The First Standalone Adjuvanted IPV
The Philippines Experience

AJVaccines

AJ VACCINES

A YOUNG COMPANY WITH 100 YEARS' EXPERIENCE

1902 STATENS SERUM INSTITUT

2017 AJVaccines

LIFE IS PRECIOUS

PREVENTING DISEASE

COUNTRY BY COUNTRY

CHILD BY CHILD

- Established in January 2017, through the acquisition of the vaccine manufacturing activities of the Danish State-owned Statens Serum Institute
- Production facilities and Global Headquarters located in the heart of Copenhagen
- Built on more than 100 years' experience of producing high quality vaccines
- Investing in our strong portfolio and production capabilities, and inaugurating our new Regional Office in Dubai in 2019
- 730 people employed globally

VISION

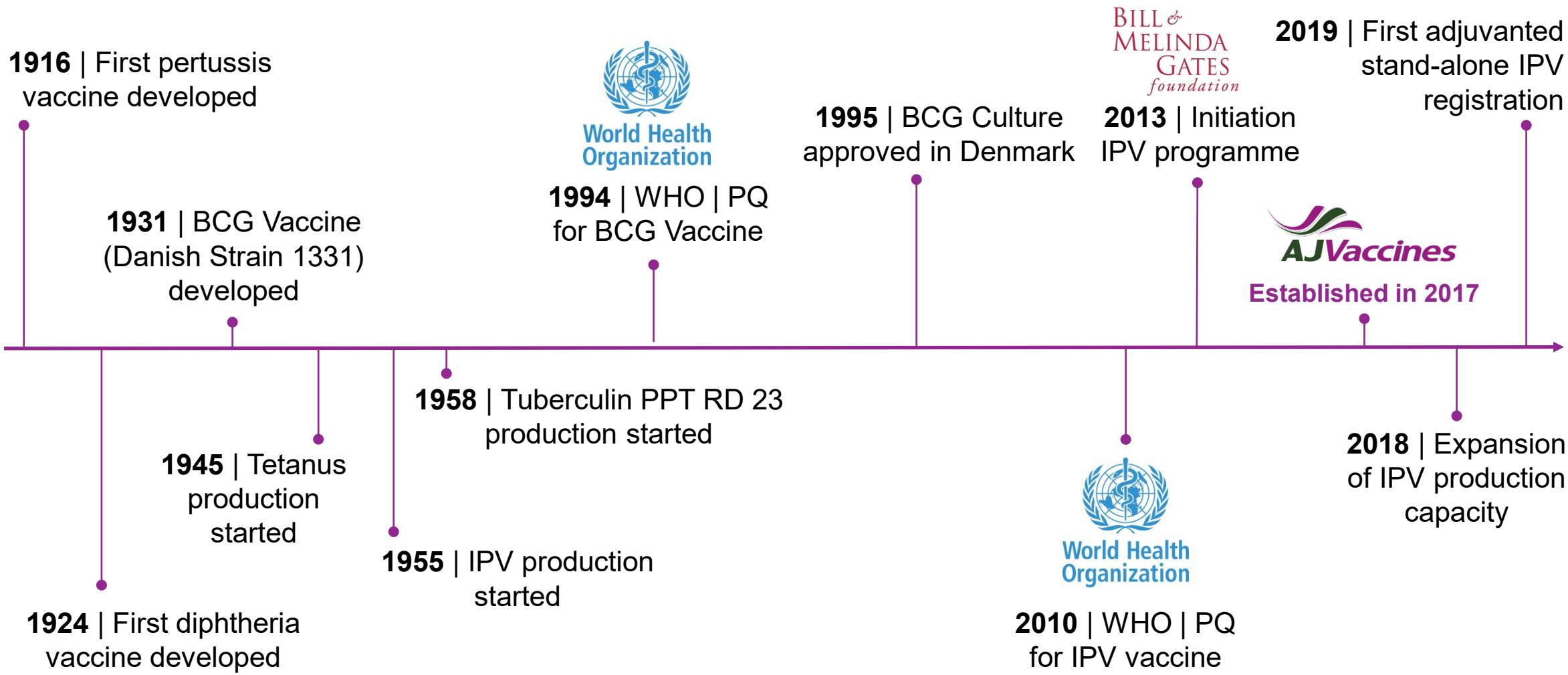
We will have a decisive influence on global health and continuously reduce diseases country by country – child by child

MISSION

Through collaboration and partnership we will develop and provide preventive vaccines and diagnostic therapy products of the highest quality

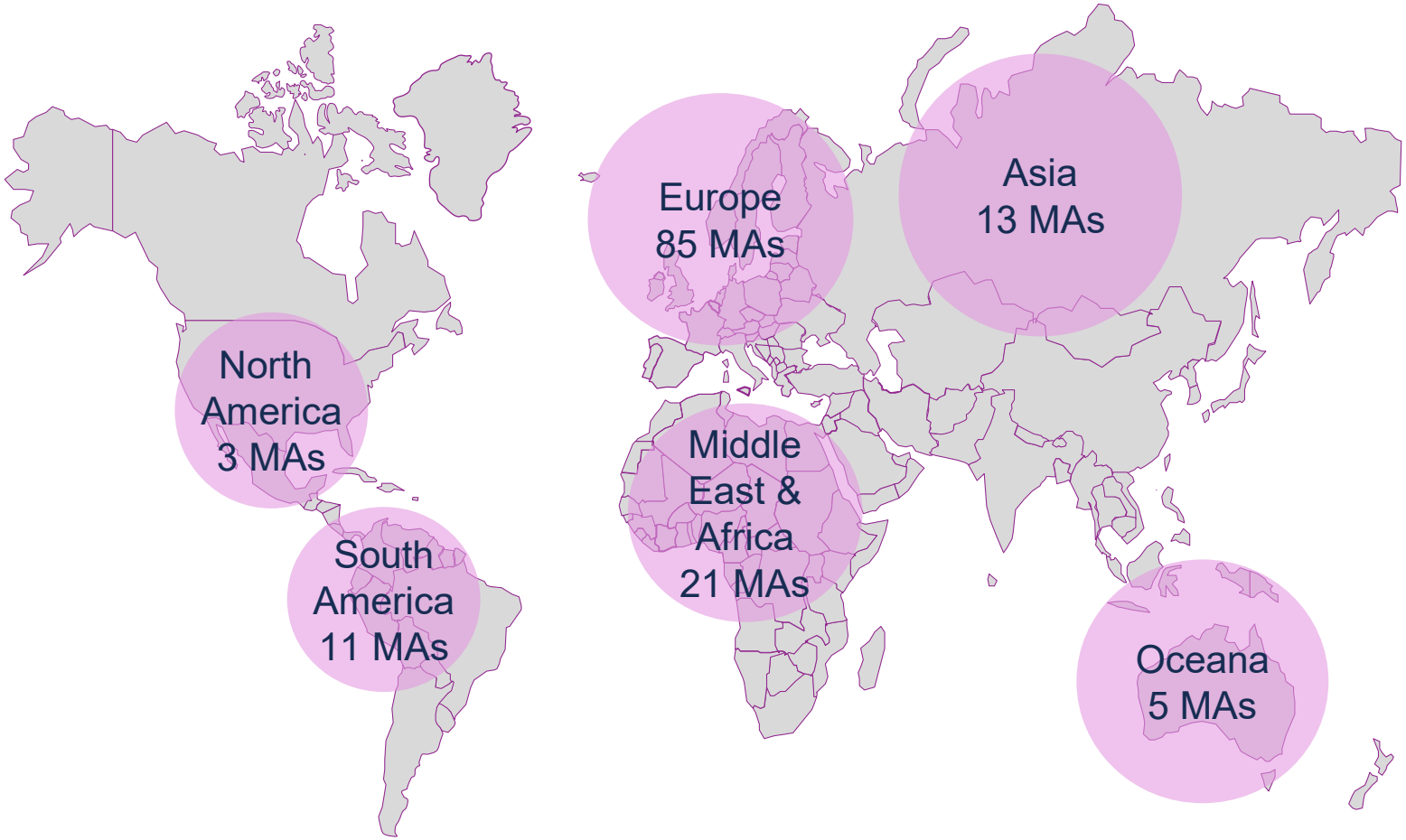
AJVaccines

DEVELOPING HIGH QUALITY VACCINES SINCE 1902



AJVaccines

OUR VACCINES | PROTECTING PEOPLE AROUND THE WORLD



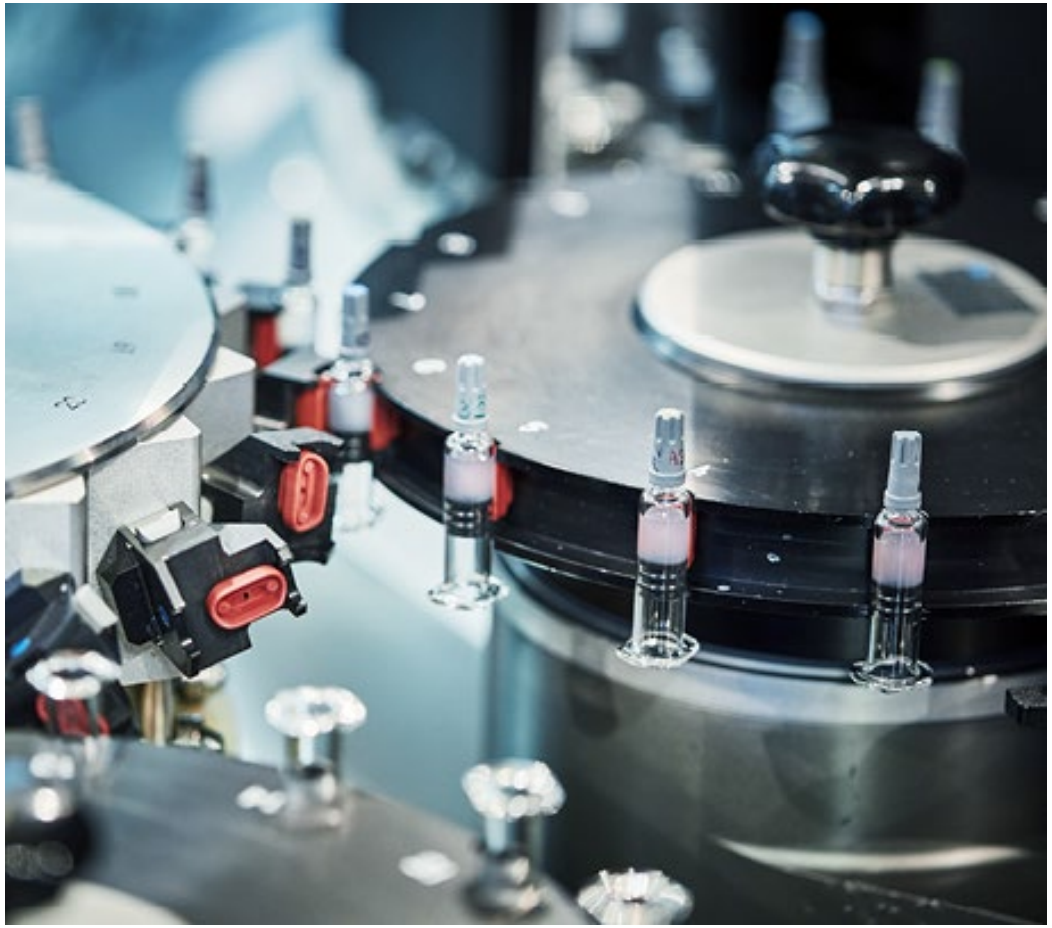
- 9 Biological products
- 138 Marketing Authorisations
- 2 WHO PQs for IPV and BCG
- MAs in 49 countries across 6 continents

AJVaccines

A GROWTH TRAJECTORY WITH AMBITIOUS GOALS

INVESTING TO INCREASE VACCINE PRODUCTION AND GROW OUR PORTFOLIO

- AJ Vaccines strives to provide as many people as possible, in every corner of the world, with a quality of life only available without the burden of infectious disease
- We have a fully GMP certified operational facility in Denmark
- We are investing heavily in production facilities to maximise capacity and help meet the growing demand for vaccines
- We continuously develop our business by expanding our product portfolio through partnerships



AJVaccines

POLIO ERADICATION

Wild poliovirus type 1 and Circulating vaccine-derived poliovirus cases

Total cases	Year-to-date 2019		Year-to-date 2018		Total in 2018	
	WPV	cVDPV	WPV	cVDPV	WPV	cVDPV
Globally	78	72	21	78	33	104
—In Endemic Countries	78	15	21	18	33	34
—In Non-Endemic Countries	0	57	0	60	0	70

http://polioeradication.org/polio-today/polio-now/this-week/ September 11th 2019

Source: http://polioeradication.org/

- Withdrawal of the oral polio vaccine (bOPV) and introduction of inactivated polio vaccine (IPV) is a key strategic step in the Polio Endgame Strategy
- The transition to IPV requires affordable IPV in quantities sufficient to secure at least 2 doses of IPV for every children

AJVaccines

ADJUVANTED POLIO VACCINE (IPV-AL)

- AJ Vaccines developed a dose-sparing aluminium hydroxide-adjuvanted IPV (IPV-Al), which secures an affordable IPV and increased the supply of IPV to the market
- The research was initiated in 2013 with financial support from the Bill & Melinda Gates Foundation
- Today, IPV-Al has been approved by the Danish Medicines Agency and is currently evaluated by WHO for prequalification
- The vaccine will provide a major contribution to the Global Polio Eradication Initiative

AJVaccines

IPV-AL | PRODUCT CHARACTERISTICS

- Contains the same IPV component as the already licensed IPV vaccine from AJ Vaccines
  - The amount of D-antigens are reduced in IPV-Al corresponding to 1/10 compared to standard IPV Vaccine AJV

- Presented in multidose vials (5 doses)

- Administered intramuscularly

- IPV-Al is indicated for active immunization against poliomyelitis (Danish approval):
  - Primary vaccination from 6 weeks of age.
  - Revaccination (boosting) of infants, children, adolescents and adults.

AJVaccines

IPV-AL CLINICAL DEVELOPMENT

Phase 1/2

Subject type	# of subjects	Country
Children and adolescents	240	Denmark

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

First-in-human safety and immunogenicity investigations of three adjuvanted reduced dose inactivated poliovirus vaccines (IPV-Al SSI) compared to full dose IPV Vaccine SSI when given as a booster vaccination to adolescents with a history of IPV vaccination at 3, 5, 12 months and 5 years of age

Line M. Lindgren [b], Pernille N. Tingskov [a], Annette H. Justesen [c], Bettina S. Nedergaard [d], Klaus J. Olsen [e], Lars V. Andreasen [a], Ingrid Kromann [a], Charlotte Sørensen [a], Jes Dietrich [a], Birgit Thierry-Carstensen [a,*]

[a] Statens Serum Institut, 5 Artillerivej, 2300 Copenhagen S., Denmark
[b] Center for Clinical and Basic Research (CCBR), Ballerup Byvej 222, 2750 Ballerup, Denmark
[c] CCBR Vejle, Orla Lehmannsgade 1[3], 7100 Vejle, Denmark
[d] CCBR Aalborg, Hobrovej 42 D[2], 9000 Aalborg, Denmark
[e] Larix A/S, Lyskær 8b, 2730 Herlev, Denmark

Phase 2

Subject type	# of subjects	Country
Infants	824	The Dominican Republic

THE LANCET
Infectious Diseases

Immunogenicity and safety of three aluminium hydroxide adjuvanted vaccines with reduced doses of inactivated polio vaccine (IPV-Al) compared with standard IPV in young infants in the Dominican Republic: a phase 2, non-inferiority, observer-blinded, randomised, and controlled dose investigation trial

Luis Rivera, Rasmus S Pedersen, Lourdes Peña, Klaus J Olsen, Lars V Andreasen, Ingrid Kromann, Pernille I Nielsen, Charlotte Sørensen, Jes Dietrich, Ananda S Bandyopadhyay, Birait Thierry-Carstensen

Phase 3

Subject type	# of subjects	Country
Infants	1.002	The Philippines
Infants	800	Panama

AJVaccines


Meet us at ASVAC
Booth A3
Contact us
sales@ajvaccines.com
AJVaccines

Getting more vaccines to more people
ASIAN VACCINE CONFERENCE
ASVAC 2019

Immunogenicity and safety of IPV-Al, a Phase 3 trial conducted in the Philippines

Dr Lulu Bravo
Professor Emeritus College of Medicine,
University of the Philippines Manila

This presentation is supported by
AJVaccines

DISCLOSURES

Dr. Lulu Bravo has received grants for the University of Philippines, Manila from Takeda, Sanofi, GSK, Novartis, LG Chem, the Bill & Melinda Gates Foundation and WHO

TRIAL DESCRIPTION

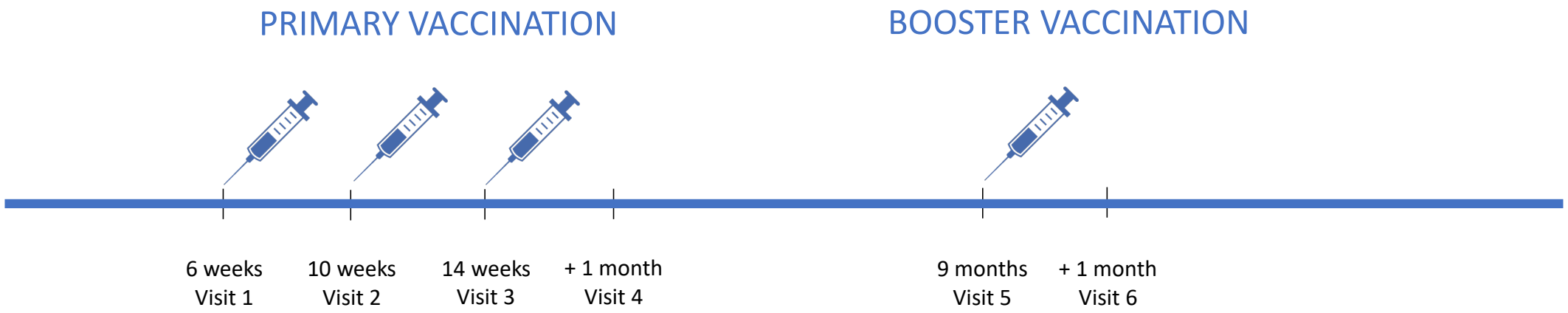
- A phase 3, non-inferiority, observer-blinded, randomised (1:1), controlled, multicentre clinical trial
- Two parallel groups received primary and booster IPV-Al or IPV vaccinations
- Healthy infants from the Philippines
- Conducted between February 2017 and March 2018
- The objective of this trial was to demonstrate the non-inferiority of IPV-Al to standard IPV

ClinicalTrials.gov identifier: NCT03032419

Antibody titre ≥8: serologic correlate of protection against polio [1,2,3]

1. Vidor E. Poliovirus Vaccine–Inactivated. In: Plotkin SA, Orenstein WA, Offit PA, Edwards KM, editors. Plotkin's Vaccines. 7th ed. Philadelphia: Elsevier; 2018. p. 841–65.
2. Plotkin SA. Correlates of protection induced by vaccination. Clin Vaccine Immunol. 2010;17(7):1055–65.
3. Robertson S. The Immunological Basis for Immunization Series Module 6: Poliomyelitis. Geneva: World Health Organization; 1993. p. 1-24

VIPV-06 SCHEDULE 6 ENDPOINTS



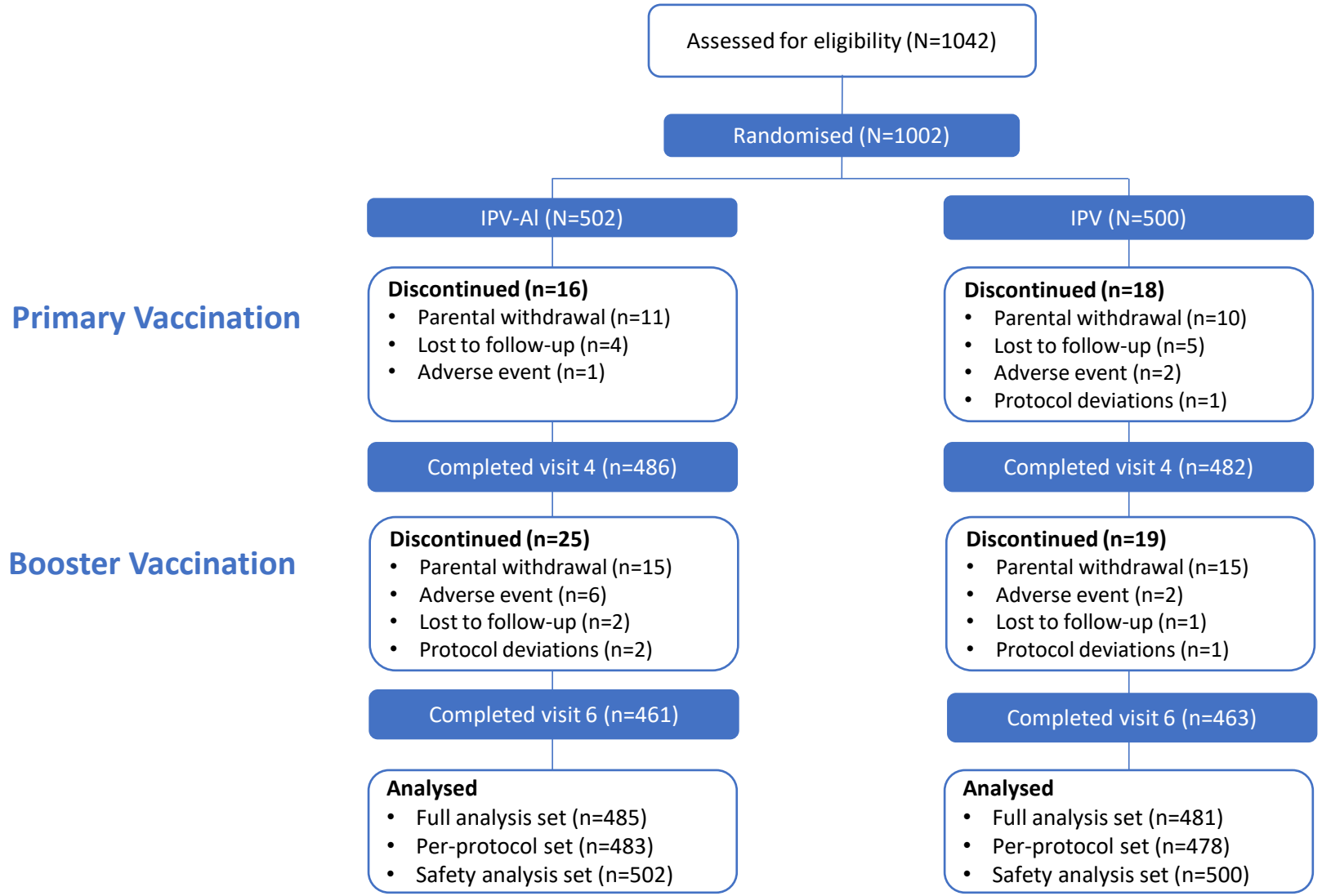
Primary endpoint:

- **Seroconversion**, defined as an antibody titre ≥4-fold higher than the estimated maternal antibody titre and a titre ≥8, one month after the primary vaccination series

Secondary endpoints:

- **Seroprotection**, defined as an antibody titre ≥8, one month after the primary and booster vaccination
- **GMT levels** one month after the primary and booster vaccination
- **Booster effect** after the booster vaccination (post-booster GMT / pre-booster GMT)
- **Safety** during primary and booster vaccination

DISPOSITION



BASELINE CHARACTERISTICS

Characteristic	IPV-AI N=502	IPV N=500
Sex		
Male	255 (51%)	255 (51%)
Female	247 (49%)	245 (49%)
Race	100% Asian	100% Asian
Age	45.06 (± 4.3) days	45.06 (± 4.6) days
Birth weight	3.05 (± 0.36) kg	3.05 (± 0.35) kg

* Data are n (%) or mean (SD) for participants in the safety analysis set
N = number of infants, SD = standard deviation

SAFETY

IPV-Al was well tolerated, with a safety profile comparable to that of IPV

Variable	IPV-Al N=502	IPV N=500
	n (%)	n (%)
Any AEs	489 (97.4%)	492 (98.4%)
Deaths	2 (0.4%)*	3 (0.6%)*
SAEs	29 (5.8%)**	28 (5.6%)**
Systemic AEs	488 (97.2%)	490 (98.0%)
Injection Site Reactions	232 (46.2%)	211 (42.2%)

Safety analysis set

*None of the deaths were assessed as being related to the trial vaccines

**All serious AEs were assessed as not related to the trial vaccine, except for one case of febrile seizure in the IPV group

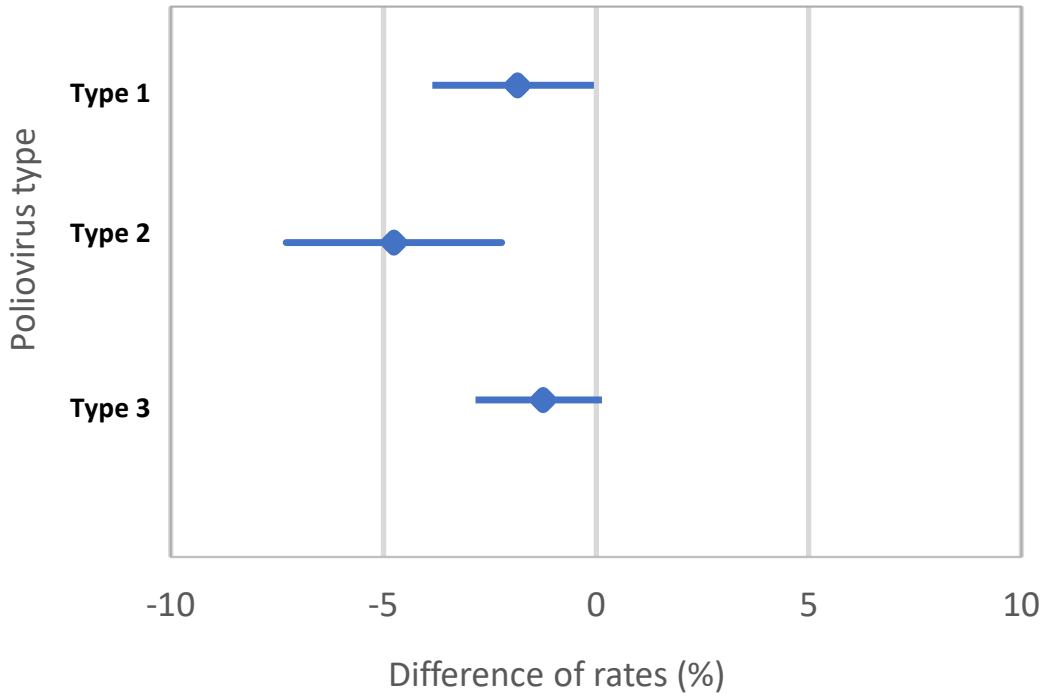
PRIMARY ENDPOINT

PRIMARY ENDPOINT: SEROCONVERSION | POST-PRIMARY VACCINATION

IPV-Al non-inferior to IPV

	Post-primary vaccination seroconversion rates	
	IPV-Al (N=483)	IPV (N=478)
Type 1	97.1%	99.0%
Type 2	94.2%	99.0%
Type 3	98.3%	99.6%

Per Protocol set



- Seroconversion defined as an antibody titre ≥4-fold higher than the estimated maternal antibody titre and a titre ≥8, one month after the primary vaccination series

- IPV-Al non-inferior to IPV
  - as the lower limit of the two-sided 95% Confidence Intervals of the rate differences was above the predefined limit of -10%-points

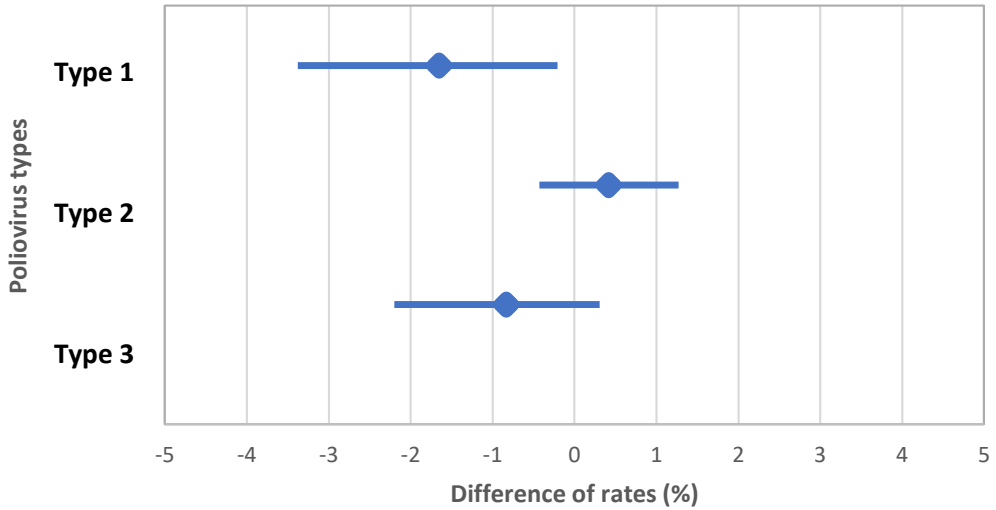
SECONDARY ENDPOINTS

SEROPROTECTION | POST-PRIMARY VACCINATION

IPV-AI non-inferior to IPV

	Post-primary vaccination seroprotection rates	
	IPV-AI (N=483)	IPV (N=478)
Type 1	97.9%	99.6%
Type 2	100 %	99.6%
Type 3	99.0%	99.8%

Per Protocol set



- Seroprotection defined as an antibody ≥8, one month after the primary and booster vaccination

- IPV-AI was non-inferior to IPV
  - the lower limit of the two-sided 95% Confidence Intervals of the rate differences was above the predefined limit of -5%-points

SEROPROTECTION | PRE-BOOSTER VACCINATION

Seroprotection rates decreased, as expected, between primary and booster vaccination

	Post-primary vaccination		Pre-booster vaccination	
	IPV-AI (N=483)	IPV (N=478)	IPV-AI (N=449)	IPV (N=449)
Type 1	97.9%	99.6%	**88.0%**	**100%**
Type 2	100 %	99.6%	**99.8%**	**99.8%**
Type 3	99.0%	99.8%	**93.5%**	**99.6%**

Per Protocol set

SEROPROTECTION | POST-BOOSTER VACCINATION

Seroprotection rates higher post-booster vaccination than post-primary vaccination

	Post-primary vaccination		Pre-booster vaccination		Post-booster vaccination	
	IPV-AI (N=483)	IPV (N=478)	IPV-AI (N=449)	IPV (N=449)	IPV-AI (N=441)	IPV (N=442)
Type 1	97.9%	99.6%	88.0%	100.0%	**99.8%**	**100%**
Type 2	100 %	99.6%	99.8%	99.8%	**100%**	**100%**
Type 3	99.0%	99.8%	93.5%	99.6%	**100%**	**100%**

Per Protocol set

GMT LEVELS | POST-PRIMARY VACCINATION

Post-primary GMTs were high for all poliovirus types

- Post-vaccination GMTs were higher with IPV than with IPV-Al
- GMTs were well in excess of the seroprotection threshold for both vaccines

	Post-primary vaccination GMT* levels	
	IPV-Al (N=483)	IPV (N=478)
Type 1	**740**	**3837**
Type 2	**1272**	**3611**
Type 3	**1110**	**4590**

Per Protocol set

*GMT: geometric mean titres

GMT LEVELS | PRE-BOOSTER VACCINATION

GMT levels decreased, as expected, between primary and booster vaccination

	Post-primary vaccination		Pre-booster vaccination	
	IPV-AI (N=483)	IPV (N=478)	IPV-AI (N=449)	IPV (N=449)
Type 1	740	3837	**132**	**746**
Type 2	1272	3611	**352**	**749**
Type 3	1110	4590	**143**	**634**

Per Protocol set

GMT LEVELS | POST-BOOSTER

Sharp increase in GMTs following the booster vaccination with both vaccines
GMTs higher post-booster vaccination than post-primary vaccination

	Post-primary vaccination		Pre-booster vaccination		Post-booster vaccination	
	IPV-AI (N=483)	IPV (N=478)	IPV-AI (N=449)	IPV (N=449)	IPV-AI (N=441)	IPV (N=442)
Type 1	740	3837	132	746	**8394**	**31558**
Type 2	1272	3611	352	749	**18933**	**35164**
Type 3	1110	4590	143	634	**15691**	**49964**

Per Protocol set

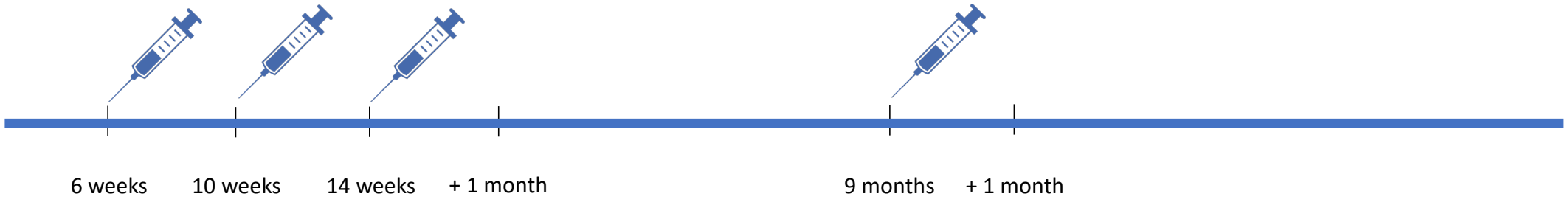
BOOSTER EFFECT

Pronounced booster effects for both vaccines

	Post-primary vaccination		Pre-booster vaccination		Post-booster vaccination		Booster effect*	
	IPV-AI (N=483)	IPV (N=478)	IPV-AI (N=449)	IPV (N=449)	IPV-AI (N=441)	IPV (N=442)	IPV-AI (N=441)	IPV (N=442)
Type 1	740	3837	132	746	8394	31558	**63**	**43**
Type 2	1272	3611	352	749	18933	35164	**54**	**47**
Type 3	1110	4590	143	634	15691	49964	**112**	**80**

Per Protocol set

* Booster effect defined as post-booster GMT / pre-booster GMT



CONCLUSIONS

PRIMARY VACCINATION

- The **IPV-Al** vaccine demonstrated **high seroconversion and seroprotection rates** after completion of the **EPI vaccination schedule comparable to those of IPV**
- Non-inferiority of IPV-Al to IPV seroconversion and seroprotection rates was confirmed for all poliovirus types

BOOSTER VACCINATION

- **IPV-Al** induced a **robust booster response** in **9-month-old** infants
- Post-vaccination GMTs were higher with IPV than with IPV-Al. GMTs were well in excess of the seroprotection threshold for both vaccines
- IPV-Al was well tolerated with a **safety profile comparable to that of IPV** following primary or booster vaccination

ACKNOWLEDGEMENTS

Thank you to …

- the trial participants and their parents
- the investigators
- trial site staff
- Bill & Melinda Gates Foundation
- Statens Serum Institut

THANK YOU FOR YOUR TIME …

QUESTIONS?