



A breakthrough high-performance viral vaccines biomanufacturing platform to countermeasure epidemic threats

Webinar

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Univercells Technologies designs and delivers state-of-the-art high-performance, scalable **bioproduction technologies** for viral products

Univercells Technologies genesis

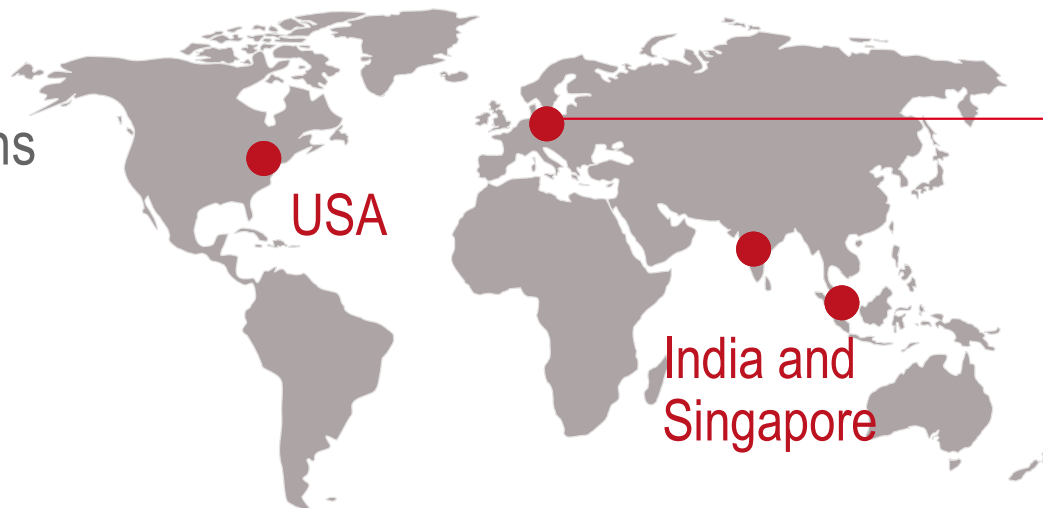


Mission	Make biologics affordable and available to all!	Design and deliver the next evolution of biomanufacturing
History	<ul style="list-style-type: none"> > Created in 2013 in Belgium > Capitalizing on unmatched bioprocessing and engineering expertise 	<ul style="list-style-type: none"> > Univercells subsidiary created in 2020 > Revolutionizing bioprocess by commercializing next generation viral manufacturing technologies
Focus	<ul style="list-style-type: none"> > Offering technologies, services and turnkey solutions to alleviate the industry's current shortfall in supply of cell and gene therapies, vaccines and biotherapeutics 	<ul style="list-style-type: none"> > Intensification of high-performance operations & chaining of unit steps into an integrated process > Key assets: NevoLine™ platform & scale-X™ bioreactor

Univercells technologies capitalizes on a **strong team of experts** and a **global footprint** for equipment dissemination and client support



Global Sales Locations



Belgium

Brussels



Head Office

Nivelles

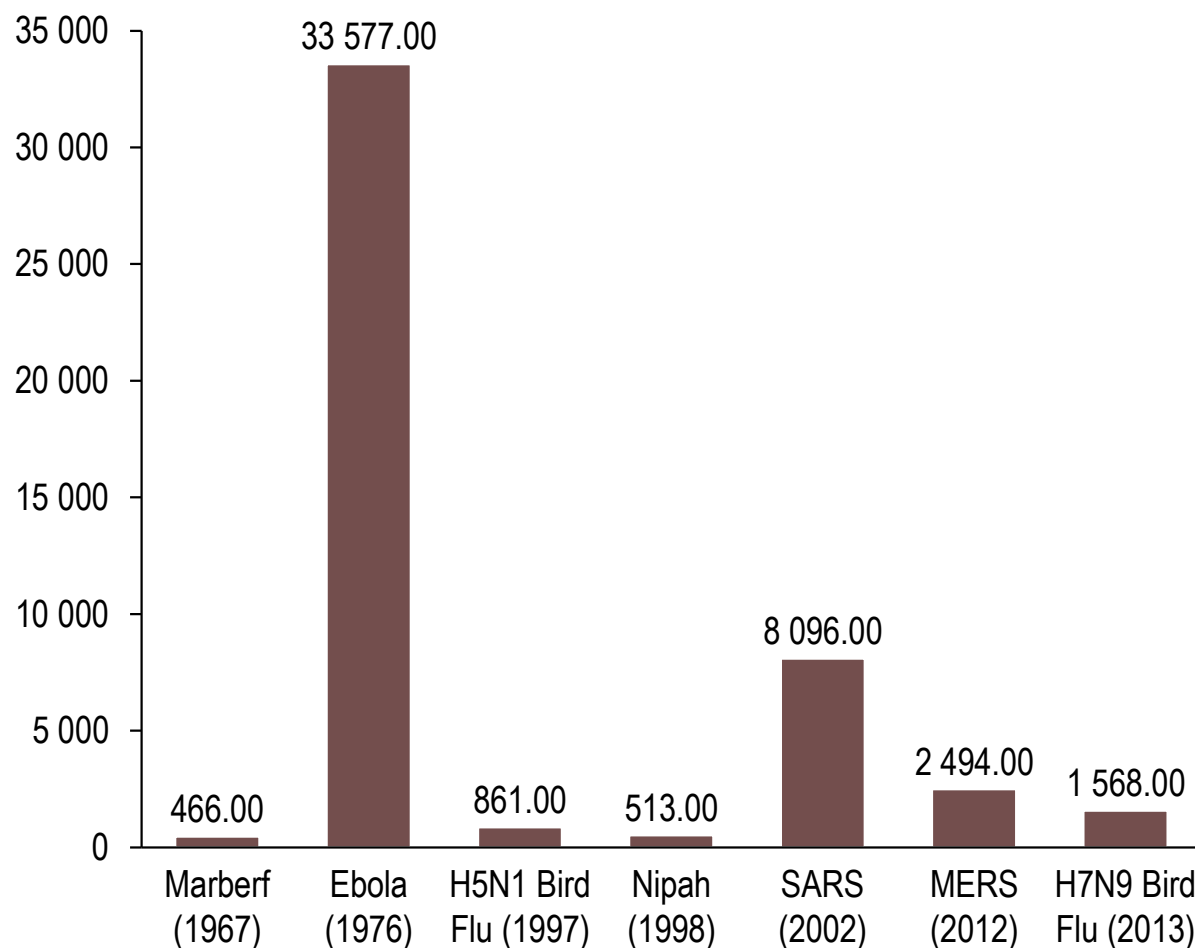


R&D and Manufacturing

India and Singapore

Variable viral outbreaks are observed throughout the years directly affecting the healthcare systems of the concerned countries

Infection of viruses involved in outbreaks worldwide as of 2020



- > **Variable number of infections** and fatality rates depending on the outbreaks
- > **Re-occurring** and **punctual** behavior outbreaks (seasonal Flu)

Challenges in outbreak management

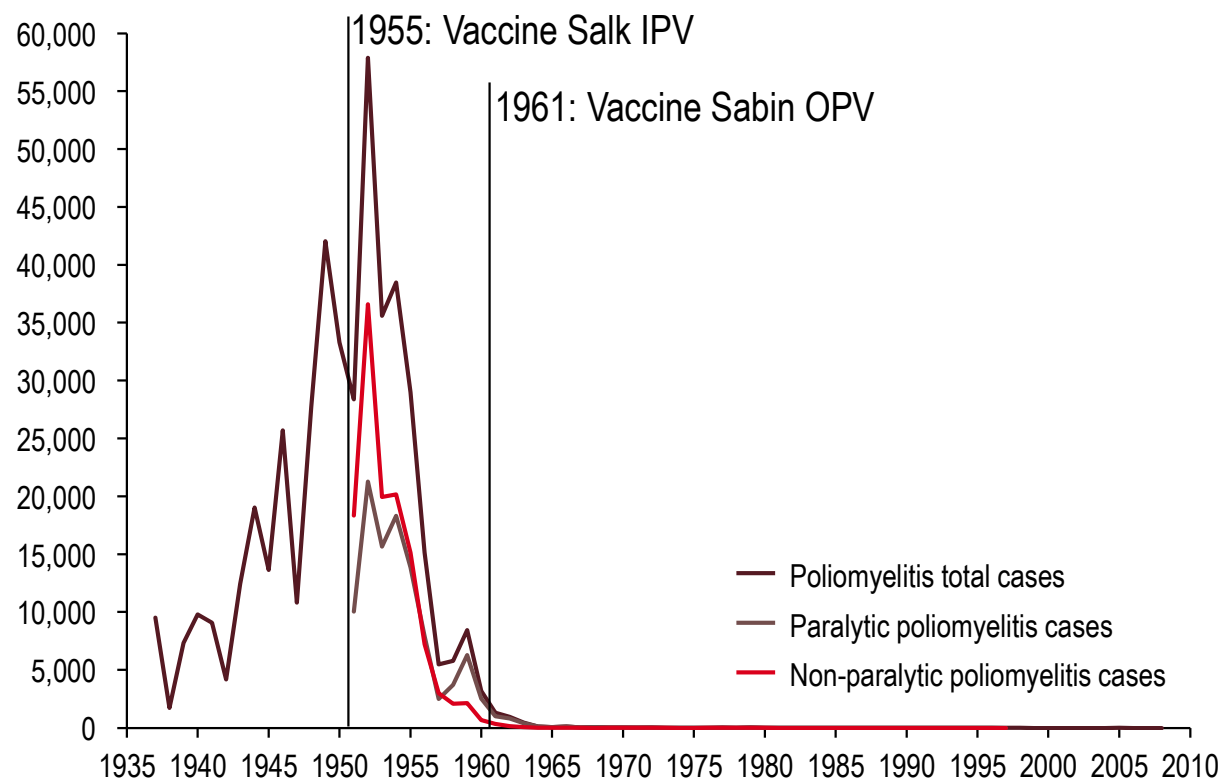
- > Need for fast development of effective vaccines
- > Lack of funding opportunities due to prioritization of diseases



Vaccines are one of the most **cost-effective** healthcare interventions ever invented

Poliomyelitis cases after vaccines introduction

Poliomyelitis reported cases after IPV and OPV vaccines introduction (USA, 1935 - 2008)



- > The introduction of **vaccination** led to a drop of poliomyelitis cases within a few decades
- > Only **global immunization campaigns** can lead to **polio eradication**



Vaccines are an effective intervention reducing mortality caused by infectious diseases

Key figures

Deaths
prevented



by immunization
every year

Diseases
preventable



by vaccines

Vaccination
coverage



remaining constant

Additional
lives

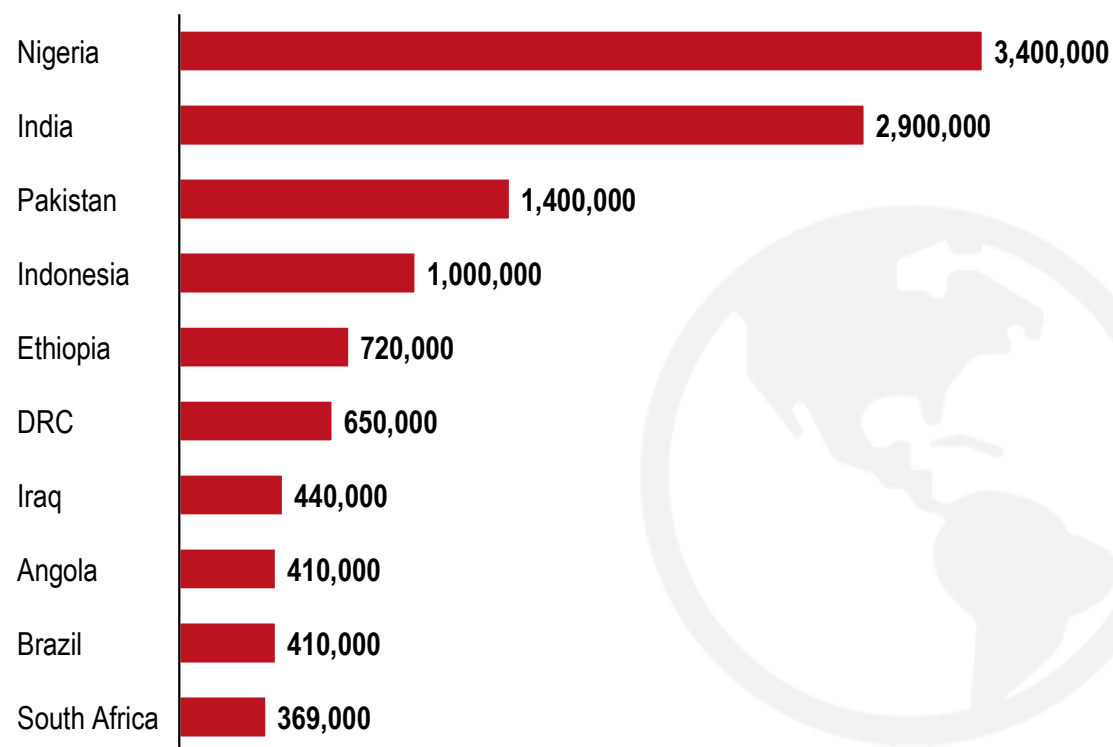


could be saved every
year by increasing
immunization globally

Global **vaccination coverage remains constant** over the past few years, requiring increased efforts in LMICs for a full immunization

Global vaccination coverage and gaps

Over 19 million children still miss out.
About **60% of these live in 10 countries**



“

Vaccines** are a miracle because with three doses, mostly given in the first two years of life, you can **prevent deadly diseases for an entire lifetime.

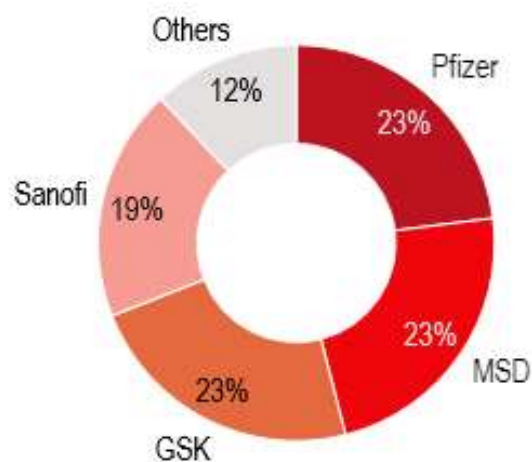
Bill Gates Annual Letter (2010)



The vaccine industry has hit a **turning point**, as the traditional approach cannot solve present and upcoming demand

Vaccine industry at a turning point

Historic **oligopoly**



- > 88% of the market is owned by Big Four vaccine manufacturers that are situated in developed countries
- > **Historically**, these four have **driven most innovation**
- > In recent years, **small biotechs and emerging-market** players have become the most important source of new vaccine development
- > Most outbreaks occur in LMICs that need to rely on 3rd party supply of vaccines

An increasing global **market growth**



Increased prevalence of **infectious diseases**



Technological advances in vaccine development



Increase **funding** from governments and international organizations

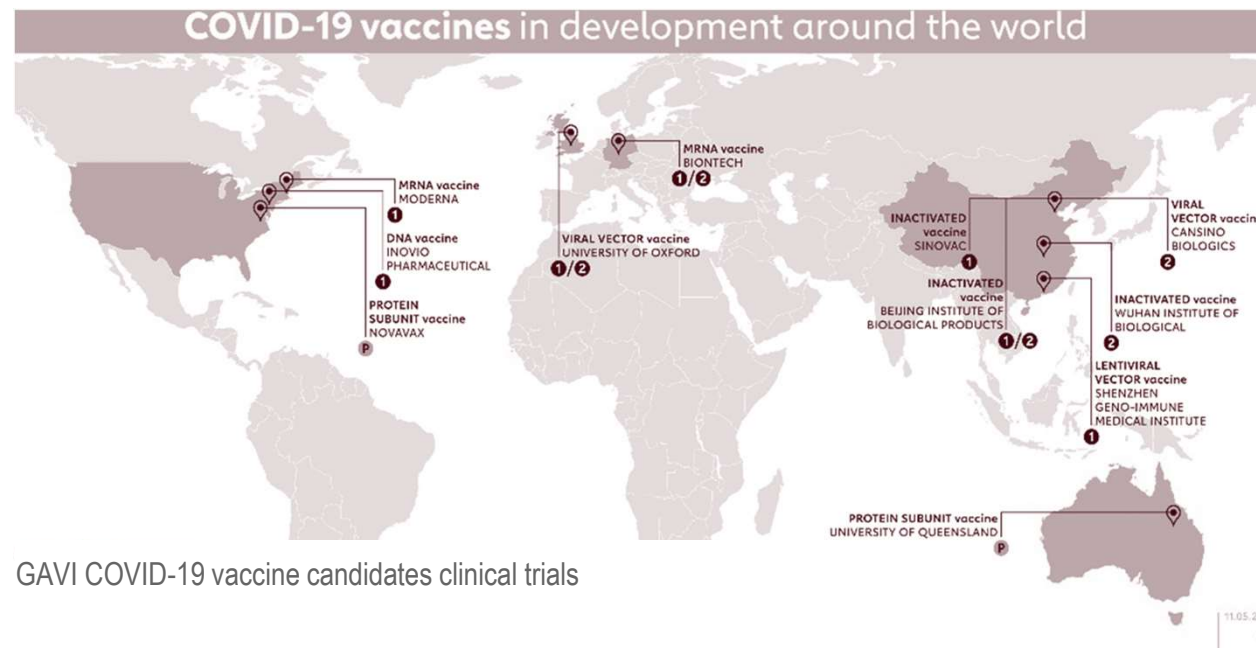


Increased **awareness** in preventative care

- > The global market size for vaccines was valued at **38.5 billion USD in 2018**
- > Growth in the market is expected to exceed **7% CAGR by 2025**
- > Vaccination coverage is rising, especially in emerging countries as a result of **vaccination efforts** by UNICEF/GAVI

Race against the clock for vaccine development and manufacture in response to coronavirus outbreak

Global epidemic outbreaks – case of COVID-19



GAVI COVID-19 vaccine candidates clinical trials

Pre-clinical (P) Testing in animals

Phase 1 Initial testing for safety and identifying dosage

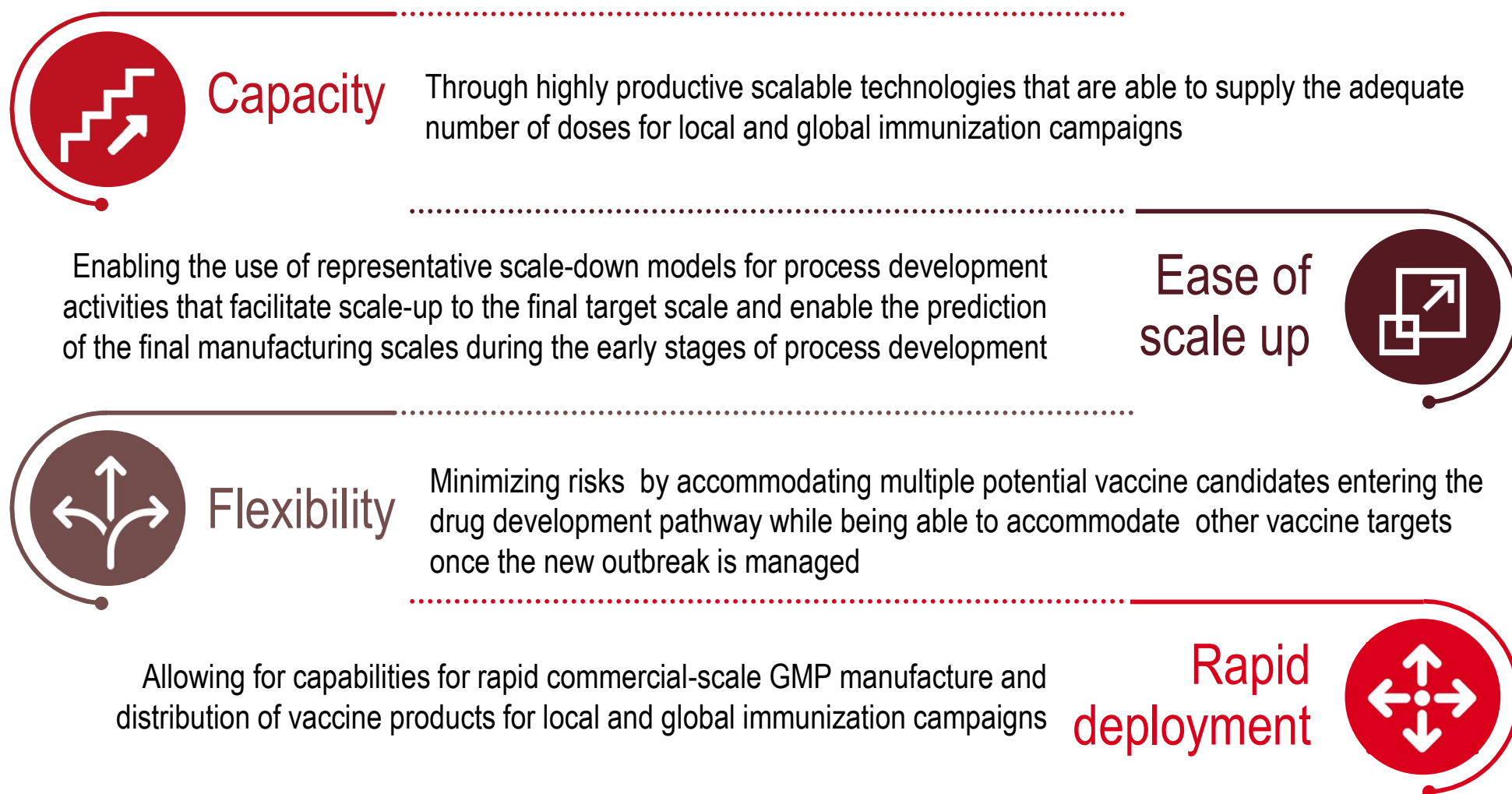
Phase 2 Testing for effectiveness and further safety testing

Phase 3 Confirm and assess effectiveness, and look for side effects

- > SARS-CoV-2 have reached **4.9 million cases worldwide** and **210 countries** impacted
- > **118 candidate vaccines** with 9 tested in clinical trials
- > Various **type of vaccines** investigated:
 - Non-replicating viral vector
 - RNA
 - DNA
 - Inactivated
 - Live attenuated virus
 - Protein subunit
 - Virus-Like Particle (VLP)
- > Clinical trials for vaccine candidates have to be **compressed** for a **rapid epidemic response** (e.g. rVSV-ZEBOV Ebola vaccine)
- > **Preclinical phases** are reduced or suppressed to accelerate the delivery of the vaccine

Rapid response to disease outbreaks requires **flexible technologies** and facility concepts able to accommodate different targets

Technology-related factors affecting the response to new disease outbreaks



Traditional technologies for vaccine manufacture require significant capital investment

Scale-up

GSK inaugure ce matin la plus grosse unité mondiale de production de ce vaccin à Wavre, dans un énorme bâtiment ultra-sécurisé. L'investissement est de 340 millions.



Mis en ligne le 24/10/2018 à 06:05 par Frédéric Soumois



- > Vaccine production using a **scale-up** approach typically rely of large bioreactors in larger facilities with **very high CAPEX**
- > Such high capital investments are incompatible with smaller vaccine producers
- > Moreover, these large facilities may **lack flexibility** to accommodate different process designs

Scale-out

T-Flasks



Roller Bottles



Eggs



- > Over 80% of viral vaccines are still manufactured by the **scaling out** of lab-scale systems
- > In order to manufacture large quantities **very high CAPEX** is needed
- > The high number of **aseptic manual operations** associated with this practice increases **risks of failure**
- > The inefficiency and manual nature of these processes result in **low production capacity and high COG**

Univercells Technologies seeks to address the common manufacturing challenges in virus production for vaccines

Restrains restricting rapid vaccine development



Manufacturing challenges

- > Process complexity: many steps and need for know-how
- > Capacity: manufacturing unit with high footprint
- > Costs : high capital and operational investments



Reactivity

- > Unforeseen events: disease outbreaks with variable needs
- > Rapid deployment: from development to commercialization
- > Available capabilities: GMP-certified facilities



Appropriate Technologies

- > Out-scaled process: most conventional technologies
- > Adapted scaling: deliver the needed amount of doses
- > Flexibility: One shot process and modular technologies

Technology principle combines **process intensification and chaining**, delivering high-performance process **achieving low CAPEX/OPEX**

Technology-driven affordability by applying chemical engineering rules



Intensification

- > Very **high cell-density** fixed-bed bioreactor technology, and high-performance chromatography columns
- > Achieving superior yield characteristics and resulting cost savings for customers



Chaining

All **unit steps** are linked into **an integrated process**, allowing continuous operation from cell culture to clarification and capture

Value creation

Designing and delivering **high performance, low footprint** bioprocessing technologies for dramatic reduction of **CAPEX & OPEX**



The scale-X bioreactor and NevoLine platform offer a range of configurations supporting vaccines development

Bioreactor product range

1 scale-X™



[hydro]
[2.4 m²]



[carbo]
[10-30 m²]

2 NevoLine™



[nitro]
[200-600 m²]

Screening

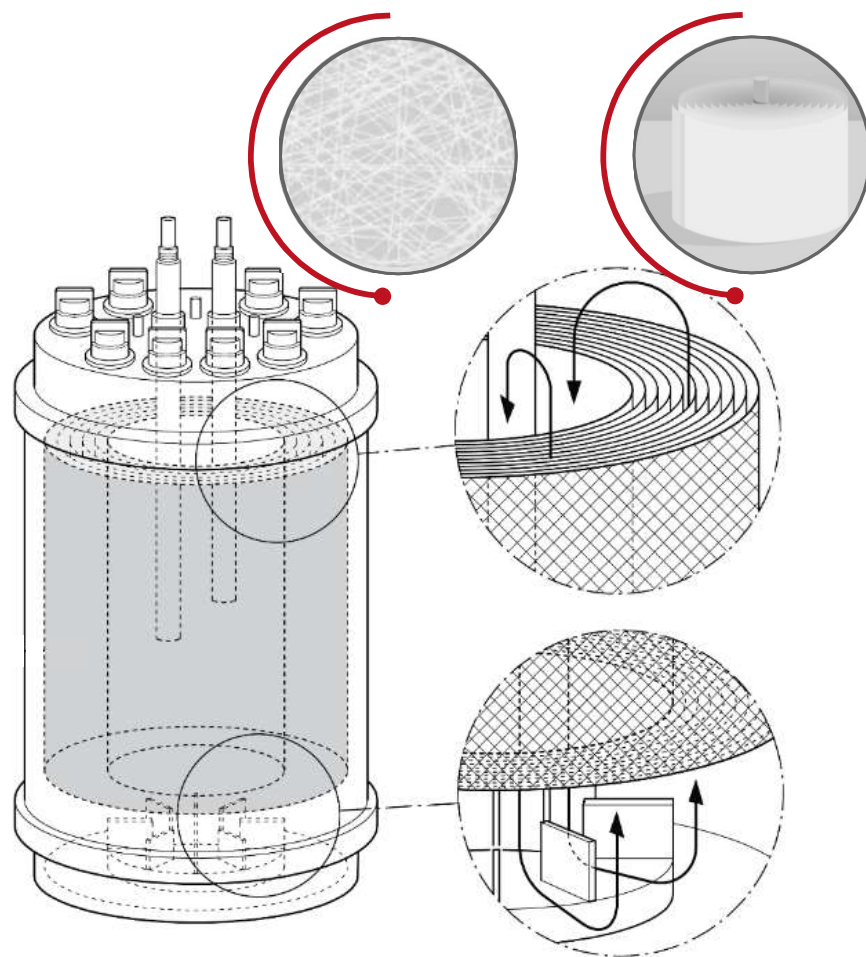
R&D

Clinical

Commercial

Process intensification is enabled by our **scale-X** fixed-bed bioreactor, a scalable solution for low COG virus manufacture

Proprietary fixed-bed technology



Features

Structured packing of rolled membrane

- > Unique dual layer structure
 - PET, non-woven fabric layer for cell adhesion
 - Polypropylene mesh spacer layer for structure and fluid flow path
- > Ensuring homogeneity and reproducibility of the culture:
 - In cell entrapment & distribution
 - In media circulation & nutrients availability
- > Adapted to a variety of cell line & viral products

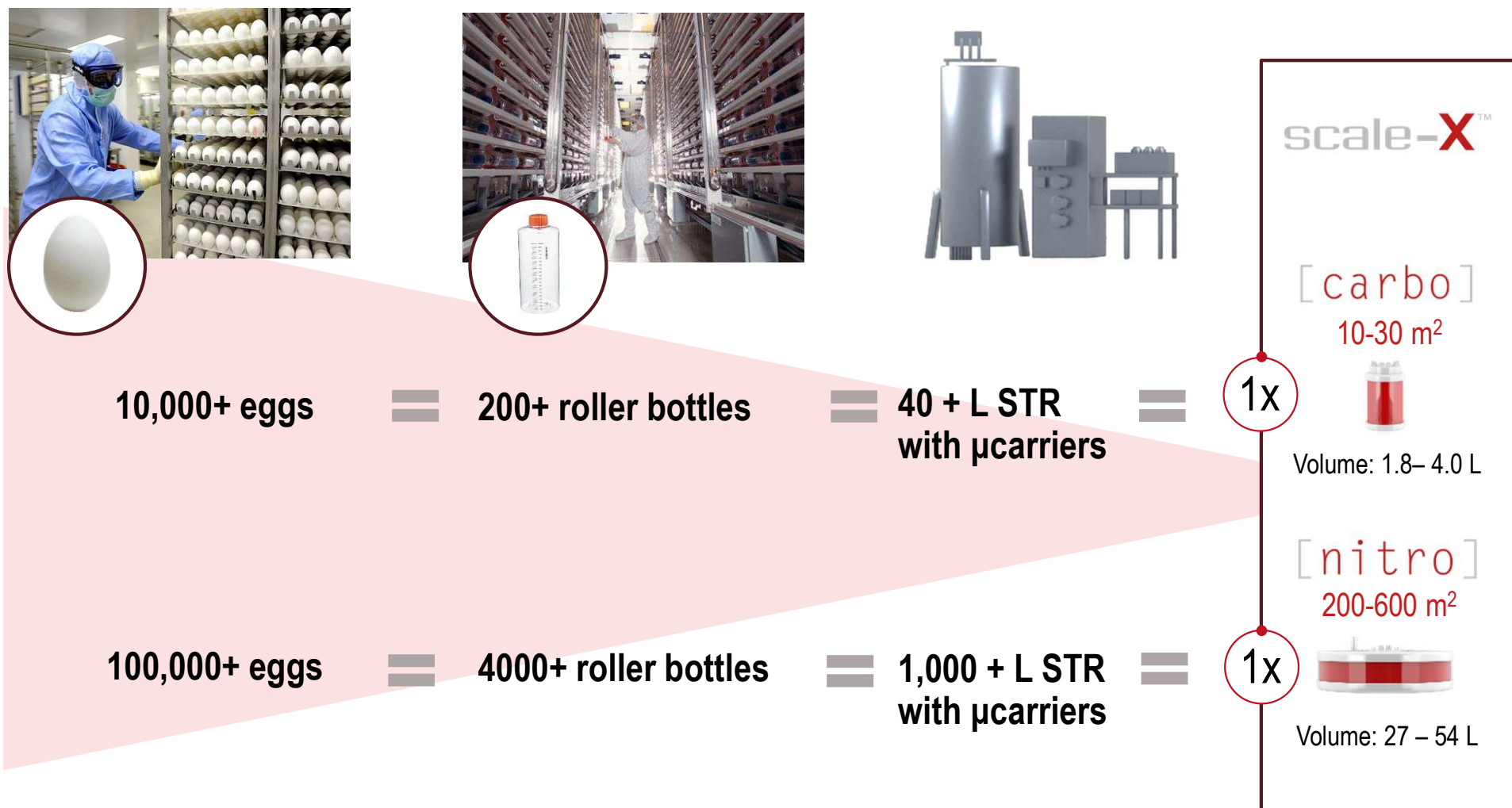
Benefits

High density

Homogeneous cell distribution

scale-X bioreactor dramatically reduces CAPEX & OPEX by replacing traditional manufacturing & associated large footprints

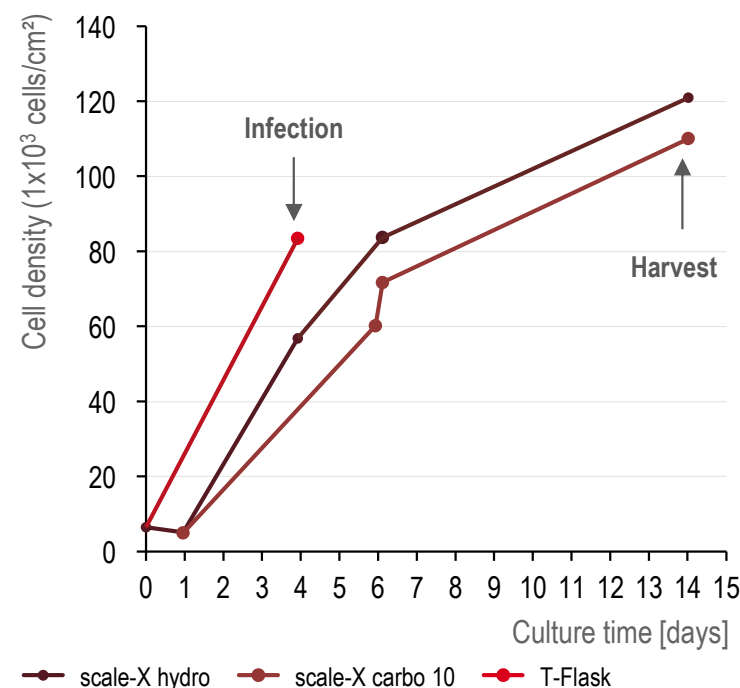
scale-X bioreactor replacing conventional technologies



scale-X bioreactor's spiral-wound fixed-bed enables **high cell densities on a small footprint** for several vaccines cell lines

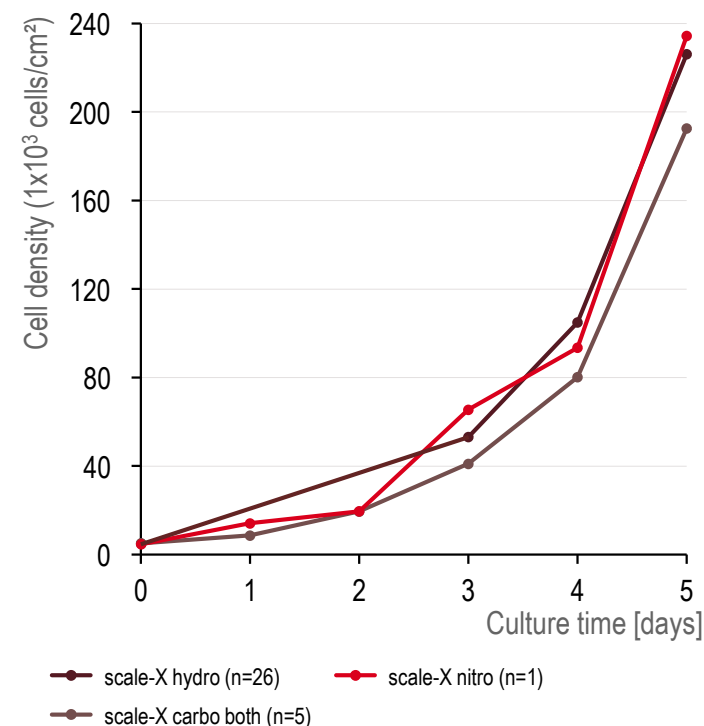
scale-X hydro | Cell growth examples (MRC5 & Vero)

MRC5 cell growth



- > **Equivalent** MRC5 cell growth profile between scale-X and classic flatware technology
- > High cell density harvested of **120,000 cells/cm²**

Scalability of cell growth Vero

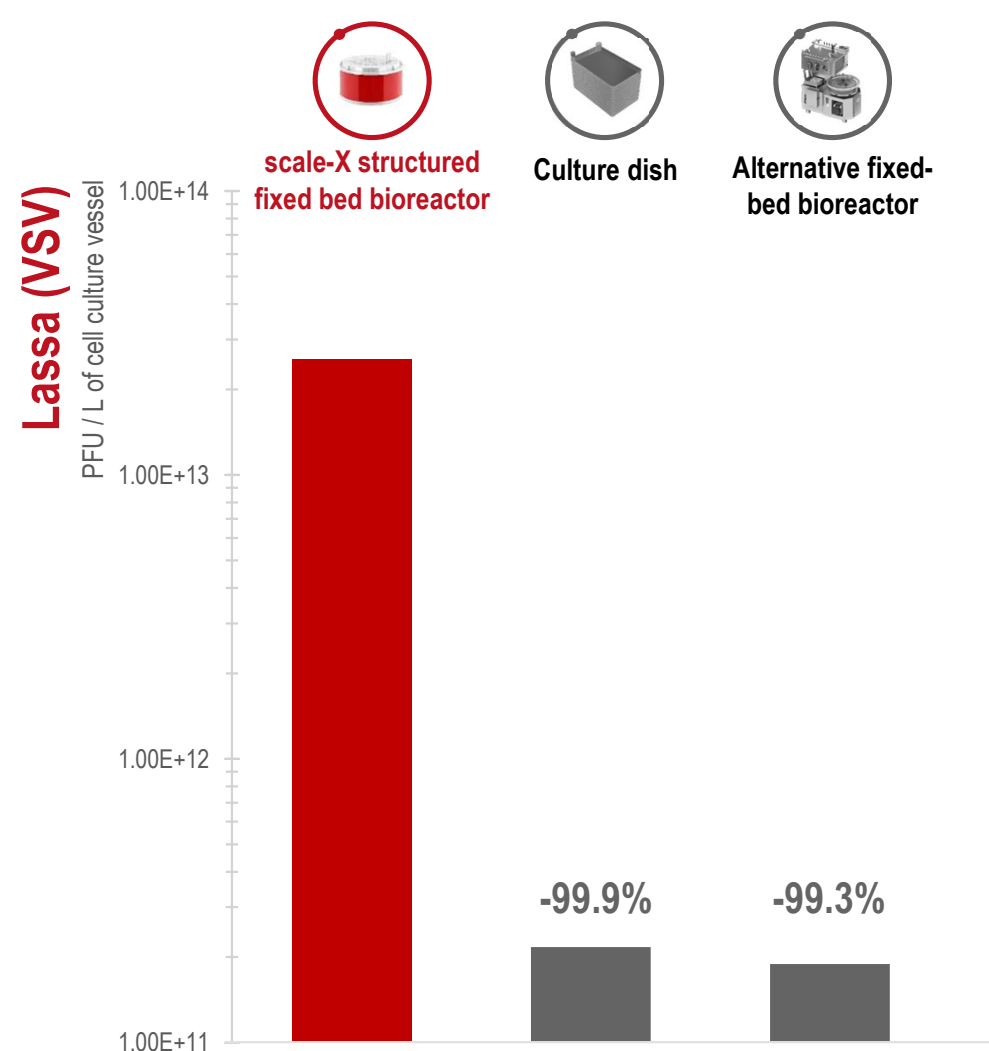
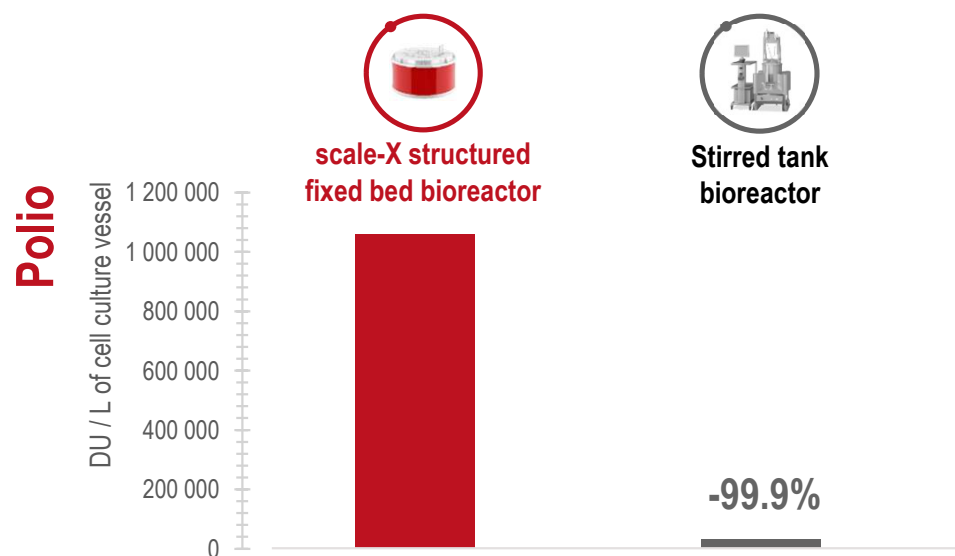


- > **Reproducible** cell growth during process scale-up
- > High cell density at infection **200,000+ cells/cm²**, or ~30 M/mL

Other biological systems grown in fixed-bed

- > **Vero** – Influenza, Newcastle, Rabies, Rotavirus
- > **MRC5** – Hepatitis A
- > **MDBK** – Bovine Herpes Virus
- > **CEF** – MVA
- > **A549** – rAAV, Adenovirus
- > **HEK 293** – Adeno, AAV, Lentivirus, Retrovirus

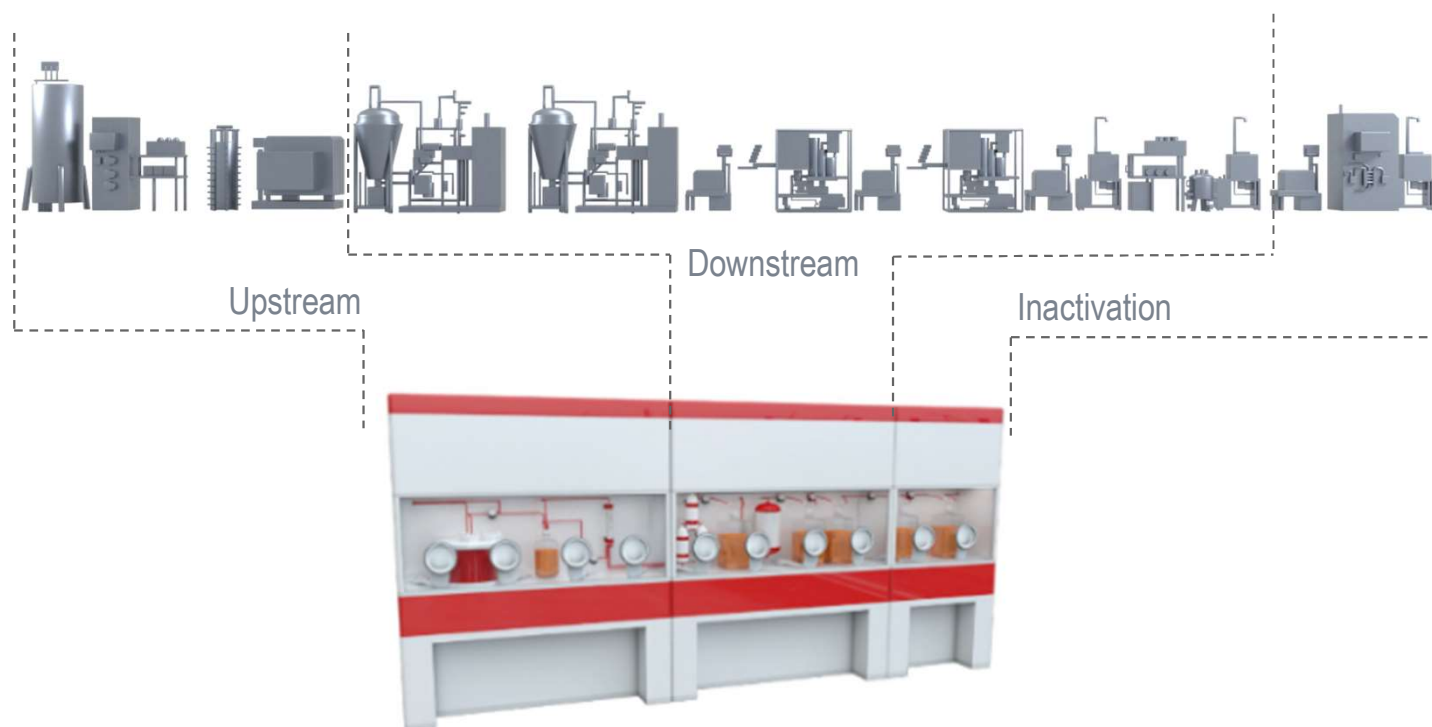
The scale-X™ bioreactor enables up to 99% higher titres compared to other technologies for Polio & VSV production



Our technology-driven approach to produce affordable vaccines enables significant **reductions in equipment footprint**

Equipment requirements for traditional vaccine processes versus NevoLine platform

NevoLineTM



Process intensification

replacing large stainless steel bioreactors with high cell density fixed-bed bioreactors

Chaining and integration

reducing the number and size of intermediate hold tanks

Process optimization

reducing the number of process steps without compromising product quality



NevoLine™ system for cost-effective viral production, chaining scale-X™ bioreactor with downstream processing

Intensified & automated viral production in 10m²

NevoLine™
NEXT EVOLUTION OF MANUFACTURING TECHNOLOGIES

Culture

scale-X™ high-performance fixed-bed bioreactor

Purification

In-line clarification and purification

Inactivation

In contained cabinet



Containment and safety

Low-footprint, closed system for process & environment safety

Cost-effective production

Low CAPEX & COGS,
Simplified infrastructure

Automated operations

And high containment for
process reliability & safety

Flexible

Modular system capable of
accommodating different process
configurations and product-specific
micro-environments

Scalable

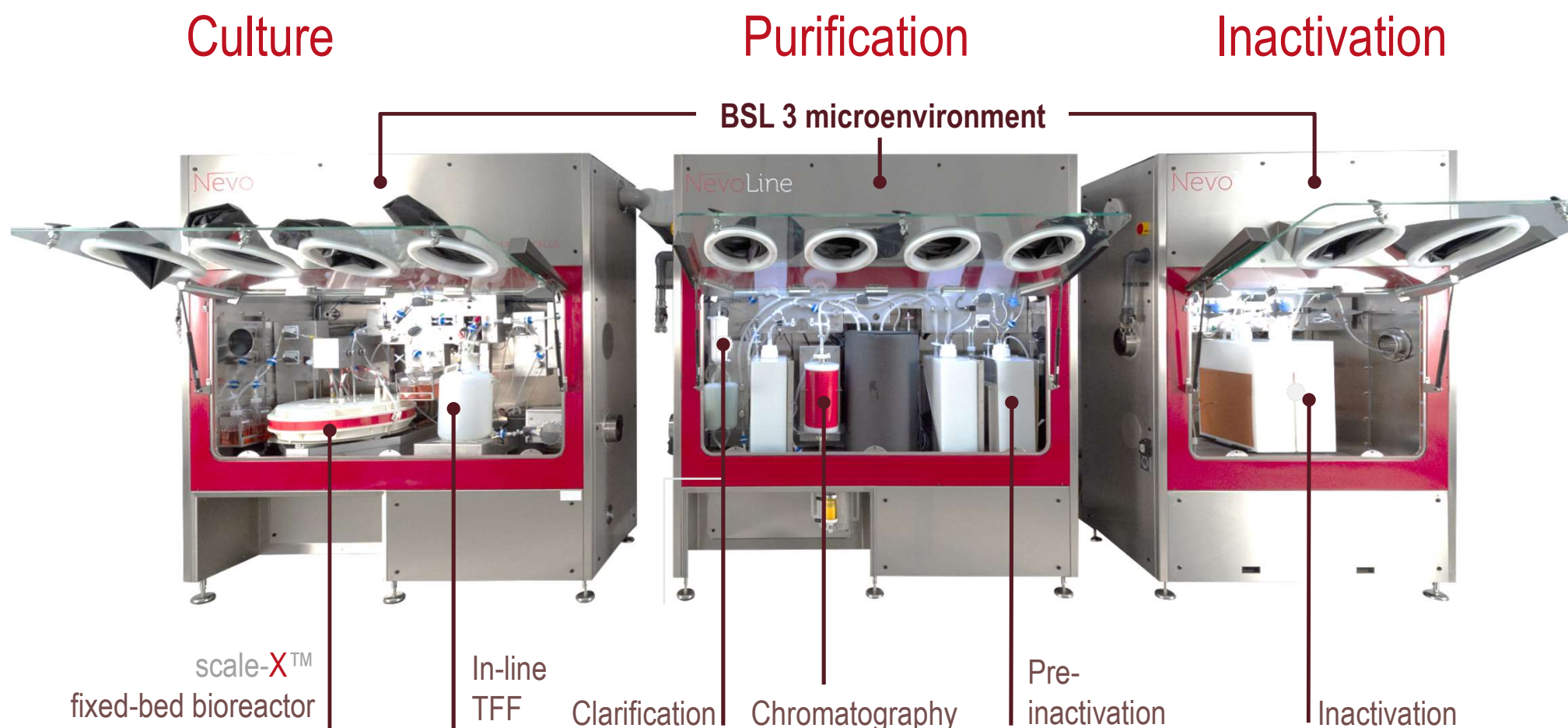
Using of process intensification to
increase manufacturing capacity
within a low footprint

Rapid deployment

In new or existing facility, reducing
time-to-market

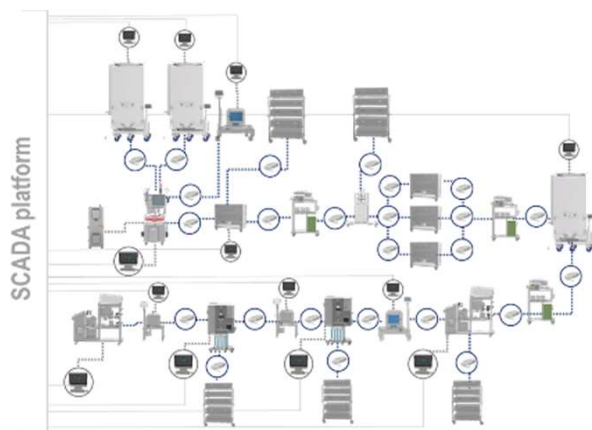
NevoLine™ system comprises all the unit operations required for "end to end" bulk drug substance manufacture

Intensified and automated viral production in 10m²



NevoLine is a streamlined, user friendly **integrated manufacturing platform** simplifying single-use design and process control

Automated, Ergonomic, Intuitive



NevoLine™



Traditional technologies

- > **Integrated USP & DSP automation controllers** in the module and across different modules
- > **Single audit trail** for the total process, USP & DSP
- > **Single consolidated automatic batch** record for the total process
- > **Accessible** connections
- > **Manifolds supported** inside the cabinet on a fixed frame
- > Short single-use fluid transfer Lines between unit operations.

- > Standalone automation controllers per unit operation and/or between USP & DSP
- > Audit trail per automated unit operation
- > Batch record per unit operation
- > Low-level connections and manipulations, below waist height
- > Unsupported manifolds often drag on the floor
- > Long fluid transfer lines between unit operations

NevoLine™ represents the next generation of vaccine manufacturing, transforming production economics & global access

Simplified equipment & facility – Trivalent Polio vaccine (50M doses/y)

Production equipment

Facility

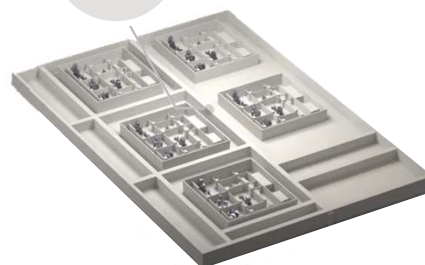
Conventional process



Complex process & equipment
High investment & operational cost



10,000 m²



NevoLine process



Intensified & contained for
reduced footprint & CAPEX



1,500 m²



Simplified infrastructure
6-fold footprint reduction

Impact

Novel **bioproduction model** transforming
vaccine production
economics



* Target values, scaled-up process under development

Overall savings in equipment costs & footprint promotes **significant reduction in CAPEX and OPEX**

Comparison with SU & SS – Case study with a trivalent polio vaccine

NevoLine



4x NevoLine
(600 m² bioreactors)
50M doses/y

Single-Use (SU)


















5x750 L bioreactors
54M doses/y

Stainless Steel (SS)



6x750 L bioreactors
54M doses/y

Equipment cost (USD M)	NevoLine		8.4
	SU		12.7
	SS		18.5
CAPEX (USD M)	NevoLine		~20
	SU		~50
	SS		~200
Footprint (m ²)	NevoLine		1,500 m²
	SU		4,000 m ²
	SS		~ 10,000 m ²
Utilities (USD/run)	NevoLine		5,400
	SU		35,500
	SS		75,000
CoGs (/dose)	NevoLine		<\$ 0.30
	SU		\$ 0.6
	SS		\$ 1.2-1.5

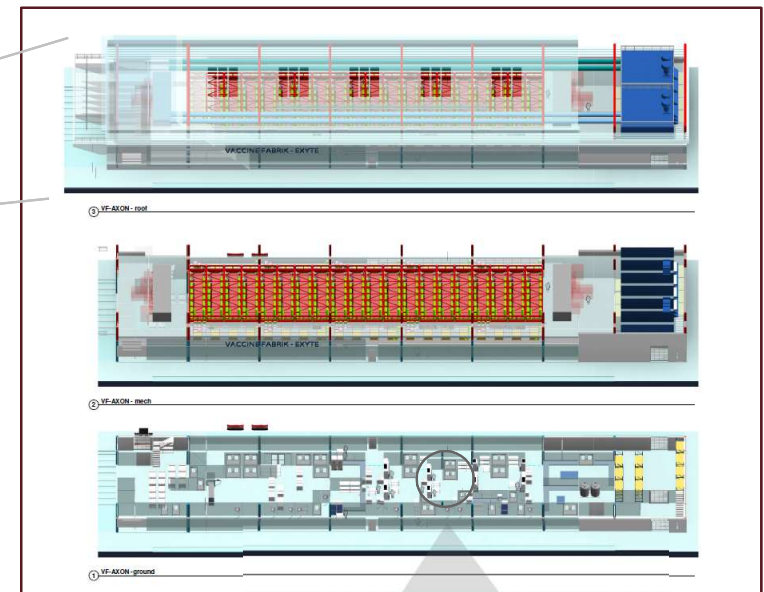
Impact

- > Intensification and chaining leading to **reduced equipment costs**
- > Lower footprint leading to **reduced facility CAPEX and operating costs**
- > **Radical reduction in drug product cost of goods**

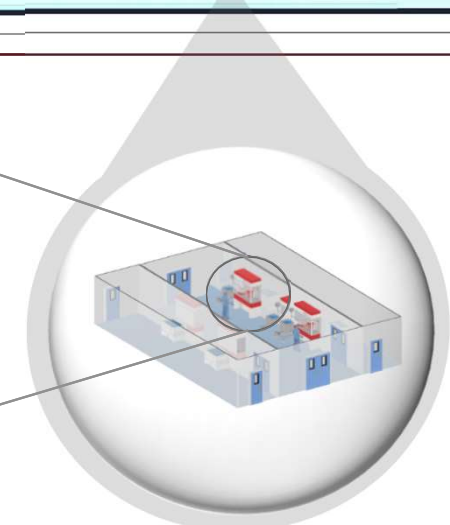


The compact design of the **NevoLine™** enables a seamless integration into novel facility concepts including prefabricated facilities

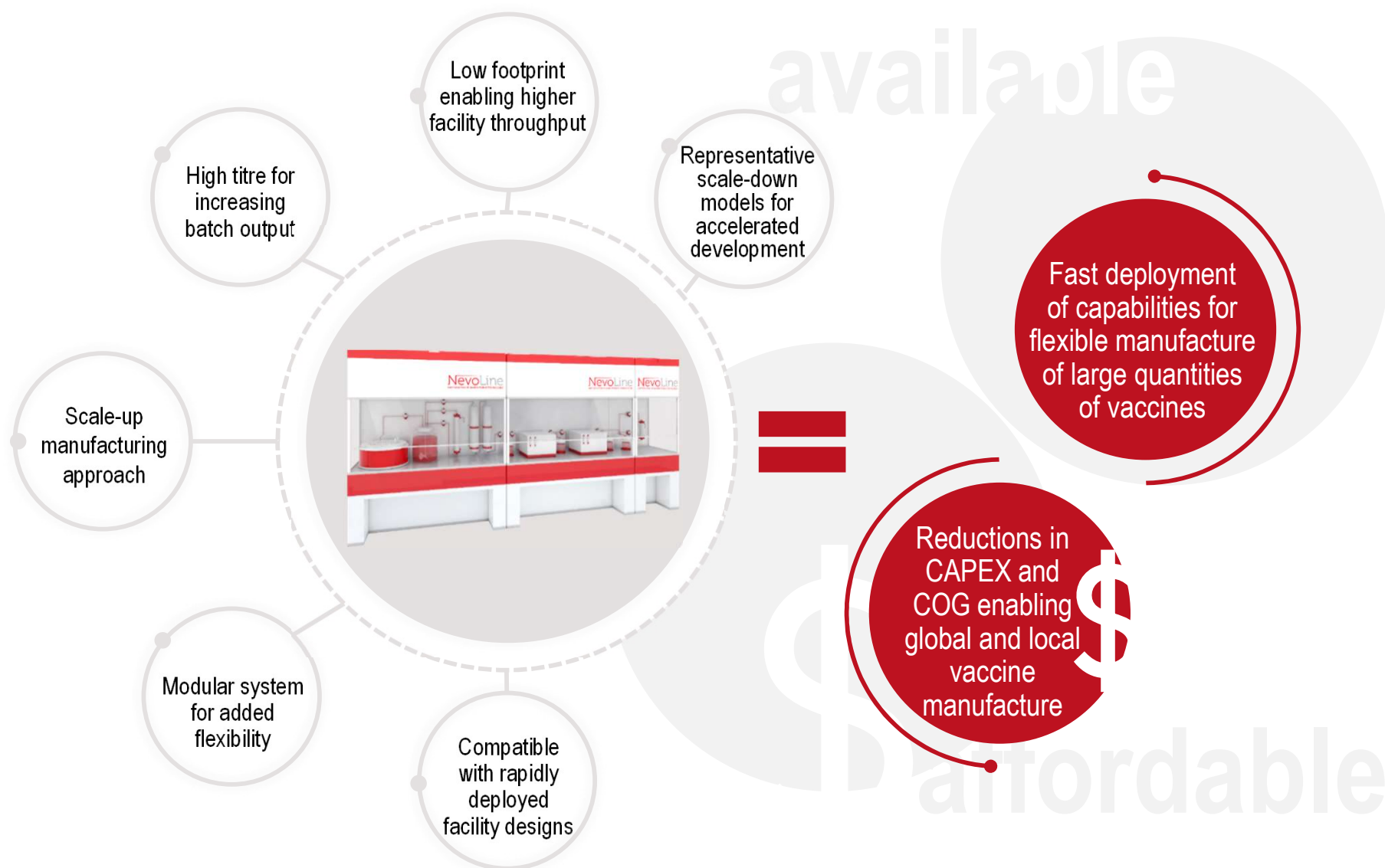
Pre-fabricated facility design integrating the NevoLine platform



The NevoLine platform is highly compatible with pre-fabricated facility designs that reduce deployment time to 6-18 months from 30-36 months



The **NevoLine™** was designed to promote **rapid deployment** of vaccine manufacture capabilities for **epidemic response**





UNIVERCELLS
Technologies

Thank you
for your attention
www.univercellstech.com

| The next evolution of biomanufacturing