Innovation (CDI)
 Non-Clinical Capabilities Network
 R&D and Proof of Concept teams

Full Clinical Development Capabilities
 Biobank and Biorepository
 +60 Clinical Sites
 Pilot plants for clinical material

cGMP Facilities for different platforms
 Reg Affairs teams
 Phase IV and pharmacovigilance

DENGUE: APPROXIMATELY 50% OF THE WORLD POPULATION AT RISK

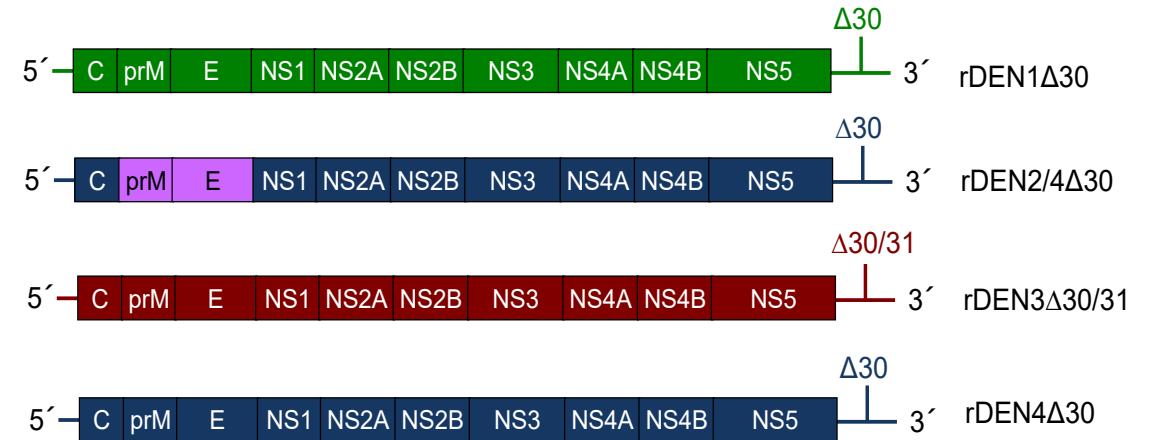


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Data Source: World Health Organization, European Centre for Disease Prevention and Control
 Map Production: WHO Health Emergencies Programme
 Map Date: 8 December 2023

BUTANTAN-DV COMPOSITION

- Lyophilized, live-attenuated, tetravalent dengue vaccine analogous to **TV003** developed by the U.S. National Institutes of Health^{1,2}
- Attenuation is based on deletion of stem loop structure(s) in the 3 prime untranslated region
- Targets delivery of 10^3 plaque forming units of each vaccine virus strain representing all four serotypes



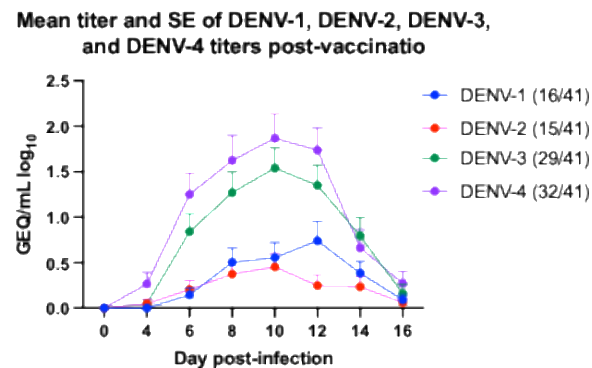
Steve Whitehead

¹Blaney, JE et al and SS Whitehead, *Viral Immunol* 2006;19(1):10-32

²Kallas, EG et al, *Lancet Infect Dis.* 2020;20(7):839-850

CLINICAL DEVELOPMENT: PHASE 2

- Safe and well tolerated
- **TV003** and **Butantan-DV** are equivalent
 - Liquid vs. lyophilized
 - Single dose vs. two doses
 - Immunogenic in seronegative and seropositive subjects
 - Cellular immune responses present

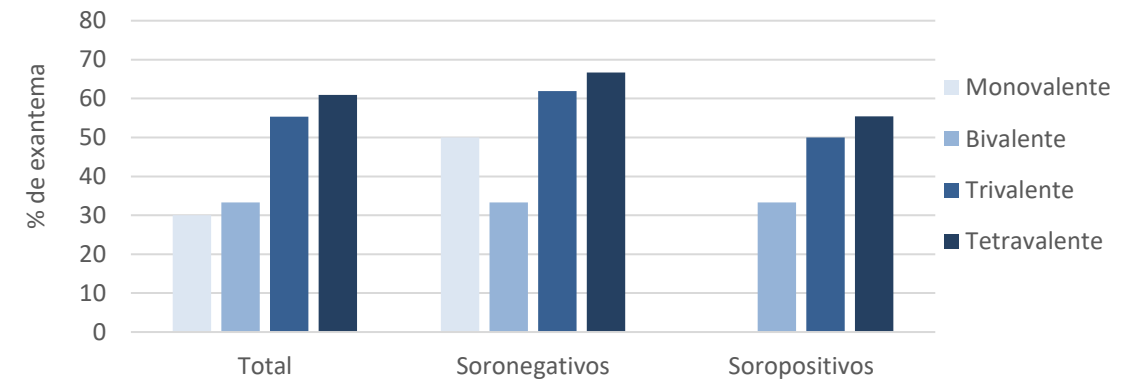


Kallas, EG et al, *Lancet Infect Dis.* 2020;20(7):839-850

Safety and immunogenicity of the tetravalent, live-attenuated dengue vaccine Butantan-DV in adults in Brazil: a two-step, double-blind, randomised placebo-controlled phase 2 trial



Esper G Kallas, Alexander Roberto Precioso, Ricardo Palacios, Beatriz Thomé, Patrícia Emilia Braga, Tazio Vanni, Lúcia M A Campos, Lilian Ferrari, Gabriella Mondini, Maria da Graça Salomão, Anderson da Silva, Heloisa M Espinola, Joane do Prado Santos, Cecília L S Santos, Maria do Carmo S T Timenetsky, João Luiz Miraglia, Neuza M F Gallina, Daniela Weiskopf, Alessandro Sette, Raphaella Goulart, Rafael Tavares Salles, Alvino Maestri, Adriana Maluf Elias Sallum, Sylvia Costa Lima Farhat, Neuza K Sakita, Juliana C O A Ferreira, Cassia G T Silveira, Priscilla R Costa, Isaías Raw, Stephen S Whitehead, Anna P Durbin, Jorge Kalil

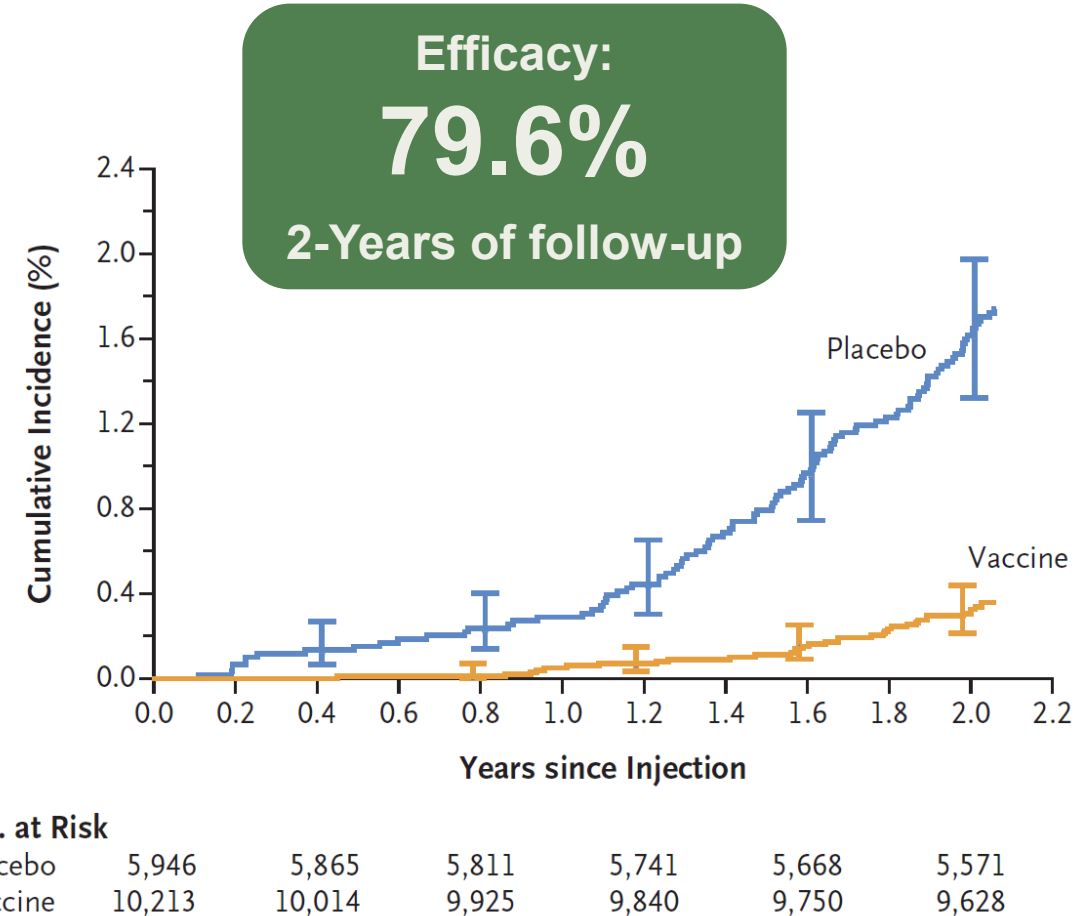


BUTANTAN-DV PHASE 3 CLINICAL TRIAL – TWO YEARS PRELIMINARY RESULTS



Live, Attenuated, Tetravalent Butantan–Dengue Vaccine in Children and Adults

E.G. Kallás, M.A.T. Cintra, J.A. Moreira, E.G. Patiño, P.E. Braga, J.C.V. Tenório, V. Infante, R. Palacios, M.V.G. de Lacerda, D.B. Pereira, A.J. da Fonseca, R.Q. Gurgel, I.C.-B. Coelho, C.J.F. Fontes, E.T.A. Marques, G.A.S. Romero, M.M. Teixeira, A.M. Siqueira, A.M.P. Barral, V.S. Boaventura, F. Ramos, E. Elias Júnior, J. Cassio de Moraes, D.T. Covas, J. Kalil, A.R. Precioso, S.S. Whitehead, A. Esteves-Jaramillo, T. Shekar, J.-J. Lee, J. Macey, S.G. Kelner, B.-A.G. Collier, F.C. Boulos, and M.L. Nogueira



CLINICAL DEVELOPMENT: BUTANTAN-DV

Média de seguimento após a vacinação: 3,7 anos

A definição de caso respeita a utilizada pelo guia do Ministério da Saúde de 2013, que adota a classificação da Organização Mundial da Saúde, de 2009

Efficacy and safety of Butantan-DV in participants aged 2–59 years through an extended follow-up: results from a double-blind, randomised, placebo-controlled, phase 3, multicentre trial in Brazil



Mauricio L Nogueira, Monica A T Cintra, José A Moreira, Elizabeth G Patiño, Patricia Emilia Braga, Juliana CV Tenório, Lucas Bassolli de Oliveira Alves, Vanessa Infante, Daniela Haydee Ramos Silveira, Marcus Vínicius Guimarães de Lacerda, Dhelio Batista Pereira, Alex Jardim da Fonseca, Ricardo Queiroz Gurgel, Ivo Castelo-Branco Coelho, Cor Jesus Fernandes Fontes, Ernesto T A Marques, Gustavo Adolfo Sierra Romero, Mauro Martins Teixeira, André M Siqueira, Viviane Sampaio Boaventura, Fabiano Ramos, Erivaldo Elias Júnior, José Cassio de Moraes, Stephen S Whitehead, Alejandra Esteves-Jaramillo, Tulin Shekar, Jung-jin Lee, Julieta Macey, Sabrina Gozlan Kelner, Beth-Ann G Collier, Fernanda Castro Boulos, Esper G Kallás, on behalf of the Phase 3 Butantan-DV Working Group*

Até a data de corte (2 ou mais anos de seguimento para cada participante)**

	Butantan-DV	Placebo		
Dengue with warning signs or severe dengue	Cases/ Total	Cases/ Total	Vaccine efficacy	(95% CI)
Regardless of serum status at baseline	2/10.215	10/5.947		88.2% (50,8 – 98,2)

BUTANTAN-DV PHASE 3 CLINICAL TRIAL – FINAL FIVE YEARS RESULTS

Long-term efficacy and safety of the single-dose tetravalent Butantan dengue vaccine

Received: 12 August 2025

Accepted: 30 January 2026

Published online: 04 March 2026

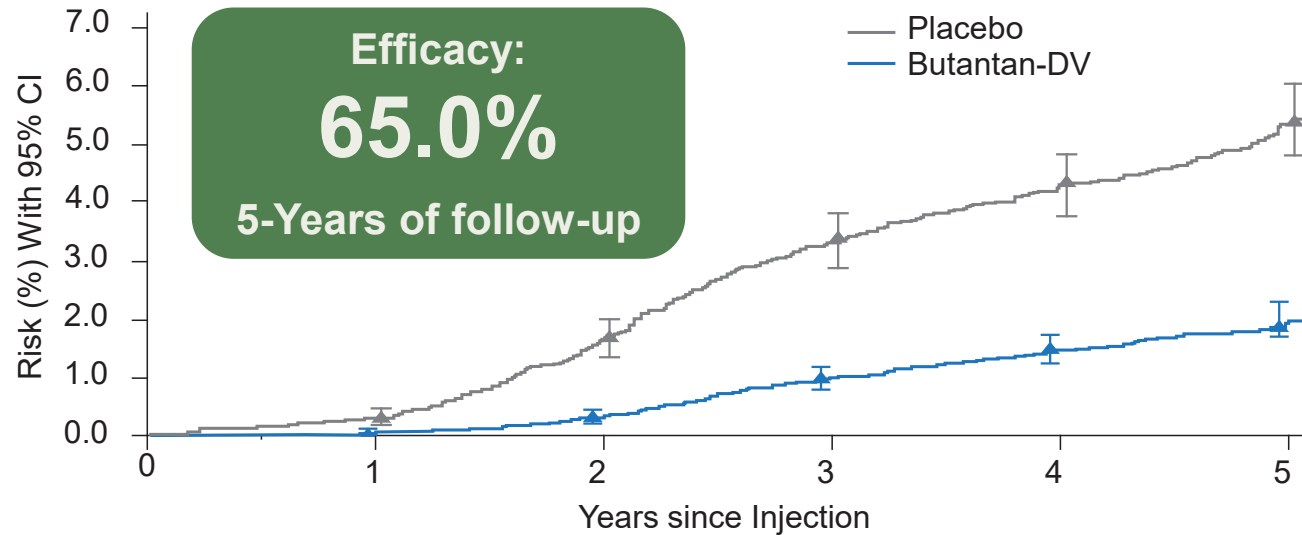
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A list of authors and their affiliations appears at the end of the paper

In individuals with prior dengue virus (DENV) exposure, subsequent heterotypic infection can increase the risk of severe disease. A single-dose dengue vaccine that protects against the four DENV serotypes across a wide age range and regardless of DENV serostatus is needed. Here we report the long-term safety and efficacy of Butantan dengue vaccine (Butantan-DV), a live, attenuated, tetravalent dengue vaccine, among participants ages 2–59 who were randomized 2:1 in a double-blind, placebo-controlled, phase 3 trial in Brazil. A primary objective was to evaluate vaccine efficacy (VE) against reverse transcription–PCR-positive symptomatic dengue 28 days after vaccination because of any DENV serotype, regardless of serostatus. Prespecified secondary endpoints included VE by serotype, by serostatus and against severe dengue or dengue with warning signs (combined). The primary and secondary objectives were met if the lower bound of the two-sided 95% confidence interval (CI) for VE was above 25%. Between 2016 and 2019, 16,235 participants received Butantan-DV ($n = 10,259$) or placebo ($n = 5,976$). The trial met the primary and secondary objectives. During the 5 years of follow-up, between 2016 and 2024, overall VE (95% CI) was 65.0% (57.8–71.0%). Secondary VE endpoints (95% CI) were 77.1% (67.6–83.9%) in dengue-experienced participants, 58.9% (48.0–67.6%) in dengue-naïve participants, 73.0% (64.3–79.7%) against DENV-1 and 55.7% (42.3–66.1%) against DENV-2. Cases of DENV-3 or DENV-4 were not observed. VE (95% CI) against dengue with warning signs or severe dengue (secondary endpoint) was 80.5% (50.8–92.4%). The most commonly reported solicited systemic adverse event (AE) was headache (36.7% of vaccine recipients and 31.1% of placebo recipients), most of which were grade 1. The proportions of participants with unsolicited vaccine-related AEs (including serious AEs) were comparable between intervention groups. A single dose of Butantan-DV was efficacious against symptomatic virologically confirmed dengue because of DENV-1 or DENV-2, regardless of dengue serostatus at baseline, with no safety concerns observed during the 5-year follow-up (ClinicalTrials.gov: [NCT02406729](https://clinicaltrials.gov/ct2/show/study/NCT02406729)).

CUMULATIVE INCIDENCE OF VIROLOGICALLY CONFIRMED DENGUE (VCD)

Any DENV Serotype



No. of participants at risk

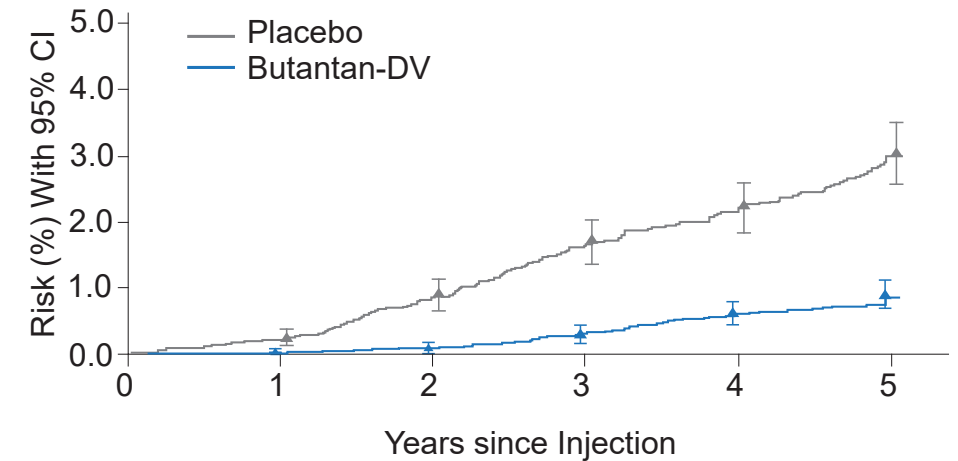
Butantan-DV:	10,202	9,832	9,581	9,358	9,144	7,728
Placebo:	5,936	5,742	5,551	5,356	5,197	4,328

*Data through the end of the five-year follow-up. Per-protocol population.

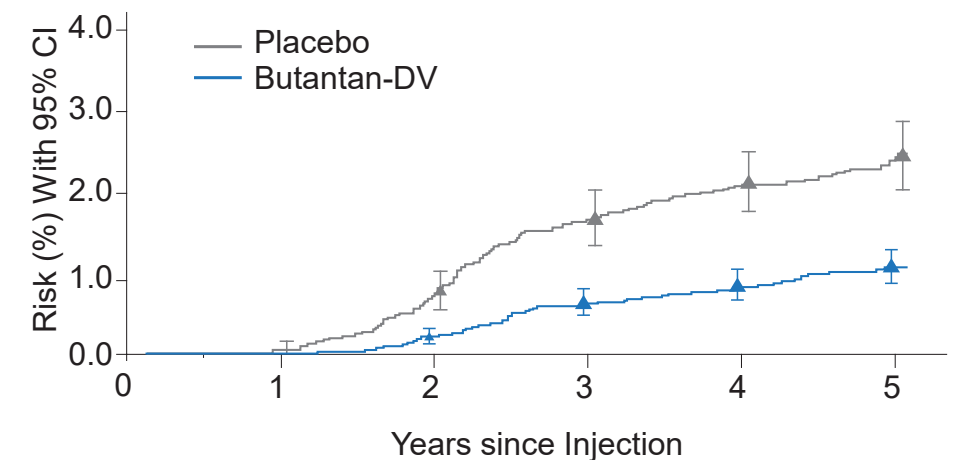
There were 9,050 participants who completed the study prior to year 5 and were no longer at risk for VCD due to any DENV serotype at year 5

Kallas *et al. Nature Medicine*, 2026

DENV-1



DENV-2



BUTANTAN-DV REGISTRATION – NOVEMBER 17, 2025



ROLLOUT – FEBRUARY 9, 2026



ANVISA APPROVES THE VACCINE FOR 12-59 YEARS-OLD

OVERALL EFFICACY

74.7%

EFFICACY TO PREVENT MORE SEVERE FORMS OF DENGUE

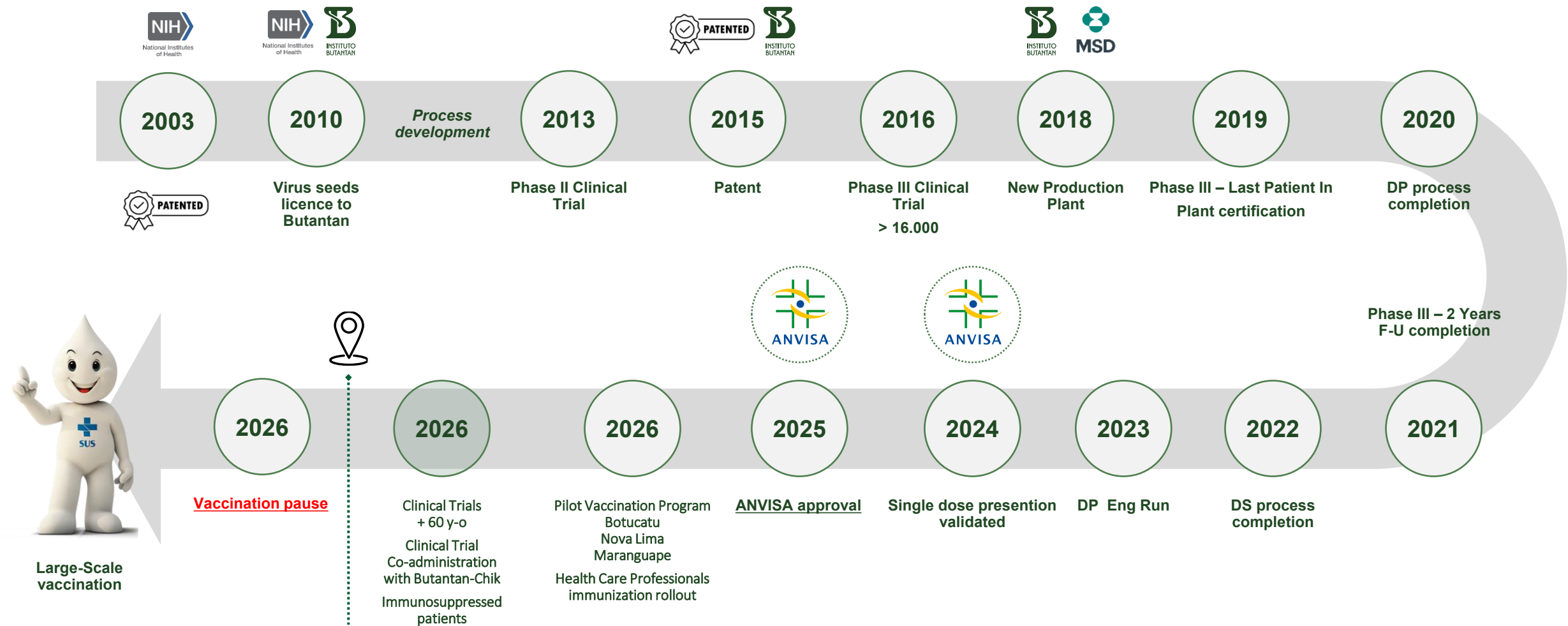
91.6%

HOSPITALIZATIONS

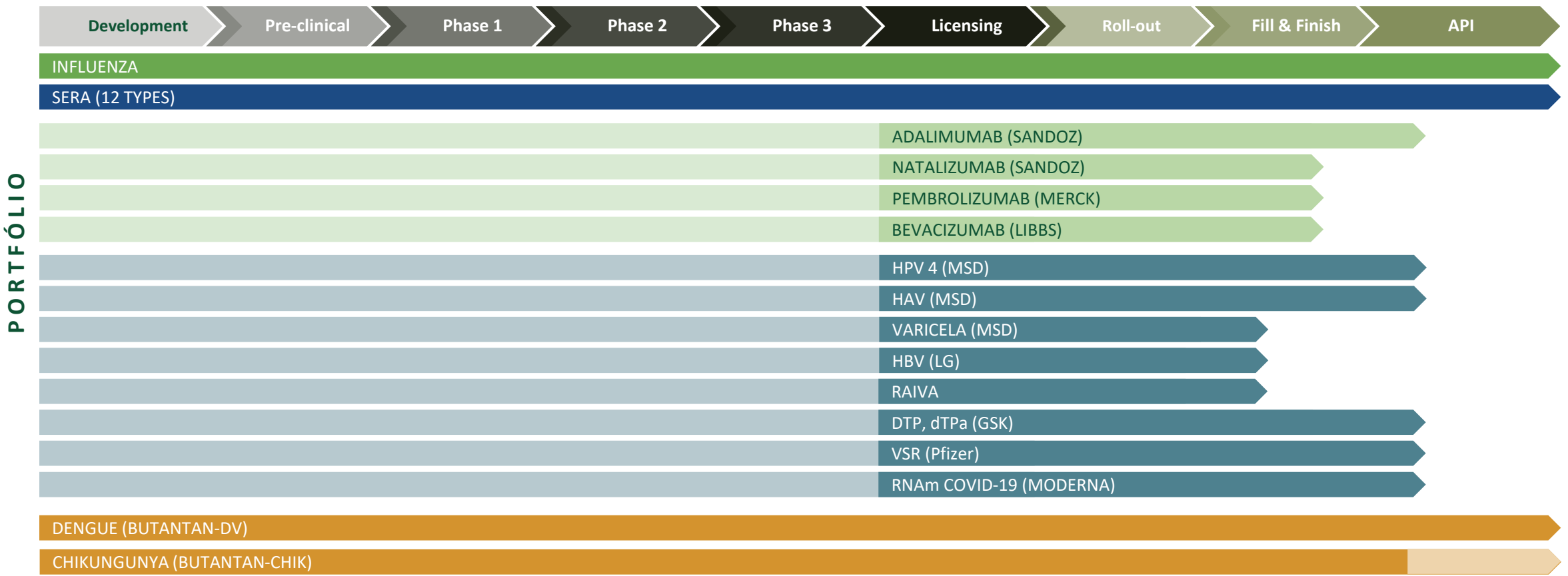
No hospital
admissions
in the
vaccinee
group

Butantan-DV

BUTANTAN-DV TIMELINE



PORTFOLIO



- MAB
- Flu vaccines
- Arbovirus vaccines
- Advanced Therapies
- Other
- Sera

PIPELINE

RESEARCH & DEVELOPMENT



- MAB
- Flu vaccines
- Arbovirus vaccines
- Advanced Therapies
- Other
- Sera



Obrigado!

www.butantan.gov.br