Intradermal Needle-free Vaccine Delivery

to reduce Ethiopia's immunization costs and improve coverage

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PharmaJet®

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Paul LaBarre, MS, MBA
Vice President,
Global Business Development

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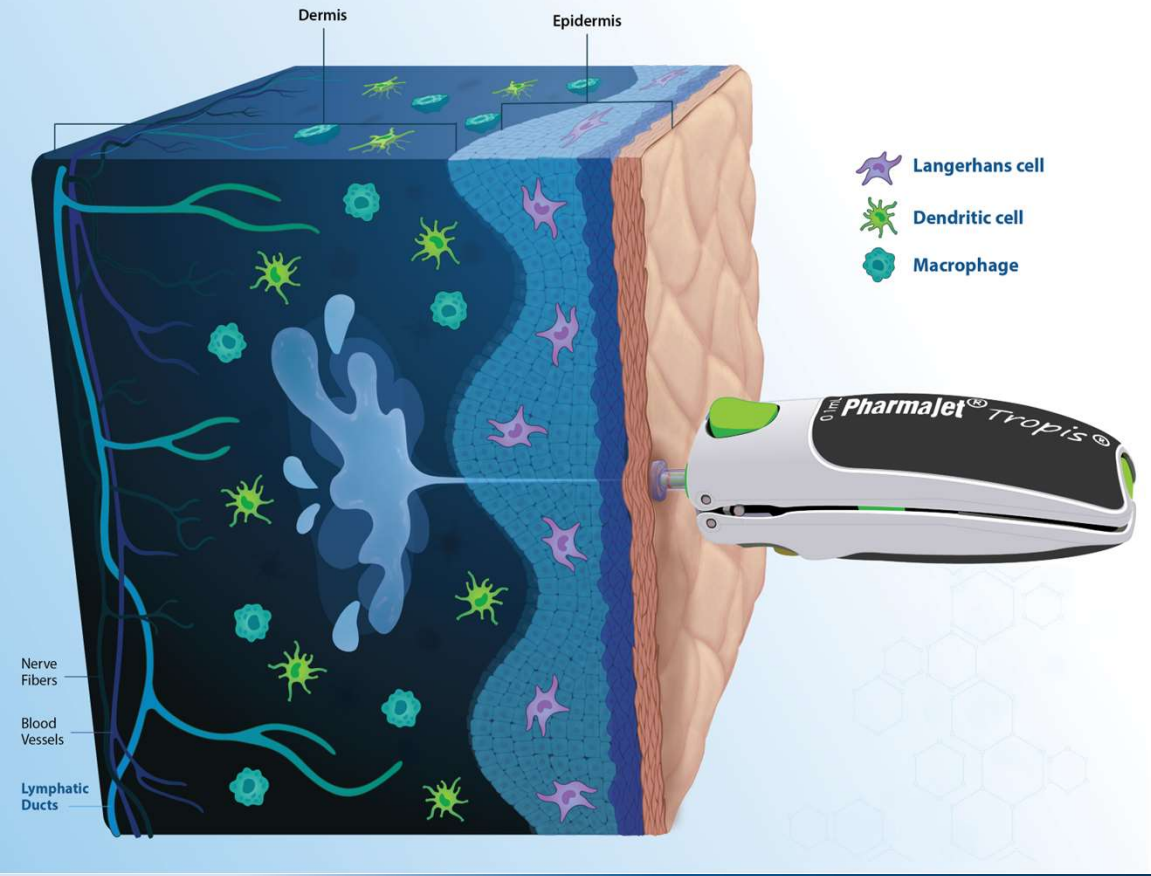
The benefits of intradermal delivery

Potential for new strategies: fractionation & decreased excipients



ID compartment

- Rich in diversity of APCs[1]
- Lymph ducts allowing migration[2]
- Induces long-lived Ab response[3]
- Promotes CD8+ T cell responses[2,4,5]

ID delivery can enhance important attributes needed for infectious disease vaccines such as:

- Duration of Ab response
- Mucosal protection
- Breadth of Ab and T cell responses

1. Kupper et al., Nat Rev Immunol, 2004.
2. Duffy et al., Immunity, 2012.
3. Levin et al., J Invest Dermatol, 2017.
4. Best et al., Vaccine, 2009.
5. Lind et al., Scand J Infect Dis, 2012.

Timeline: Evidence for ID fIPV* and needle-free delivery (Non-adjuvanted Salk)

2015

Tropis is highly effective at triggering the immune response compared with needle and syringe.[1]

2017

- *"Data from Pakistan, Cuba and Gambia confirmed that Tropis is a device that is feasible to use in a vaccination campaign."*[2]
- *"Tropis provides for better comfort for children, is quicker to use than tradition BCG needle and syringe and is easy to train."*[2]
- *"Important to gain more implementation experience both in routine and campaign settings to guide future policy"*[2]

2018

- *"fIPV* is safe, effective and immunogenic"*[5]
- *"fIPV can be used in routine immunization, in supplementary immunization activities (SIAs), and in outbreak response"*[5]
- *"Data … demonstrated that using needle-free ID injection is equally immunogenic as when using a syringe alone and is clearly preferred by health workers for ease of ID administration."*[5]

2021

A meta-analysis of 10 studies found with a high level of certainty that there was : *"No substantial difference in seroconversion between 2 and 3 doses of ID fIPV, and 2 and 3 doses of full-dose IPV."*[3]

"Programmatic challenges of ID administration are eased by needle-free injectors."[6]

2022

"ID fractional IPV can be used instead of full dose IPV IM injection."[7]

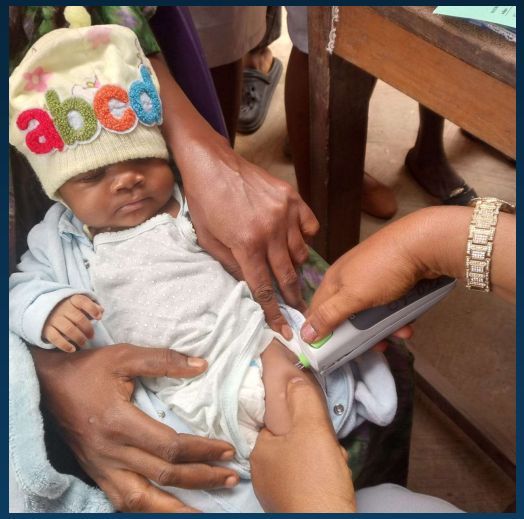
2023

"Administering an injectable vaccine in a house-to-house campaign with needle-free jet injector devices is feasible and can achieve high coverage."[4]

1. Resik et al., Vaccine, 2015.
2. 16th meeting SAGE Polio Working Group.
3. Mashunye et al., Lancet, 2021.
4. Biya et al., WHO MWWR, 2023.
5. GPEI, Considerations for fIPV decision making, 2017.
6. Macklin, et al., Lancet, 2021.
7. WHO, Position paper, polio vaccines, 2022.

* fIPV = fractional dose inactivated polio vaccine


dios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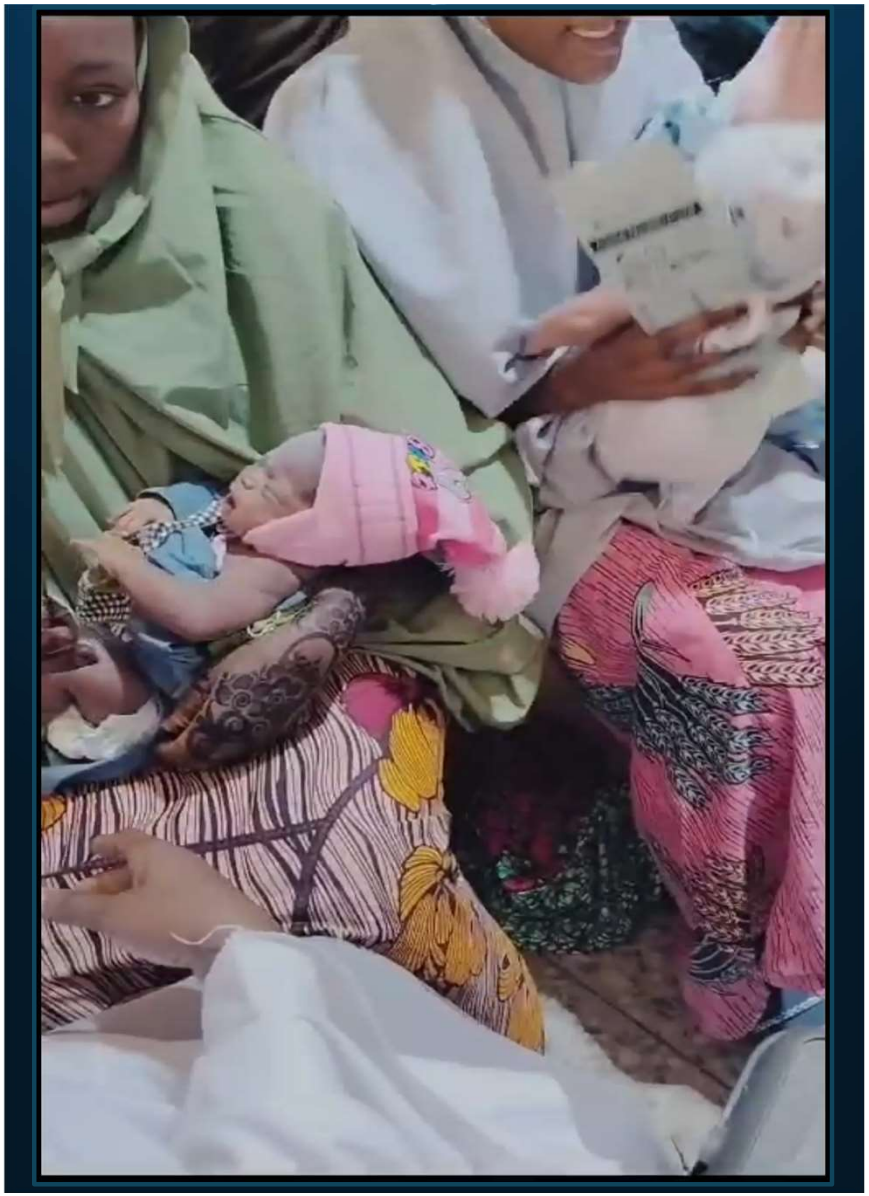


N/S ID Mantoux delivery Nigeria, 2023

Link to 20 second video we recorded in Nigeria.

In this video, intradermal injection using the **Mantoux technique takes 18 seconds** from needle insertion to completion.

Tropis injection duration is 0.1 seconds.[1]

[1] PharmaJet data on file.

PharmaJet's ID Precision Delivery System

delivers a spring-powered injection in a 10th of a second by means of a narrow stream of fluid that penetrates the skin with a **precise dose and depth**.

NO needle

NO external power source

Tropis® ID

Precision Intradermal Delivery System for 0.1 ml Injections

INJECTOR

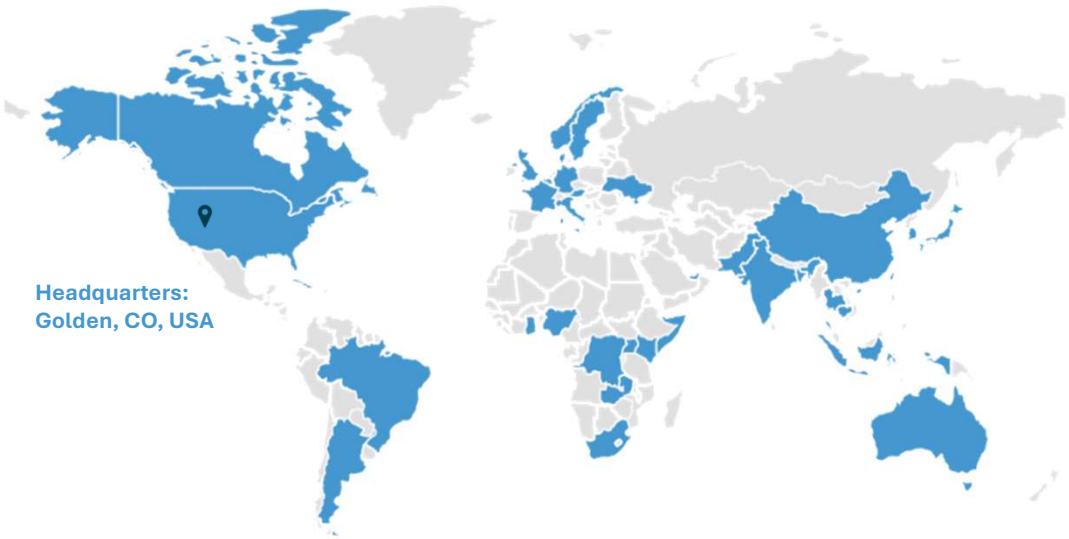
0.1ml SYRINGE

ADAPTER

Tropis® Workflow

Market access through global partners and regulatory clearances

Global Development and Commercial Partnerships



Regulatory Clearances

PharmaJet's Precision Delivery Systems are validated with several regulatory clearances across the globe.

Tropis® Registrations:

- US FDA Master File
- European Union CE
- WHO/PQS
- Brazil
- Vietnam
- India
- Indonesia
- Kenya
- Ghana
- Nigeria
- ***Pending: Ethiopia, Iraq, Pakistan and Egypt***

PharmaJet's needle-free injection devices are the first ***and only*** to achieve **World Health Organization** standards for **Pre-qualification (PQS)**

Tropis ID delivery for campaigns - > 10M pediatric fIPV injections

Reference	Application	Results	Author comments
Yousafzai et al., Heliyon, 2017.	Campaign use, Pakistan 	**High acceptability among infants:** All the vaccinators reported that crying among children was less common with needle-free compared with SoC **High acceptability among non-traditional HCWs:** all vaccinators reported that filling the device was easy, device was appropriate size, and giving the injection was easy.	*"The device is **safe, efficient** in dose sparing, **quick** in administration of fIPV, and needs **minimal training** to use in campaign settings."*
Bullo et al., BMC Public Health, 2021.		**Improved coverage:** 7.3% higher in areas using needle-free compared with regions concurrently using SoC.	*"Our analysis supports the use of IPV in mass campaigns to maintain an immunity level that would diminish the number of paralytic cases in the occurrence of endemic transmission of poliovirus as **good vaccination coverage is feasible especially by using a fractional dose of IPV**."*
Daly et al., Vaccine, 2020.		**Improved coverage:** 18.4% higher than previous IPV campaign **High acceptability among caregivers:** 95.6% prefer needle-free **High acceptability among non-traditional HCWs:** 97.6% prefer needle-free over SoC	*"The **high coverage and strong acceptability** of the jet-injectors in this setting provide support for use of this mode to administer fIPV in areas with community resistance to vaccination – a key challenge to interrupting WPV1 transmission in Pakistan and in particular, the city of Karachi."*
Bashoran et al. Lancet, 2022.	Campaign use, The Gambia 	**Acceptability among infants:** Significantly less infant crying (17%) compared with full dose IM with needles (SoC @55%) **Immunogenicity:** Non-inferior to SoC across all serotypes **Throughput:** 55% of injections administered in < 1 min **Low wastage:** 26% increase in useable vaccine	*"Intradermal fIPV is safe and **generates consistent immune responses** that are not dependent on vaccinator experience."*
Biya et al., WHO MMWR, 2023.	House-to-house, Nigeria 	**High coverage:** Surveys indicated that 87% of children in the target age group received fIPV during the campaign.	*"This pilot study demonstrated that administering an injectable vaccine in a **house-to-house campaign** with needle-free jet injector devices is feasible and can **achieve high coverage**."*
Nouh et al, BMC Global and Public Health, 2024.	Campaign use, Somalia 	**High coverage:** 96% in each of 2 rounds (administrative data); 98.7% reported **Acceptability among caregivers:** In one region, 42.6% of parents brought their children for immunization because they heard about the new delivery method. **Needle-free future:** 97% of interviewees thought that all injectable vaccines should be administered using this needle-free injector.	*"The evidence from this study suggests that the **impressively high coverage** post-campaign was mainly due to preference for the use of intradermal needle-free injectors in addition to other factors, including the low quantity of vaccine required, the speed and ease of administration by vaccinators and the willingness of parents to bring their children due to the painless administration of the vaccine."*

Tropis ID delivery for routine administration of fIPV

Reference	Application	Results	Author comments
Resik et al., Vaccine, 2015.	Routine use, Cuba 	**Acceptability with HCWs:** HCWs preferred over BCG needle and syringe (Mantoux) for intradermal administration.	*"PharmaJet needle-free demonstrated its ability to streamline intradermal fIPV administration. No safety concerns….produced similar immune response to BCG needle."*
Mvundura et al., Vaccine, 2019.	Cost comparison modeling, multi-country	**Cost savings:** Costs per child vaccinated with fractional doses was 15% to 48% lower than that with SoC full doses in routine settings.	*"The analysis also showed that even when accounting for higher wastage due to using fractional doses and the costs of the devices facilitating ID administration, fIPV was always less expensive than full-dose administration for all vial sizes in routine settings."*
Mvundura et al., 2021 (unpublished, with permission)	Cost comparison, Uganda 	**Cost savings:** Assuming 3 devices per health facility, 5 years (5 birth cohorts); 1200 uses per device; 42% cost savings.	
PharmaJet modeling, 2025 (data on file, available upon request)	Cost comparison, Ethiopia 	**Cost savings:** Assuming 2 devices per clinic, 46% total immunization cost savings totaling $130M over 10 years.	
USAID-funded RCT (PACTR202308820044137; manuscript in preparation,)	Routine use scaled to 22 clinics, Nigeria 	**Coverage:** up to 20% improved coverage compared with needle delivery **Cost savings:** all scaled scenarios show needle-free is cost saving up to 47%; could save ~US $50 million over a 5-year period **Clinic throughput:** 11% faster than SoC **High acceptability among caregivers:** 94% like the device with 84% noting the child's response (less or no crying compared with SoC) **High acceptability among HCWs:** 95% prefer needle-free over SoC; 89% said it was easier to use; 90% said there was less discomfort.	*"Yes. In fact, I will even love it if we use the device to give other antigens because it is faster and effective and it reduced the noise of the children."* *"So, this device is very easy for the children, and it is very easy for the health workers. Then you can only immunize 10 children but now you can immunize up to 50 children without knowing that they have done anything."*

Evaluating the impact of needle-free delivery of inactivated polio vaccine on Nigeria's routine immunization program[1]

This study is made possible by the support of the American people through the United States Agency for International Development (USAID). The contents are the responsibility of PharmaJet and the Project Partners and do not necessarily reflect the views of USAID or the United States Government.

1. Pan African Clinical Trials Registry. (2024, April 10). Evaluating the impact of an Intradermal Needle-free Delivery Device on a Polio Routine Immunization Program. Trial ID: PACTR202308820044137. Available online: pactr.samrc.ac.za/Search.aspx (accessed on 27 December, 2024). Manuscript in progress

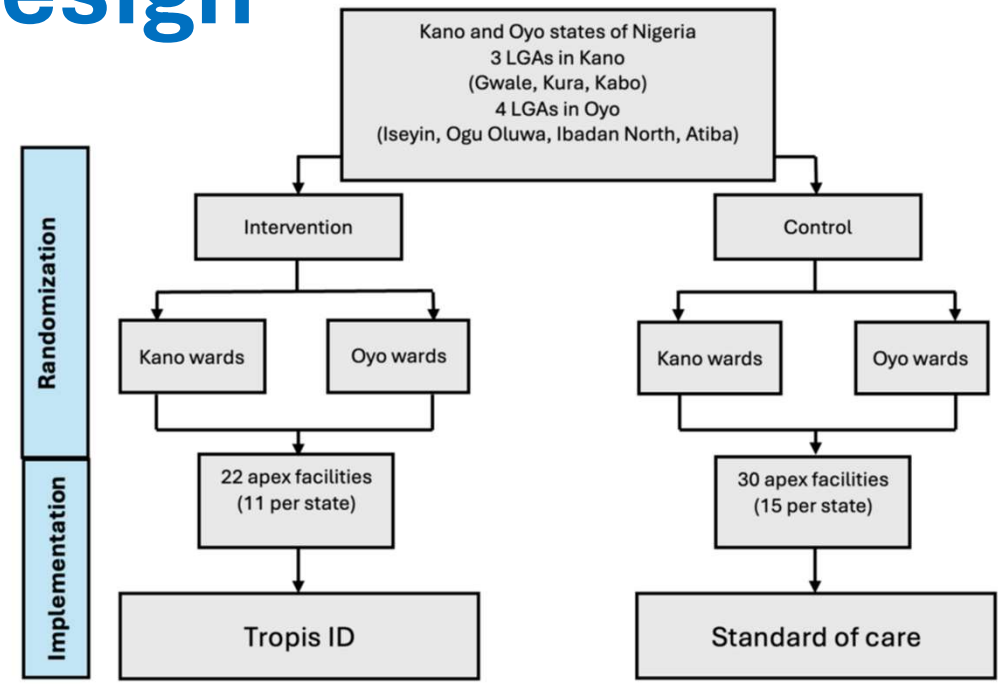
Three study aims

Aim 1: To test the **comparative effectiveness** of Tropis for fIPV in routine immunization services as compared to standard-of-care (SoC) vaccination practice (0.5 ml IM injection with traditional needle and syringe) **in improving 2-dose IPV coverage** (IPV2) among children aged less than one year

Aim 2: To assess the **total immunization cost impact** of using Tropis for fIPV delivery as compared to SoC vaccination practice

Aim 3: To understand the **acceptability, feasibility, scalability, and sustainability** of fIPV Tropis delivery

Design

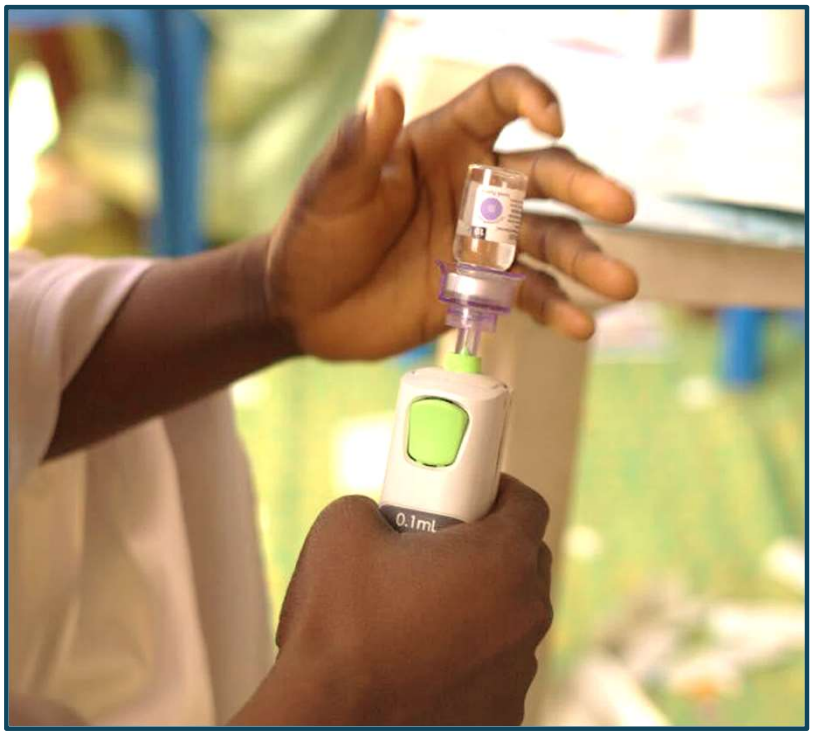


Design: Cluster randomized trial
Intervention units (Randomization): 52 Apex facilities (22 intervention, 30 control)
Intervention: Tropis used for intradermal delivery at intervention sites (0.1 ml ID)
Control: Standard of care (0.5 ml IM)

Results (coverage*)

Tropis is an effective intervention for increasing coverage of IPV2⁺

- There was no difference in IPV2 coverage between the randomized study arms (intention to treat), due to low compliance to intervention.
- Among those vaccinated with Tropis, IPV2 coverage was **11.2%** higher compared to the SoC.
- On a relative basis, the **odds of receiving 2 doses of IPV are doubled when Tropis is used.**



** 3433 children (14 weeks to 12 months) from 97,165 households surveyed.*

+ IPV2 is 2nd dose of IPV in any form (IPV or fIPV)

Results (cost)

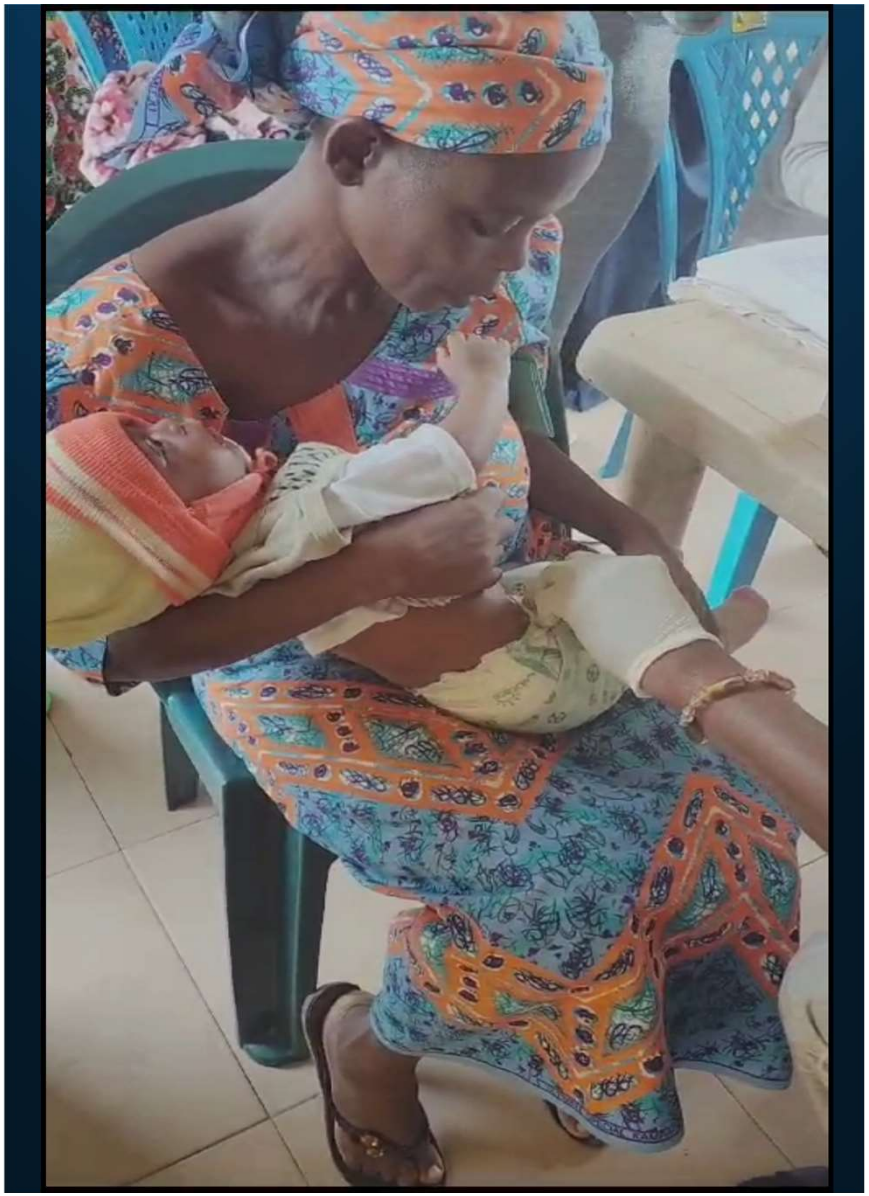
All intervention scenarios demonstrate cost savings compared to SoC.

- Incremental savings with needle-free could range from $0.07 to $1.00 per dose administered across evaluated scenarios with **up to 47% total immunization cost savings** compared to SoC at full scale.
- Switching to needle-free delivered fIPV could **save the Nigeria immunization program ~$50M USD** over a 5-year period.

Results (feasibility)

Needle-free was highly valued compared with SoC

- Caregivers: **94% acceptability.**
- Healthcare workers: **95% (preference)**, 89% (easier), 78% (safer).
- Tropis **reduced administration time by five seconds** on average compared to standard of care.
- **Zero device malfunctions** (6-month period)
- Tropis was **successfully integrated into routine immunization sessions** where other vaccines were being administered.



Needle and syringe compared with needle-free delivery

Here is a 20 second video from our work in Nigeria.

- The 1st 10 seconds show a baby responding to MR injection with a needle and syringe
- The next 10 seconds show same child receiving IPV intradermally using needle-free Tropis.

What a difference! This ties into our theory of change: ease of workflow in the clinic + high acceptance = improved coverage. (behavior change with mothers AND vaccinators)

In summary:

The study results indicate increased coverage of IPV2 among those receiving vaccination through Tropis. Its use shows a potential decrease in program costs, and when coupled with high acceptability can be scaled for routine immunization use.

jhpiego

PharmaJet®

USAID
FROM THE AMERICAN PEOPLE

PATH

SYDANI GROUP

Improved performance of various products & technologies

Many Applications

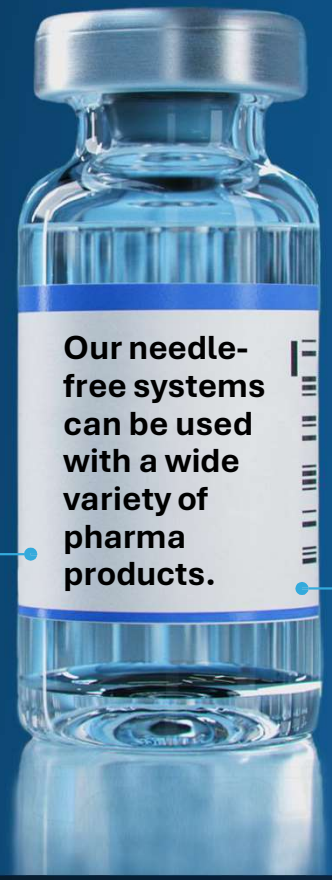
- Vaccines
- Therapeutics
- Select drug products

Any Level of Research

- Bench testing
- Pre-clinical studies
- Clinical trials

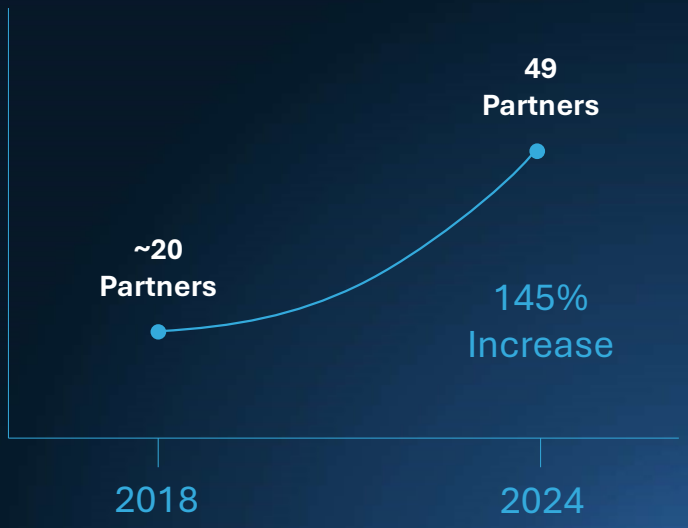
Various Formulations

- **Fluid** injectables (same as needle & syringe)
- **No need to re-formulate or re-package**
- **Viscosity** up to 70 cP (mineral oil consistency)
- Partners have used:
  - **Adjuvants**
  - **Microcarriers** (microspheres, **LNPs**)
  - Plasmid and doggybone DNA



- Nucleic Acid
- Inactivated
- Subunit
- Live Attenuated
- Viral Vector
- Bacteria

PharmaJet Clinical Data: Dramatic Growth Over Six Years



TODAY:

3 **Approved Products**

Afluria	Split egg-derived vaccine, influenza, Stratis
ZyCoV-D	EUA approval World's first approved DNA vaccine, COVID-19, Tropis
GEMCOVAC-OM	EUA approval, mRNA vaccine, COVID-19, Tropis

98 **Publications**

- 96 Partner published
- 2 PharmaJet published
- 19 Clinical studies
- 79 Preclinical studies

51 **Active Studies**

- 40 Preclinical
- 6 Phase 1
- 4 Phase 2
- 24 Infectious Disease
- 13 Oncology
- 14 Other / Preliminary

EUA of Nucleic Acid Vaccines Exclusively Administered Intradermally with Tropis

ZyCov-D, the first DNA vaccine approved for Covid

Gemcovac-OM, the first self-amplifying mRNA vaccine approved as a booster dose for Covid

Clinical benefits of ID delivery of vaccines with Tropis

- **More effective vaccine delivery across multiple vaccine platforms:** Stronger immune response and enhanced immunogenicity for DNA and mRNA vaccine delivery compared with traditional needle and syringe.[1,2]
- **Higher T-cell response:** ID Vaccination of a therapeutic DNA-based HPV vaccine provides higher CD8+ T Cell responses than intramuscular delivery[3]
- **Higher mucosal immunity and greater cross protection:** compared with IM delivery with needle and syringe (multi-valent inactivated platform)[4]
- **Faster seroconversion:** Seroconversion of multivalent live vaccine was more rapid with a single dose delivered by Tropis compared with needle and syringe.[5]

1. Momin, T. et al., (2021). https://doi.org/10.1016/j.eclinm.2021.101020
2. Alberer, M. et al., (2017). https://doi.org/10.1016/s0140-6736(17)31665-3
3. Peng, et al., (2023). https://doi.org/10.1128/mbio.02121-23
4. Hernandez-Franco, *et al.,* (2023). https://doi.org/10.3390/vaccines11111699
5. Jackson, L., et al., (2018). https://doi.org/10.1016/j.vaccine.2018.05.028

Conclusions: PharmaJet Precision ID Delivery Systems

Tropis is the only commercially-scaled technology for needle-free ID administration

- Over **10 million** vaccinations given
- **CE mark** and **WHO pre-qualification**

Improve the performance of prophylactic and therapeutics vaccines

- Cross-protection, duration of immune responses, and mucosal immunity

Flexible delivery platform for various vaccine technologies

- mRNA, DNA, LIAV, protein, etc.
- No need for reformulation or extensive CMC development

Can be used for **delivery of treatments** (mAb and others)

THANK YOU!

PharmaJet®
Needle-Free Injection™

PharmaJet Team

Paul LaBarre, MBA
Vice President, Global Business Development
Paul.LaBarre@PharmaJet.com