Vaccine development Strategies in Korea; from R&D to Production

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Background of Vaccine Self sufficiency

Importance of stable vaccine supply due to increased threat of emerging diseases

- SARS-CoV (2002, 775/8273 global, total damage 30 billion USD)
- Avian Influenza (2003, damage 1.5 billion USD Korea, recurrence in 2013)
- Pandemic influenza (2009, 270/750,000 Korea, estimated 5 to 30 billion USD in damage in Korea)
- FMDV (2011-2015, damage 4 billion USD Korea)
- MERS-CoV, (2015, 38/186 Korea, 10 billion USD in damage in Korea)

Vaccine self sufficiency; allows stable and low-cost supply of vaccines when you need it

Korea Experience: Influenza vaccine

MoTIE

Egg-based flu vaccine facilities (2005):

- Domestic flu vaccine production of 2009
- influenza pandemic outbreak; Failed to import vaccines on time

→ Supply of pandemic influenza vaccine; GC Biopharma, 26 million dose, 2010.01.05

MoHW

TEPIK established (Transgovernmental Enterprise of Pandemic Influenza in Korea):

- R&D (65M US$/6 yrs) (2010~2016)

→ Development of cell-based influenza vaccine; SK bioscience,
First cell-based vaccine for WHO PQ certification

MoHW: Ministry of Health & Welfare
MoTIE: Ministry of Trade, Industry and Energy

Vaccine R&D and manufacturing capacity plan by Korean Government

2016

"Vaccine 3.0"
Infrastructure building project for vaccine self sufficiency 2016-2020

2018

RIGHT FUND
Research Investment for Global Health Technology Fund

- Funded by ROK government, BMGF, Korean manufacturers
- Focuses on global health R&D
- E.g. Cholera Conjugate Vaccine (CCV)

2020

VITAL-Korea
Vaccine Innovative Technology ALliance Korea

- Partner with Vaccine Innovative Technology Alliance (VITAL) Korea to promote R&D for global health
- Promote vaccine sovereignty of Korea and preparedness against EID

2021

"K-Vaccine Hub"

Center of Excellence, providing essential support required in establishing K-Bio Hub

- **Vaccine research**: platform technology (mRNA, viral vector), adjuvant
- **Innovation center**: vaccine evaluation system through standard assays and reagents
- **Translational hub**: clinical development, regulatory affairs, and quality assurance
- **Globalization**: provide networking to industry to move to the next level

Research Investment for Global Health Technology Foundation

Vaccine product development partnerships with Korean manufacturers & agencies

OCV, TCV, HEP B, HEP A, MERS Vaccine

SK bioscience
- Vi-DT TCV
- iNTS

경북바이오산업연구원 Gyeongbuk Institute for Bio industry
- Hep A

eubiologics
- Euvichol® & Euvichol-Plus® OCV

QuadMedicine
- Hep B microneedle patch

GENEONE LIFE SCIENCE
- MERS

COVID-19 Vaccine[1]

CEPI New vaccines for a safer world

LG Chem

SK bioscience

eubiologics

Genexine

CELLTRION

sumagen

CELLID

National Institute of Health

KDCA

SNUH SEOUL NATIONAL UNIVERSITY HOSPITAL

2011: 20%

2022: 40%

2030: 80%

1. Additional partners include Hanmi Pharmaceuticals, NeoImmuneTech, Bioapp, GI Cell, GI Innovation, POSVAX, GeneMatrix and Korea Mouse Phenotyping Center (KMPC)

SKYCovione

SK bioscience co-developed SKYCovione™;

Korea, UK, WHO

- A recombinant protein vaccine, the Institute for Protein Design (IPD) at the University of Washington

- ASO3 adjuvant from GSK

- The Bill & Melinda Gates Foundation funded for early development

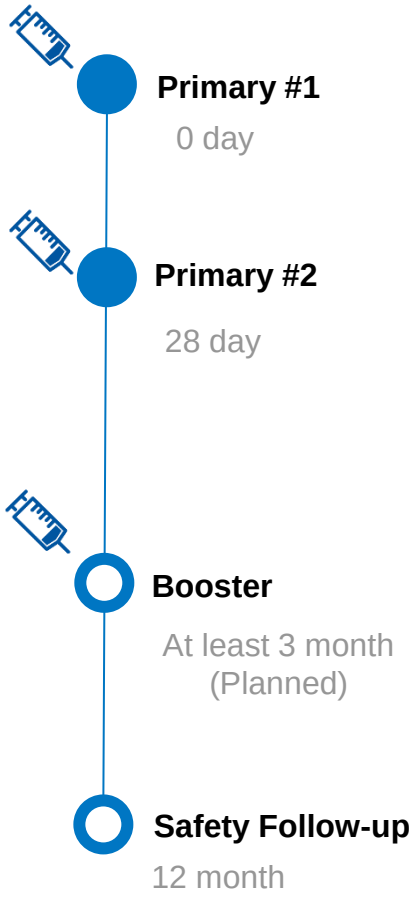
- CEPI Fund for clinical trials, variants research, and manufacturing process development.

- IVI supported the global clinical trial, sample analysis (with KDCA), and the regulatory process for the vaccine's licensure

Phase 3 clinical study design of SKYCovione

- **SKYCovione conducted global clinical trials using ChAdOx1-S (AstraZeneca Covid-19 vaccine) as a reference vaccine for the purpose of evaluating humoral/cellular immunogenicity and safety in adults over 18 years of age**

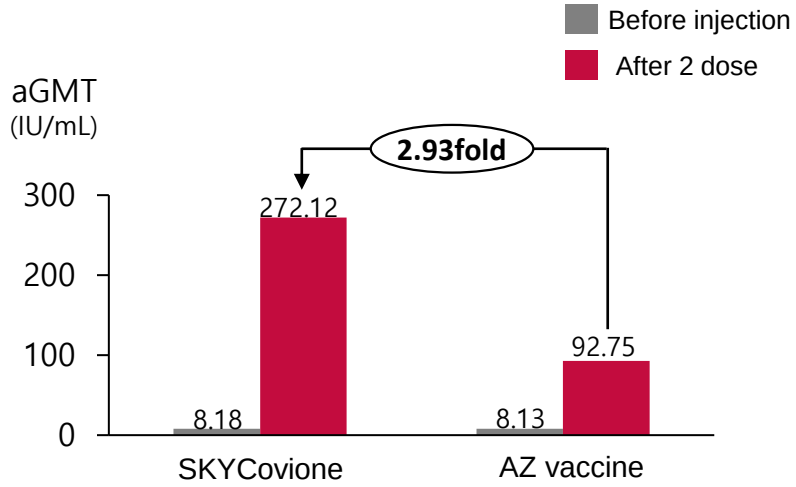
Title	Multicenter, parallel comparison, observer-blind, active-controlled, randomized, phase 2, phase 3 clinical trial to evaluate the immunogenicity and safety of SARS-CoV-2 recombinant protein nanoparticle vaccine (GBP510) in adults 18 years of age or older.
Purpose	Humoral/Cellular Immunogenicity and safety evaluation of SARS-CoV-2 recombinant protein nanoparticle vaccine (GBP510) in adults 18 Years or older
Subjects	• Target subjects: 3,990 adults 18 years of age or older • Countries participating in clinical trials: Korea, New Zealand, Ukraine, Philippines, Thailand, Vietnam
Dose	GBP510-AS03 (25μg), reference vaccine: ChAdOx1-S (AstraZeneca Covid-19 vaccine) • 2-Primary doses 4 weeks apart (on Day 0 & 28 for each)
Endpoints	**Safety** • Solicited AE, Unsolicited AE, AESI, SAE, COVID-19 cases **Immunogenicity** • GMT(Superiority)/GMFR(Non-inferiority)/seroconversion of IgG antibody and Neutralizing antibody, and Cell-mediated response



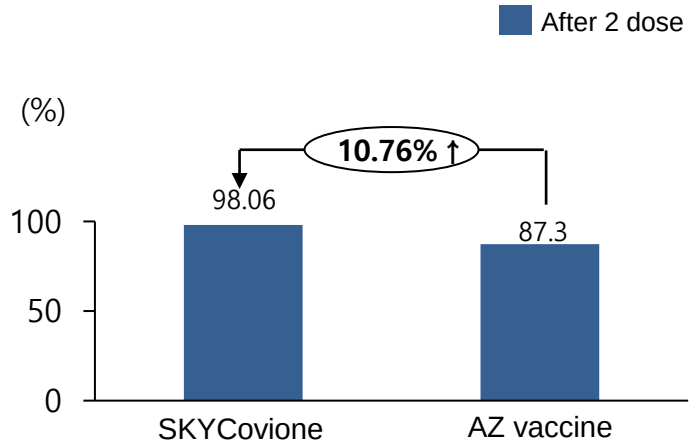
Phase 3 study results – Primary endpoint

- **The results of the phase 3 clinical trial of SKYCovione confirmed the superiority of immunogenicity compared to the reference vaccine, the same as the results of the phase 1/2**

FRNT[1] Neutralizing Ab – Superiority



SCR[2] - Non-inferiority



			GBP510		AZ Vaccine		P-value**
			N	Post- GMT	N	Post- GMT	
	Baseline	GMT (SD)	877	8.18(1.08)	441	8.13(1.06)	0.0936
		GMR (95% CI)	1.01 [1.00, 1.01]				
GMT (FRNT)	2W after Dose 2	Adjusted GMT (SE)*	877	272.12(1.07)	441	92.75(1.07)	<0.0001
		GMR (95% CI)	2.93 [**2.63**, 3.27]				
SCR	2W after Dose 2	SCR	877	98.06%	441	87.30%	<0.0001
		Diff. (95% CI)	10.76% [**7.68**, 14.32]				

1. FRNT (Focus Reduction Neutralization Test) : SARS-CoV-2 Wild type virus ND50 Titer converted to IU/mL
2. SCR (Seroconversion Rate) : Ratio of subjects whose neutralizing antibody titers increased 4 times or more compared to before administration

** GMTs adjusted with treatment group, age group (18~64, ≥65) as factors, and baseline antibody level as covariate*

***P-value for baseline GMT : t-test / P-value for adjusted GMT : ANCOVA / P-value for SCR : Chi-square test*

SKYCovione

- June 29, 2022, Skycovione was approved for use in South Korea
- May 26 2023 authorised by the Medicines and Healthcare products Regulatory Agency (MHRA), UK
- June 23, 2023, listed on the WHO Emergency Use Listing (EUL)
- South Korean government purchased 10 million doses of SKYCovione of which 600,000 doses released into hospitals

Lessons Learned; for successful vaccine development

- International Collaborations for public sector funding and development efforts: IPD at the University of Washington, GSK, The Bill & Melinda Gates Foundation, CEPI, IVI, AstraZeneca, Korea Government
- Good antigen and adjuvant
- Rigorous regulatory process for vaccine manufacturing and clinical evaluation
- Need Vaccine experts and trained staffs

Global Equity in Access and Development?

International Vaccinology Course by IVI

- Established in 2000, one of the longest-running vaccinology courses in the Asia-Pacific region.
- Trained nearly 5,000 vaccine professionals from LMIC worldwide
- Collaborators: Karolinska Institutet, Sweden

GTH-B: Global Training Hub for Biomanufacturing

- Launched in 2022, the trainings are supported by the Ministry of Health and Welfare of Republic of Korea and the WHO
- Aims to equip participants with the critical skills and knowledge needed for biomanufacturing.
- 400+ participants have taken part in the trainings.
- The entire training course is free of charge to all participants. (exclusive travel and visa costs)

GTH-B: Introductory Course for Biologics Development and Manufacturing

- **2-week, in-person training on introduction to all aspects of biomanufacturing.**
  - Includes didactic training and interactive activities (e.g., case studies, presentations, panel discussions, etc.)
- **Participants start to build the skills and competencies needed to work along the entire cycle of vaccine development, production and licensing.**
- **Includes excursion to and networking sessions with Korea Biopharmaceutical companies and networking**
- **Two trainings held**

2022	2023
• July 18-29 • 138 participants: 106 participants from 24 LMICs • Scholarships provided by: PAVM, IDB	• June 19-30 • 187 participants: 150 participants from 40 LMICs • Scholarships provided by: PAVM, IDB, EAC RCE-VIHSCM, PAHO

GTH-B: Introductory Course for Standard Practice (GxP)

- **3-week, in-person training**
  - Provide participants with a strong understanding of global standards for biomanufacturing (GMP, GCP, GLP, GCLP, and biosafety)
  - Includes didactic training and interactive activities (e.g., case studies, presentations, panel discussions, etc.)
  - Includes excursion to and networking sessions with Korea Biopharmaceutical companies and networking
- **First training held in Oct-Nov 2022**
  - 151 participants from 31 LMICs and 36 participants from South Korea
- **Next training is scheduled for Oct 30-Nov 17**
  - Participant confirmation ongoing: Expecting 180 participants

Development of training programs for WHO global bio-training hub (GTH-B) in Korea (Global Bio Campus program development and planning) : Proposed training program

Scope of GBC program

Scope of GBC Training

Jobs throughout the entire cycle of biopharmaceutical and vaccine development, manufacturing, commercialization, and supply

Manufacturing (Hands-on under GMP)	GMP	Pre-clinical (GLP)	Regulatory Affairs (WHOPQ+RAPS)	Clinical (GCP)	Supply and Marketing

Job diversity in GBC training programs
Specialized training by career unit

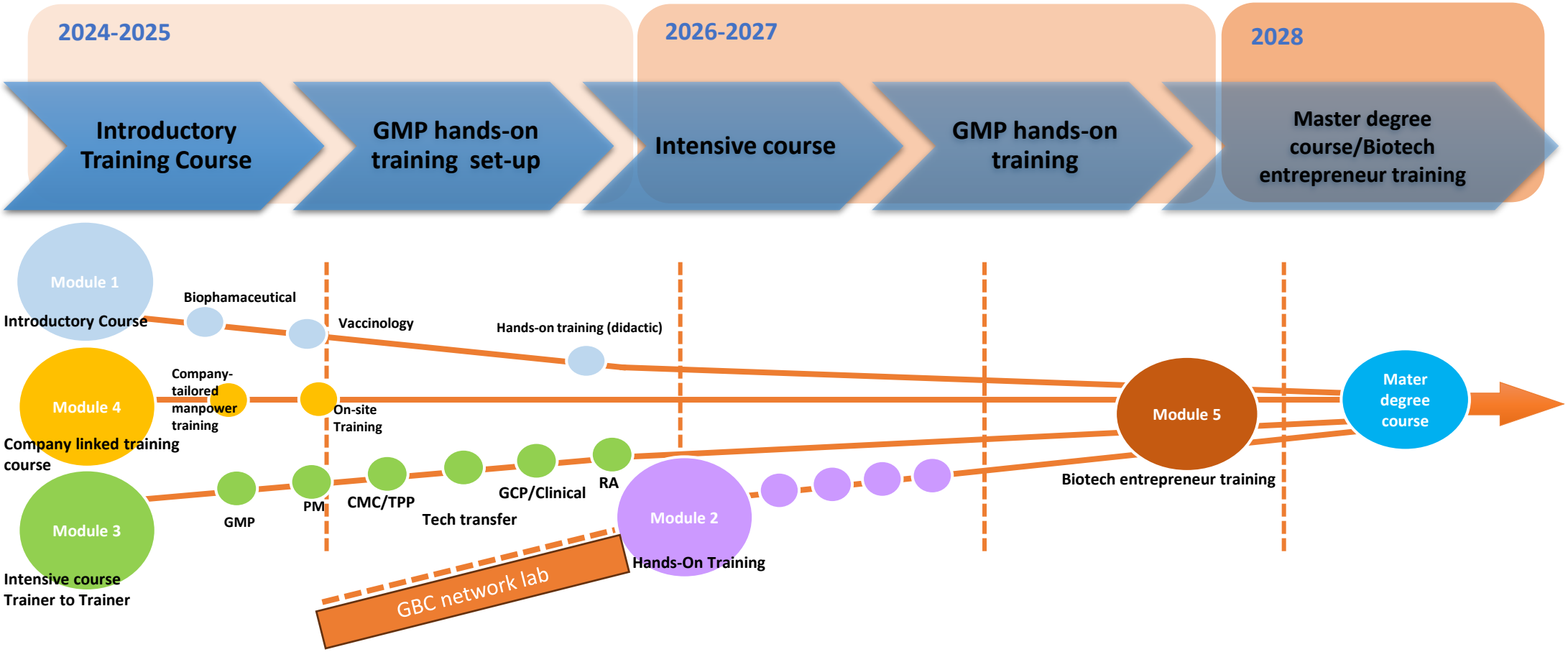
Entry Level / Junior specialist		Senior / Manager	Director/C-Level
Basic/intermediate level overview program	Hands-on training session	Intensive / advanced program Trainer to Trainer Training (TTT)	Biotech entrepreneur training

Major 6 modules of GBC Training Program

GBC Training Program Module					
Module 1	**Module 2**	**Module 3**	**Module 4**	**Module 5**	**Module 6**
Introductory training course	**Hands-on training**	**Intensive course**	**Company-linked training program**	**Biotech entrepreneur training**	**Master Degree**
Training to strengthen basic knowledge of biopharmaceutical and vaccine development	Vaccine and biopharmaceutical hands-on training at GMP-like facility	Trainer to Trainer level training, In-depth training for each job of vaccine/biopharmaceutical industry	Training based on industry needs and on-site training programs	Biopharmaceutical entrepreneurship training to build a domestic biopharmaceutical ecosystem	Master's degree program combining GBC training program and internship Master degree in biopharmaceutical science and Vaccinology

Development of training programs for WHO global bio-training hub (GTH-B) in Korea (Global Bio Campus program development and planning): Operation model

Propose the efficient 6 biomanufacturing training module programs and operation model contributing to global bio campus.

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