AFRICA IN THE GLOBAL VACCINE MANUFACTURING LANDSCAPE: ADVANCEMENTS

Innovative Biotech (Nig) LTD

Freetown, Sierra Leone Simon Agwale, Ph. D 24-25 September 2018

Company Overview

Mission Statement: To build a new business area in Nigeria through the development of world quality vaccines, diagnostic products and the provision of excellent clinical services.

Key Objectives:

1. Market Leader: Provide High Quality and Affordable vaccines, across all critical disease segments.

2. Leadership Development: Develop one of the first modern African owned vaccine of international standards with world-class business leadership.

3. Sustainable Growth: Deliver and maintain growth at a minimum of 10% CAGR over the next 10 years.

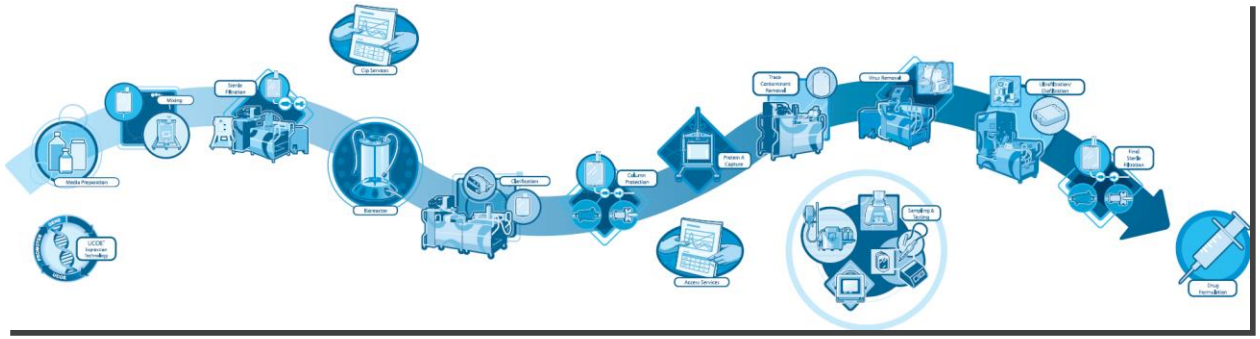
Why Manufacture Locally?

- Over 35 new vaccines introduced into developing countries gradually adopted from developed world.
- The most devastating diseases in developing countries are generally rare or do not occur at all in the developed world.
- Communicable diseases make up 56% of the disease burden in developing vs 6% for developed countries.
- Developing countries can no longer count on hand-me down vaccines from the developed world.
- Developing countries will have to focus on localized manufacture of vaccines at affordable to ensure sustainability.
- Developing countries have to wait for longer period (>18 months) until the vaccine becomes available for them as recently evidenced by Ebola and MERS cases.

Setting up a Vaccine Company: The approach)

- Partnership between public and life science private sectors provides the advantage of bringing high value innovation to the market and to the patients.
- Through the creation of a partnership between Merck (Life Science business), and Innovative Biotech LTD a privately held company registered and operating in Nigeria, **the goal of this project is to create an integrated vaccine development and production platform in Nigeria** to address the needs of priority diseases: **Lassa, Ebola, HIV, Cancers etc**.
- The project is based on a stepwise approach: first Innovative Biotech will build-up a vaccine fill/finish facility in Nigeria (Bosch and Merck)to respond quickly to epidemics needs.
- As a second step, the development and scale up of LASSA, EBOLA, HIV, Cancers etc candidate vaccines will be conducted between the partners to reach the point of scaling up the process and transferring it to the local manufacturing in Nigeria.
- Innovative technologies such as the recombinant Virus-like –particle (VLP) will allow for easy combination of the required antigens on the surface of a VLP structure thereby making it a flexible platform technology for the development of current and emerging infectious diseases threats locally and globally.

Develop a manufacturing process



Upstream Processing	Downstream Processing	Formulation
Cell line generation Media and feed selection Clone selection Cell line adaptation Bank generation Bank storage Upstream definition	Chromatography media screening Viral inactivation // filtration step design Sterile filtration optimization TFF step design Precipitation step design Single-use implementation	Bioavailability enhancement

Set the Ground for VLP in Nigeria

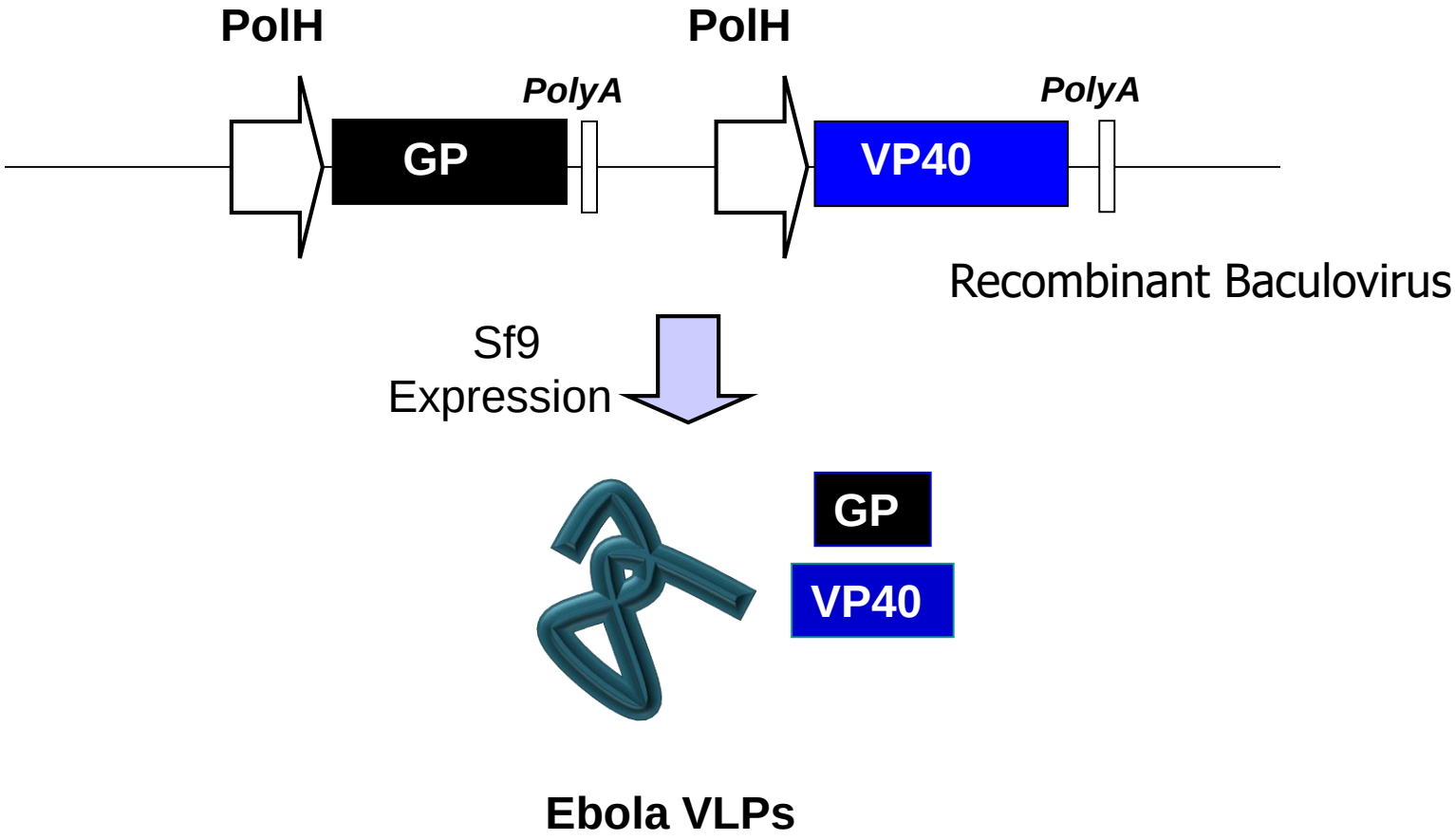
Virus-like particles (VLPs) represent an appealing model for vaccine development, as they resemble native viruses but are not infectious. VLP-based vaccines are in high demand and being actively pursued by many vaccine companies worldwide.

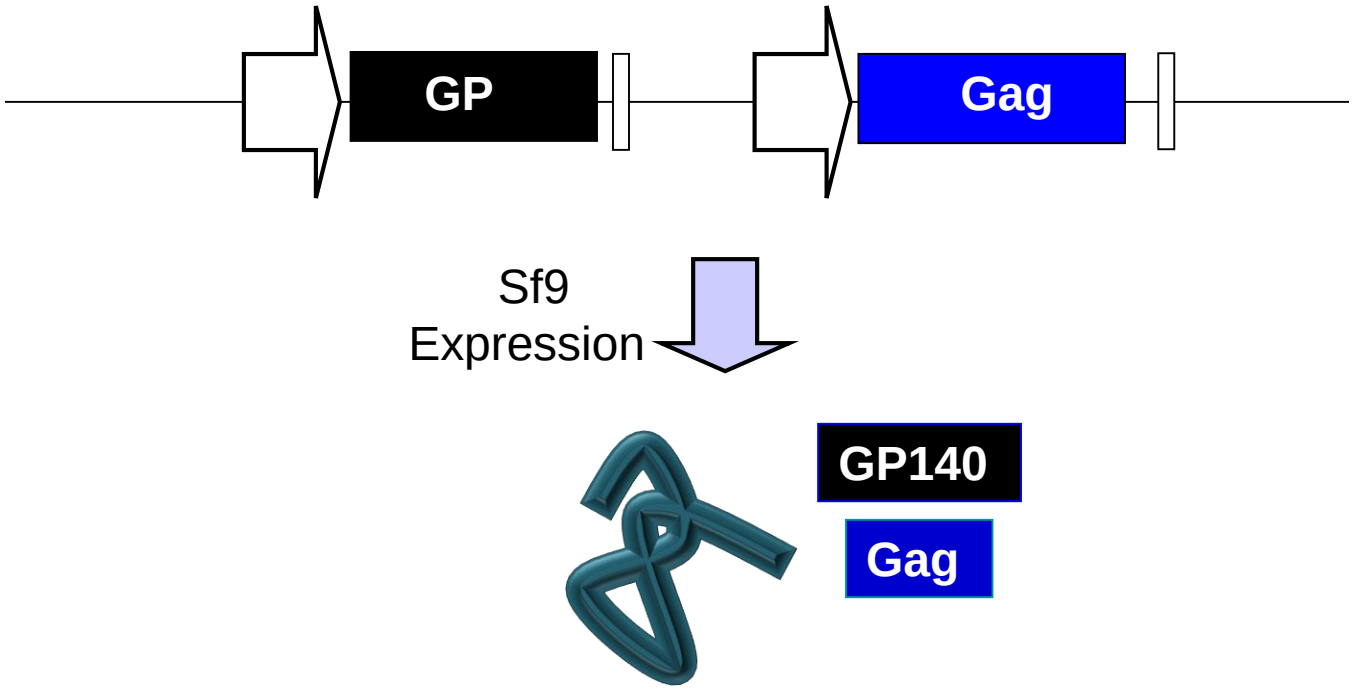
VLPs can be produced by various methods such as mammalian cell culture, insect cell culture, and bacterial and yeast-based systems. While these systems can result in good production yields, purification requires particular attention.

Regulatory bodies are concerned about the level of the process-related impurities and their overall impact. For this reason, key impurities such as host cell proteins (HCP), host cell DNA (hcDNA), and baculovirus must be removed during the VLP production processes. The challenge is to develop a scalable upstream process, together with clarification steps and effective purification, while ensuring product quality and reproducibility.

Based on these challenges, it is important to work with a partner who understands these challenges. Merck Millipore's regulatory expertise, integrated portfolio of development and manufacturing solutions, and proven applications experience will help us overcome challenges in our VLP vaccines process.

Baculovirus Expression of Ebola VLP




GP
Gag
Sf9
Expression
GP140
Gag

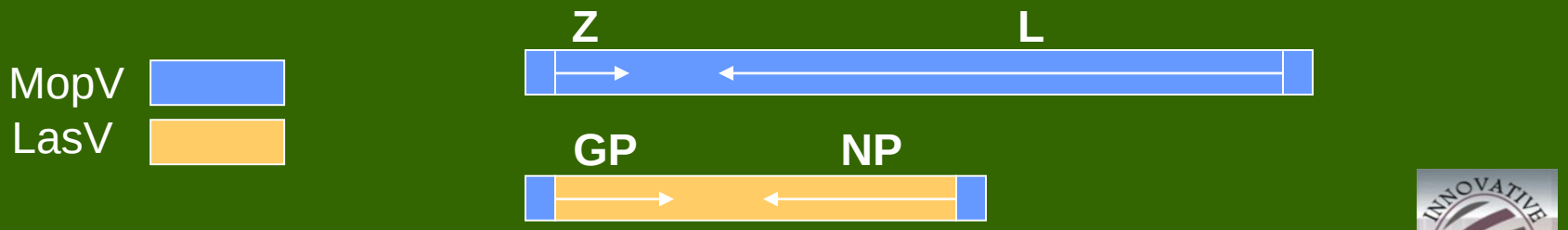
VLP-HIV CRF02_AG candidate vaccine induced broadly neutralizing antibodies in mice model

	IC50 (1/diln)					
	IBHIV001	IBHIV002	IBHIV003	IBHIV004	IBHIV005	Z23
SF162	<100	<100	<100	<100	<100	20773
MN	2506	1454	1811	4129	2846	8840
BAL	<100	<100	<100	<100	<100	919
MGRM-AG-002	5580	3048	3944	7915	5412	387
MGRM-AG-006	7930	3010	3697	9477	6280	227
94UG103	7366	3042	3112	6437	5972	149
MGRM-C-026	3578	2092	1641	3499	3128	299
92TH021	4939	2205	1945	7008	4820	233
93IN905	2613	2232	1654	3831	3171	523
6535.3	596	247	321	1126	549	312
VSVg	1208	494	775	2063	920	<100
aMLV	13228	6150	7218	17153	14331	<100
JRCSF	3277	1636	2397	5377	4286	199
NL43	<100	<100	<100	<100	<100	2047
SIVmac239	559	328	387	1088	523	<100

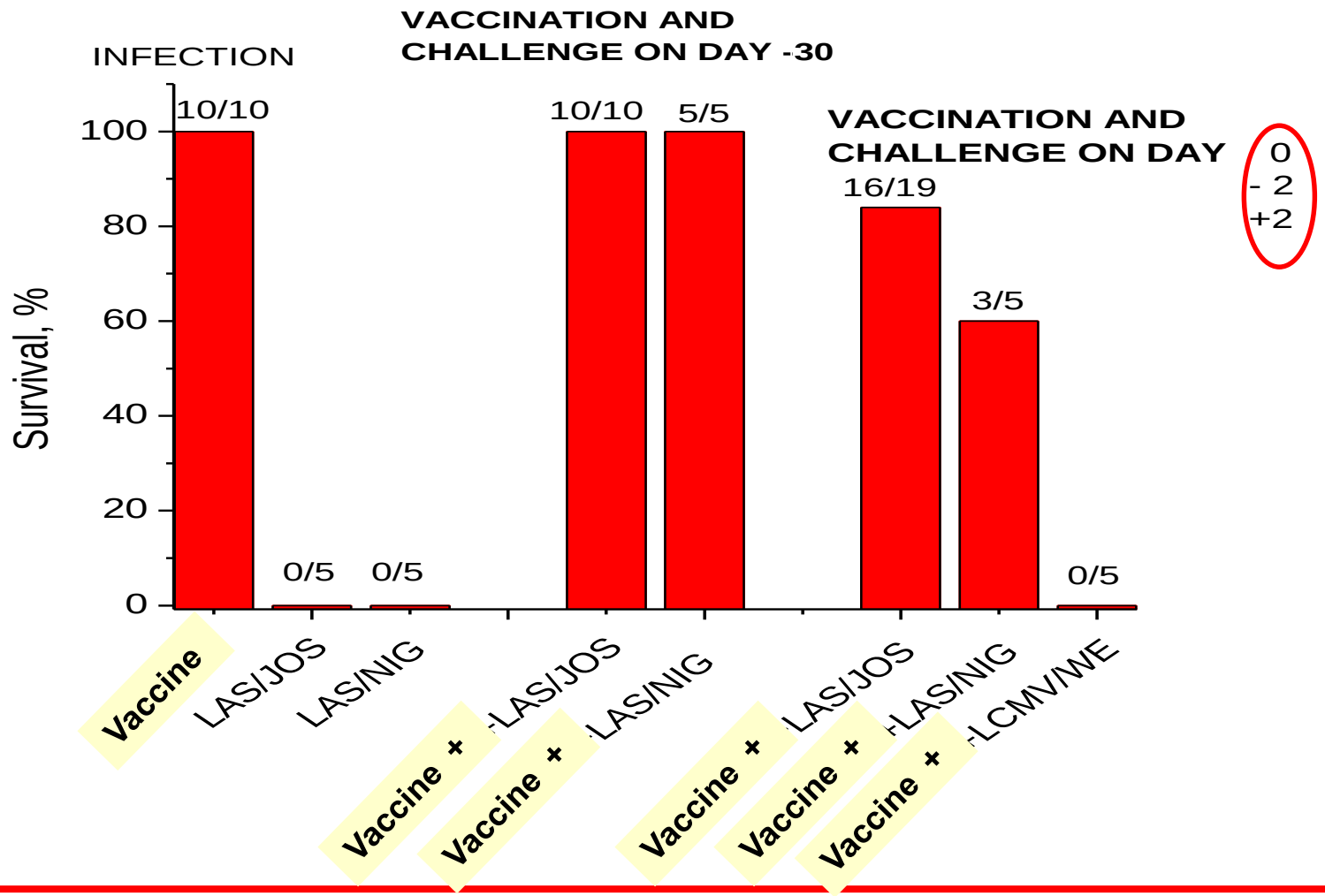
LasV Vaccine:
Live Reassortant Mopeia Virus (MopV) Expressing Lassa Fever Virus Structural Proteins

- LasV ML29 Vaccine: 68% MopV genome + 32% LasV Genes
- Reassortant vaccine against Lassa fever
- Vaccine is safe in rodent and NHP models

Genetic Structure of Reassortant Vaccine against LasV



Vaccination-Challenge Experiments in Guinea Pigs: Preventive and Therapeutic Applications of LasV Vaccine



1
2

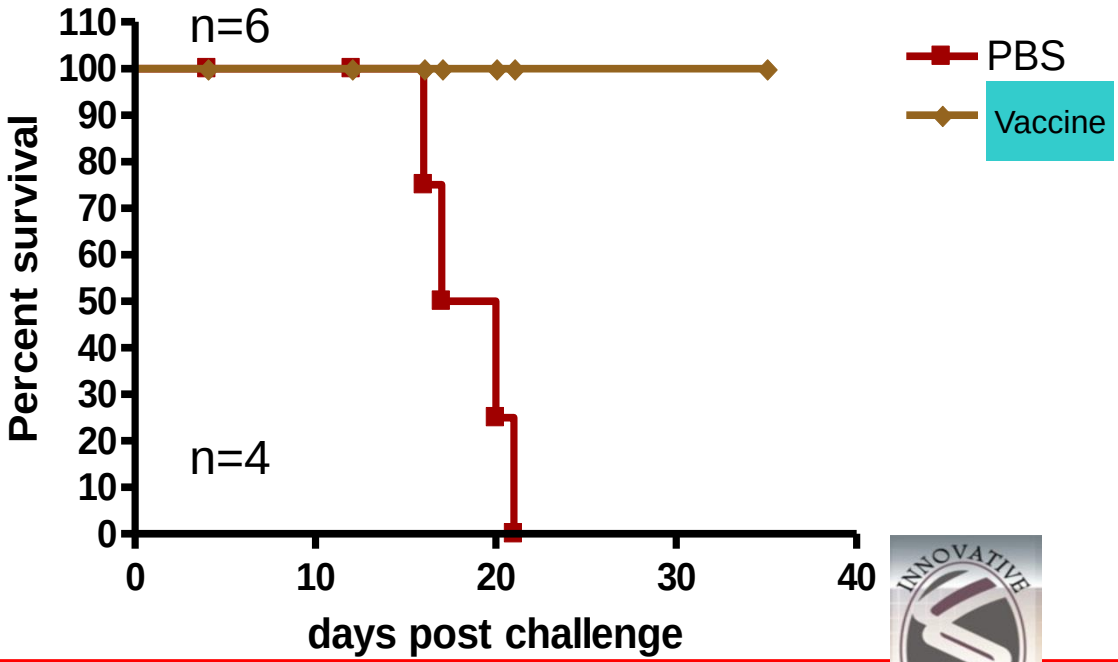
Vaccination with reasortant vaccine protects marmosets against fatal disease

Vaccination
1,000 PFU, s.c.

Challenge
1,000 LD50, s.c.

0 30 35 45 50 65 bleed. days

Efficacy in Marmosets



Future Plans

- We have developed and evaluated an EBOV VLP candidate vaccine that is highly immunogenic in mice.
- We have developed and evaluated an HIV VLP candidate vaccine that induced broadly neutralizing antibodies in mice.
- The primary immune response was boosted after a second dose and our proprietary adjuvant enhanced the immunogenicity at both time points.
- Given the immediate need for Ebola/HIV vaccines and the efficiency, safety and adaptability of our VLP platform technology we are confident in producing a high yield, high quality product using the most cost effective methodologies available.
- Recombinant VLPs have inherent advantages in safety, which is especially important for patients with immune system disorders including AIDS.
- This is critical for mass vaccination in Africa where HIV/AIDS represent a significant fraction of population.
- The proposed innovative approach is expected to increase yields of VLPs and to improve manufacturing to meet regulatory standards for a human vaccine.
- Such optimized VLPs would represent an ideal candidate for rapid scale-up and cGMP manufacturing of vaccines suitable for clinical trials and human vaccination.

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African Vaccine Manufacturing Initiative

Freetown, Sierra Leone 24 – 25 September 2018

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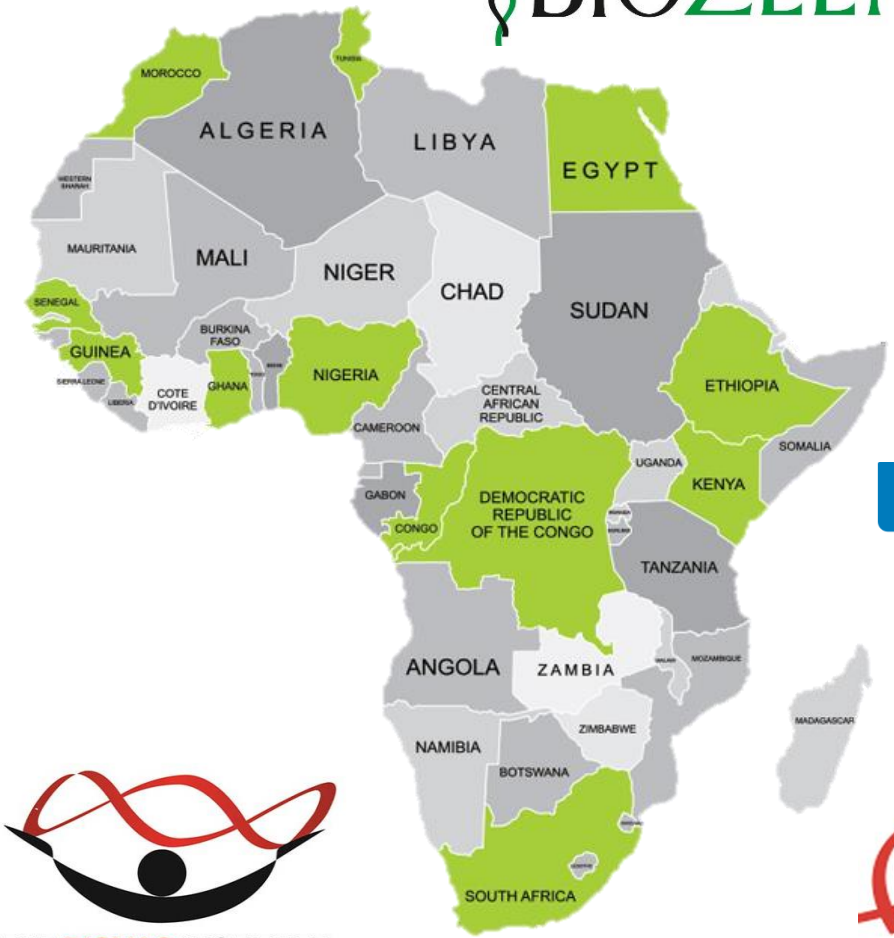

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