



Disclaimer

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- The presentation provides an overview of the subject and does not intend to be complete in every detail and in all options.
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Role of CDMOs from CRO, Dx, Vaccines and Therapeutics



Viral isolation

Real-time PCR

Test for Genetic Material

(DNA/RNA) with primers

directed against the

genome

Inoculation of viral isolates from swabs, tissue homogenates, body fluids in host cell lines to enable replication



Bacterial isolation

Inoculation of bacterial isolates into liquid /solid media and identification by staining



Identification of bacteria

- Stain and Examine under microscope
- · Gram +ve (Blue)
- · Gram -ve (Red)

Sample Collection (Urine, Stool, Blood, Swab, Sputum, Other Fluid/ Tissue from Field Specimen)

Microbial Identification thru diagnostic techniques



Sequencing

Detection of novel, divergent species with homology to sequenced organisms



ELISA multiplex

· Confirmatory test against antigens

*The selection and sequence of diagnostic methods for proper identification both depend on the sample. This set of tests complement each other for the screening and confirmation of pathogens



Diagnostics: Commercial Production and Services

IVD Manufacturing: ISO 13485/EU DX/FDA 820

Diagnostic Testing Services: CAP/ISO 15189



Diagnostics: R&D Clinical Development

Real-time PCR kit (Design Primers and Probes against novel genetic sequence as a rapid screening method)



Diagnostics: **R&D** Clinical Development

Microfluidics, Paper, Lateral Flow



Recombinant protein expression and purification Bacterial, yeast, mammalian systems



Isolation of patient/ animal-derived antibodies, screening of Abs with best binding affinity, single clone expansion, MaB production for therapeutic purposes

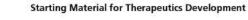


Storage of Isolates and mAbs

Strains and mAbs are preserved as references for 1-1.5 years



Purified monoclonal antibodies (mAbs)/ Antigens for coating/dispensing to



Antibody Discovery Lab

- · Antigen administration to animals for hybridoma generation
- Positive clone selection and expansion using selective medium
- Harvest of Monoclonal antibodies



and SPR for Binding affinity

"high

by ELISA

· Expansion of "high producing hybridomas" - adherent or suspension platform

Vaccine Development in

- Viral isolation
- · Reverse genetics
- Reassorted virus (passaged and rescued from host cells)
- Immunological evaluation in animal models(adjuvanted Vaccines)
- Formulation
- CQAs/ Correlates of protection





Determine Suitable Expression Platform















Scale Up Process Development

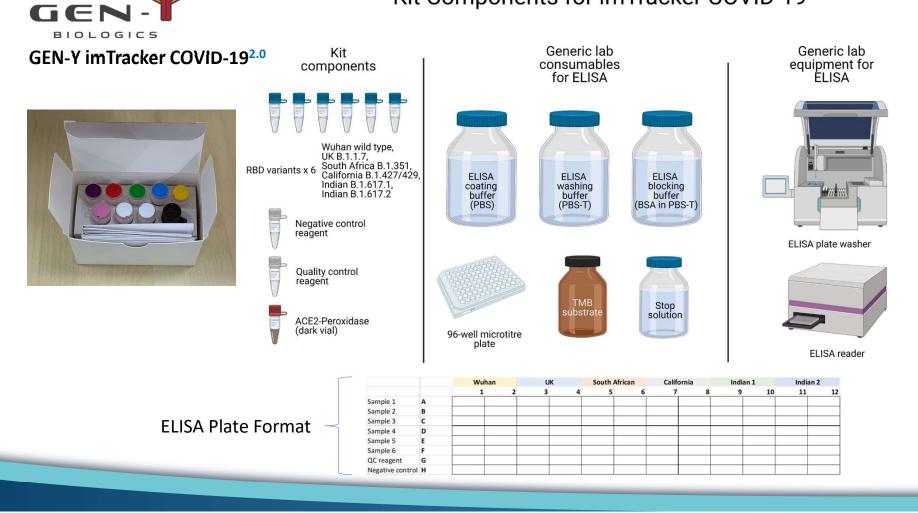
- · GLP/cGMP compliant TOX in animal facility
- cGMP compliant phase 1/2
- · CGMP certified Phase 3 commercial







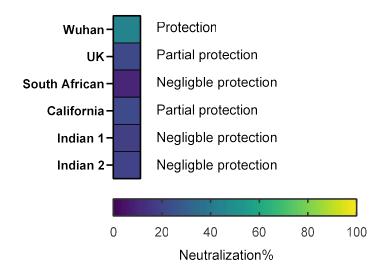
E.G of MDX When to boost. (Beyond vaccine self sufficiency) Kit Components for imTracker COVID-19





imTracker MULTI Provides Broader Deeper Insights

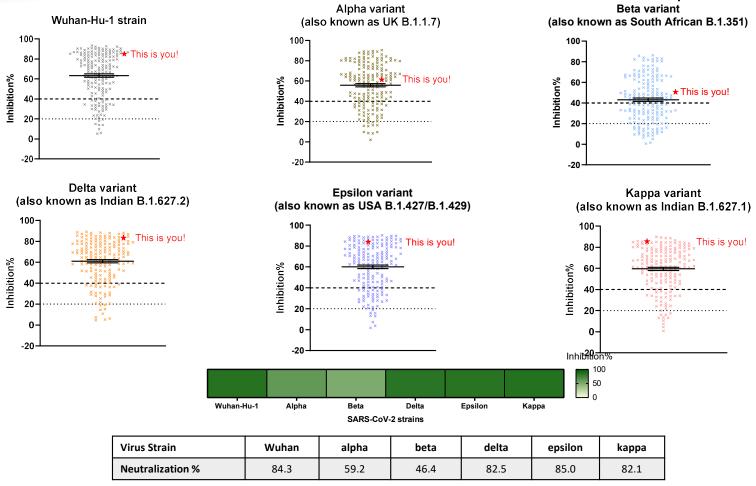




- Colour coding identifies an individual's personal antibody neutralizing ability versus the most concerning viral variants
- For example, from the read out;
 - Yellow color means there is good neutralizing antibody protection whereas dark blue indicates levels that may be below the threshold of protection or have no protection leading to reinfection with that variant
 - The evolution of the neutralizing antibody capability in these patients can be tracked further with repeated tests – say 3/6/9 months following the 2nd vaccine dose
 - By understanding the current status of an individual's neutralizing antibodies against multiple viral variants, this will enable the ability to:
 - --> Track Travel Appropriateness
 - Track Vaccine Effectiveness
 - Track Booster Requirement
 - Track Vaccination Status at Border for Entry
 - Track Data on Immunity against Multiple Variants
 - Track Data Differences in Groups; by gender, blood type, ethnicity, age ...



Gen-Y imTracker MULTI for Covid-19 – Sample Test Result



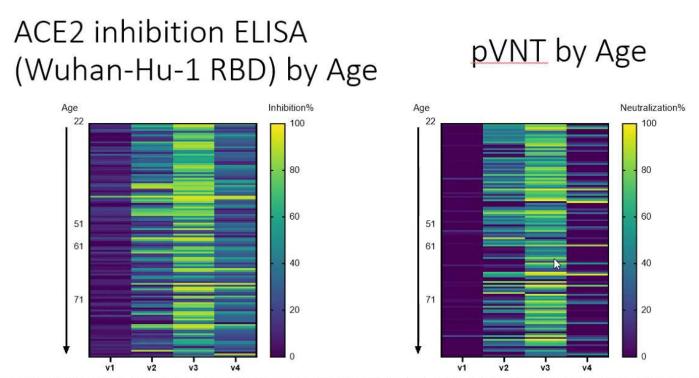
Over 40% = Good neutralization

20-40% =Weak Neutralization

Under 20% = No Neutralization

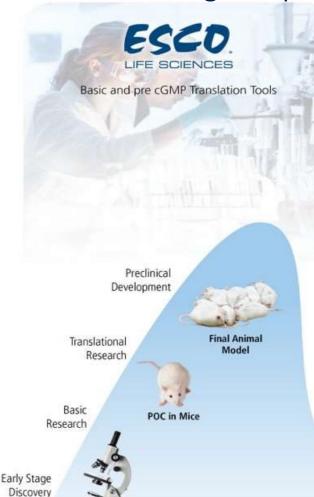


Population Cohort Studies.



Please note that this is only a preliminary result. Some data are affected by outliers in triplicates so there will be some changes. Some samples became very neutralizing at v4. Suspected infection after v3. Need to check anti-NC antibody titer at v4.

CDMOs Enabling Companies to Overcome Valley of Death in Commercialization





Esco Aster bridging non GMP lab processes into GLP/cGMP. Process development of bench scale into cGMP scale for CMC package leading to IND Phase 1 and 2. CRO work to enable scale up.

Highest Yield
Affordable Cost
Linearly Scalable
Quality by Design

FTO

Safety, Efficacy Clinical Cohort larger number

Phase 2

Safety Clinical Cohort small number

File IND with CMC

GLP Tox Non Human Primate or Large animals (Rabbit, Pig) GLP Material.

Process Valley of Death 1 Lab-GLP/GMP

- Identify Critical Quality attributes
- Process Analytical Techniques
- Identify cGMP Assays and Analytical Methods to guide and inform cGMP PD

Healthcare



Phase 3/ Commercial is either continued on by Esco Aster Commercial Sites or tech transfer into client own site built by Esco

Phase 4

Also known as post market surveillance. e.g. Safety for up to 10 years post gene therapy.

Commercial

Cohort largest number

Process Valley of Death 3 Commercialization roll out

- · Lack of reimbursement
- · Anti-movements (e.g. Anti Vaxxers)
- · Lack of public awareness
- Slow introduction into NHIP or approval by regulatory (e.g. biosimilars)
- Lack of infrastructure (e.g. Central Diagnostic Labs or ICUs for Car T, autologous facilities), viral vector shortage globally, etc

Process Valley of Death 2 Lab-GLP/GMP

· GMP to full cGMP

Phase 3

Safety, Efficacy Clinical

/ Challenge study (if applicable e.g. Flu

Vaccine). Process

locked in and will not

change.

 In some instances processes that work in phase 2 are not repeatable or consistent when scaling up into Phase 3 / Commercial

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	А	S	Т	Ε	R

Current Landscape and use cases of Covid-19 Therapies

	Asymptomatic or presymptomatic	Mild Illness	Moderate Illness	Severe Illness	Critical Illness		
Features	Positive SARS-COV- 2 test; no symptoms	Mild symptoms (e.g. fever, cough or change in taste or smell no dyspnea)	Clinical or radiographic evidence of lower respiratory tract disease; oxygen saturation ≥94%	Oxygen Saturation<94% respiratory rate ≥30 breathes / min lung infiltrates >50%	Respiratory failure, shock, and multiorgan dysfunction of failure		

Proposed
Disease
Pathogenesis

Inflammation

Antiviral Therapy

Antibody Therapy

Management **Anti-inflammatory Therapy** Considerations Home based monitoring tele-Clinical monitoring: if patient is Monitoring Hospitilization, oxygen Critical care and medicine. hospitalized and at high risk for for therapy and specific specific EUA therapy deterioration suggest EUA symptoms Palliative care. therapy e.g. exosomes. e.g. exosomes. Prophylactic usage if staying with at risk individuals

Adapted from Wild or Moderate Covid-19 | NEJMAntiviral pill: How close are we to a drug to treat Covid-19?, Opinion News & Top Stories - The Straits Times



Current Landscape and use cases of Covid-19 Therapies including stage of clinical trials

	Asymptomatic or presymptomatic	Mild Illness	Moderate Illness	Severe Illness	Critical Illness
Proposed Disease		Viral Replication			
Pathogenes	sis			Inflammation	

Antiviral Therapy



III/EU: Merck Molnupiravir

Antibody Therapy

Do not require supplemental oxygen, but are at risk of progression to severe forms of the disease.

III: GlaxoSmithKline (GSK) and Vir Biotechnology, sotrovimab

III: Casirivimab-imdevimab, made by Roche-Regeneron

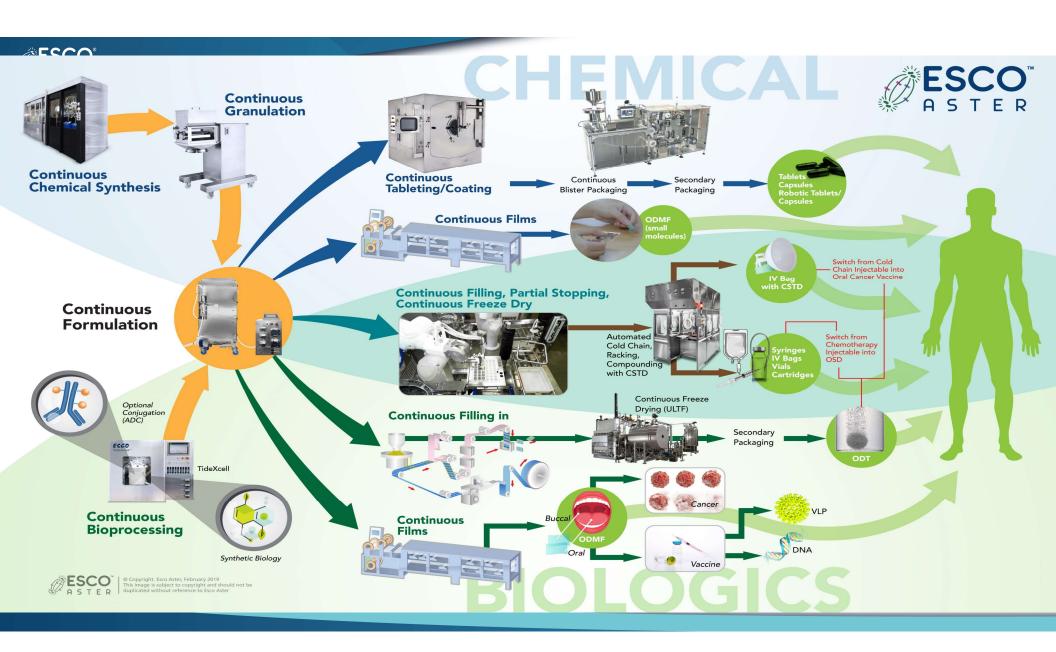
EU: Hospitalized, Repurposed Tocilizumab_

Anti-inflammatory Therapy

Phase 2: OBCTCD24 EXO-CD24 Treat CRS (occu 19 Patients)

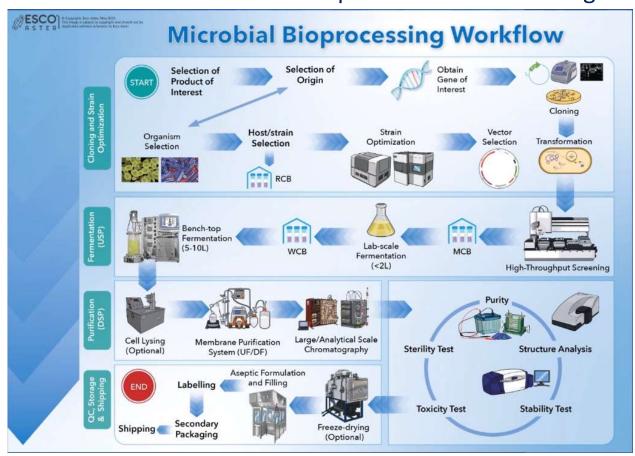
Antiviral pill: How close Repurposed Cogticosteraids (Pexamethasone

Opinion News & Top Stories - The Straits Times





Esco Aster Microbial Process for LMIC Open-Source Vaccines e.g. RBD219-N1C1

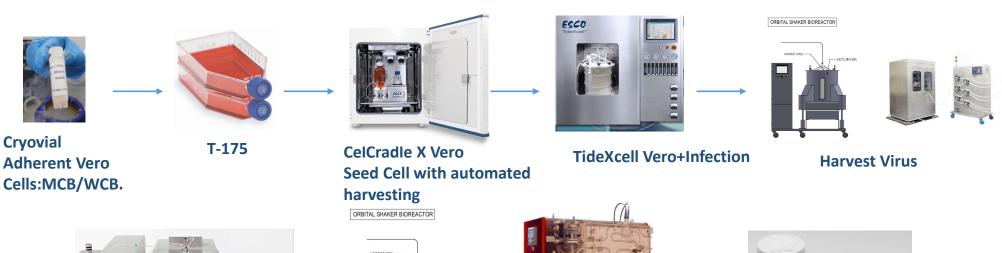


New operational paradigm from traditional CDMO to DBOT?





Esco Aster Single Use Adherent Vero Virus/Oncolytic Virus/Viral Vector Production





TFDF/TFF or Single Use continuous centrifuge



DNA Digest Benzonase

One step ion exchange Chromatography SO3 or Precipitation

Formulation
0.2µ Filtration
& Filling in Glass or COP
vial.

Freeze -60 or thermostable TBD if CRF or BF.



mRNA/LNP Vaccines













Plasmid DNA manufacturing

Extraction and purification of plasmid DNA

pDNA linearization Chromatography and TFF In-vitro transcription Capping and poly-A tail addition

Chromatography and TFF

Encapsulation and Formulation

TFF and sterile filtration

mRNA vaccine

Plasmid DNA production

Typically done by CDMO

mRNA production and purification

Typically done by Biotech company up to final DS Formulation into LNP

LNP Formulation PD and CTM typically done by CDMO

DP Typically done by CDMO

PROVAXUS COVID-19

Preparing for future COVID-19 variants and the need for booster shots against these variants



Developing novel mRNA vaccine



Fraction of the cost of current vaccines, less than US\$10 per dose



Planned deployment 2023



Provaxus Vaccine Advantages: High-Tech Low-Cost



highly effective



mRNA vaccines







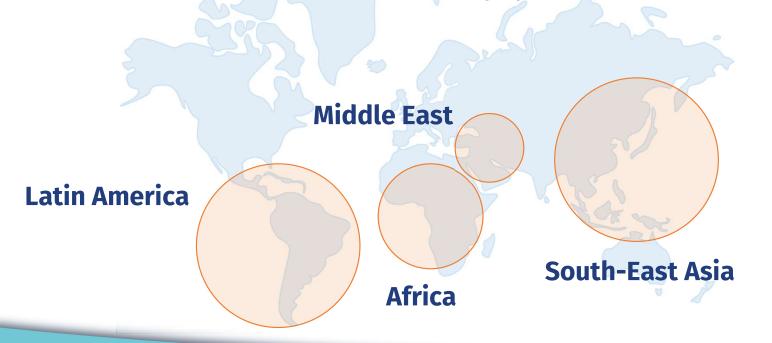
Removal of ultra-low temperature cold chain



Local Manufacturing

Early target markets for Provaxus Vaccines

Cost-enabled Provaxus vaccines are designed with the intent to provide access to superior vaccine technology to the world's most vulnerable and underserved populations.



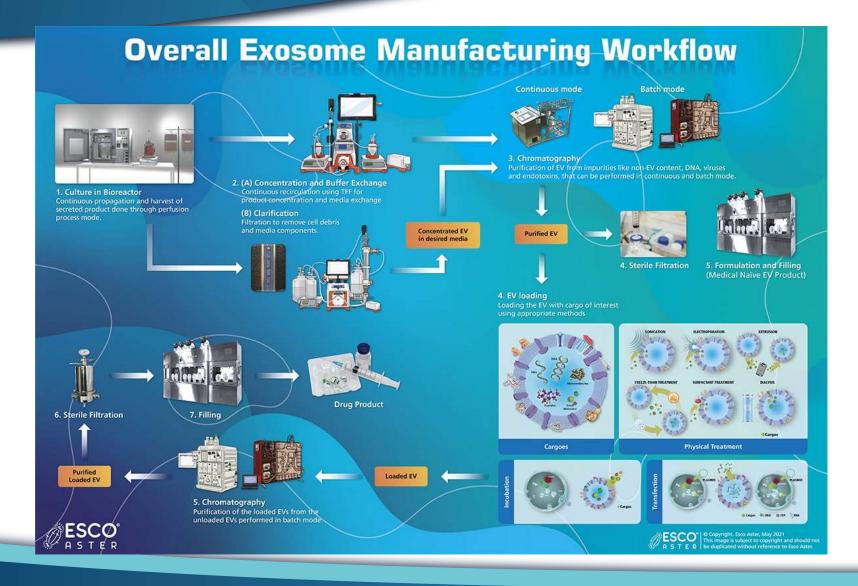














CDMOs play an important role in vaccine self sufficiency.

- Esco Aster has variety of mfg platforms and partners to help in early stage development and tech transfer from CDMO model to DBOT model.
 - Fermentation of sub-unit vaccines (Gen-Y)
 - Adherent VERO for LAIV/LAV (Vivaldi Biosciences)
 - Suspension for Covid-19 Mabs for Dx Antigens and Therapeutics (Gen-Y)
 - mRNA-LNP platform (Provaxus)
- Esco Aster is the only life sciences company that is neutral and operates within African continent for African from our base in South Africa.
- We are here to support you in your vaccine self sufficiency journey from tools, technologies, platforms, human resources, training.
- Contact us to collaborate!





