



Disruptive micro-facility for affordable vaccines manufacturing

Benjamin DAMIEN, PhD, MBA
Director of Business Development

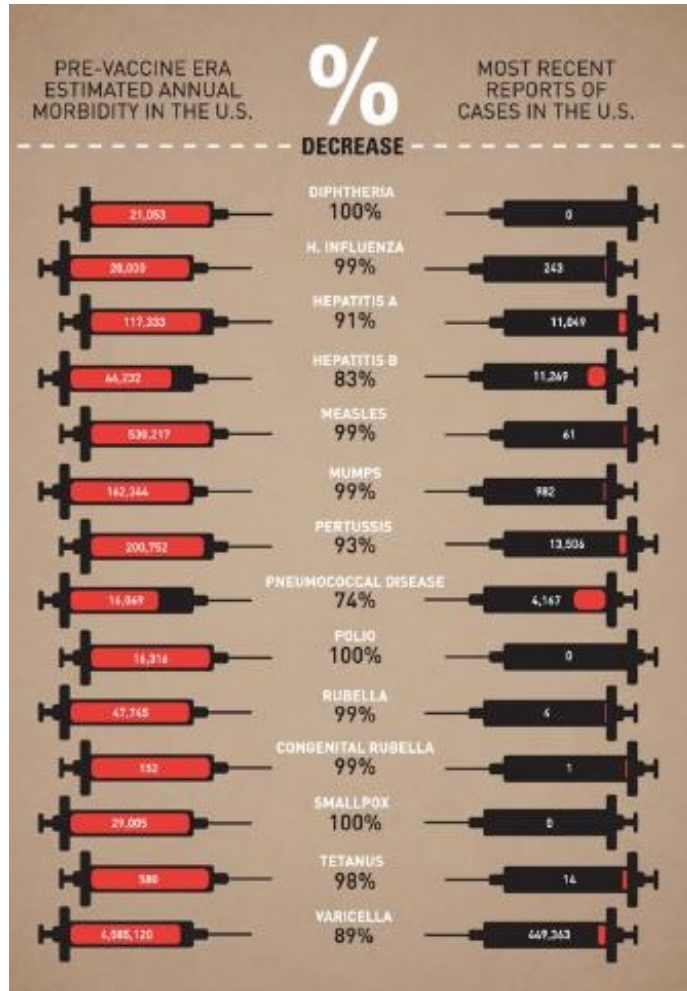
WCBP 2018
February 1st | Washington, D.C.

Vaccine manufacturing
today





Vaccines are the most efficient tools to prevent infectious diseases, yet a number of factors prevent global coverage



Global immunization

- > Averts ~ 2 to 3 million deaths every year (of DTP and Measles)
- > An **additional 1.5 million deaths** could be avoided, by improving vaccination coverage
- > An estimated **19.4 million infants** worldwide are still missing out on basic vaccines

Insufficient supply and late availability (i.e.)

- > Prevnar in 2011, USA
- > BCG in 2015, France
- > Meningitis C in 2015, Africa
- > DTP in 2015, India

Crisis

- > Zika virus spread
- > Ebola epidemic

- > Urgent need for **increased production capacity and cheaper vaccines**
- > The global vaccine market will reach **USD 48 bn in 2021**, and 90% in the developed countries
- > **Emerging countries** must become able to **manufacture their own vaccines more efficiently**




Vaccine Manufacturing Today...



- > Over 80% of viral vaccines are still manufactured by the **scaling out** of lab-scale systems
- > Barrier: **Very high CAPEX**
- > Risk: High number of **aseptic manual operations**
- > **Production capacity**↓↓, **cost** ↑

- > Some vaccines are manufactured in bioreactors – **scaling up**
- > Barrier: **Extremely high CAPEX**
- > Reduced risk: Limited aseptic manual operations
- > **Production capacity**↑↑, **cost**↑↑





Univercells ambitions to
make biologics
available to all

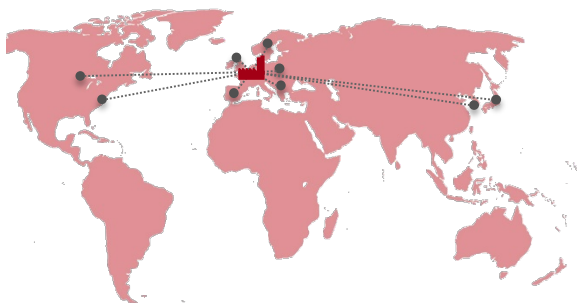


Univercells exists to make **biologics available and affordable** to all – Its mission embodies the ongoing industry **paradigm shift**

Biologics for all – Industry paradigm shift

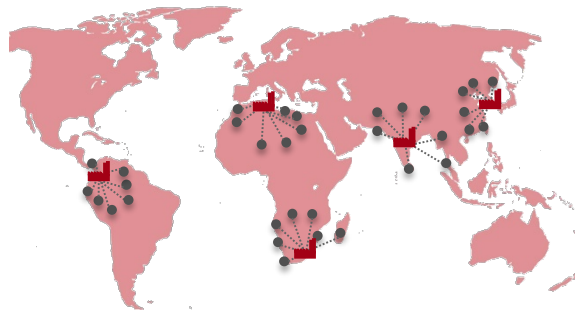
Old paradigm

Centralized manufacturing for developed economies
(e.g. USA, EU, Japan)



New paradigm

Distributed manufacturing for local markets
(e.g. Asia, Africa, Latin America)



Paradigm shift supported and promoted by all health-related NGOs and academics, i.e. WHO, BMGF, Wellcome Trust and MIT, UCL

Univercells **mission** supported by key strategic partnerships

Viral vaccines

- > **Bill & Melinda Gates Foundation** (BMGF) – Grant for integrated micro facility for vaccine production in GAVI countries

Monoclonal antibodies

- > **Network in LMIC countries** through Key Opinion Leaders, Strategic Consulting firms, WHO and other NGOs

Enzyme Replacement Therapies

- > **Private health insurance companies** to leverage antibodies platform to dramatically reduce the cost of orphan drugs, to be produced in hospitals



This is achieved by bringing out the **best of technology innovations** allowing a **rapid deployment** of **low CAPEX/OPEX** production facilities

Technology-driven affordability by applying chemical engineering rules



Intensification



Chaining

Use of high-density fixed-bed bioreactors operated in perfusion, and high-performance chromatography columns

The perfusion process and the integration of steps allow continuous operation from cell culture to clarification and capture

LOW-FOOTPRINT, HIGH-PERFORMANCE PROCESS



Value creation



Dramatic reduction of **CAPEX & OPEX**





Rapid deployment of multiproduct facilities with a capacity of :

- **5-40M doses/year** for Vaccines
- **50-500 kg/year** for mAbs



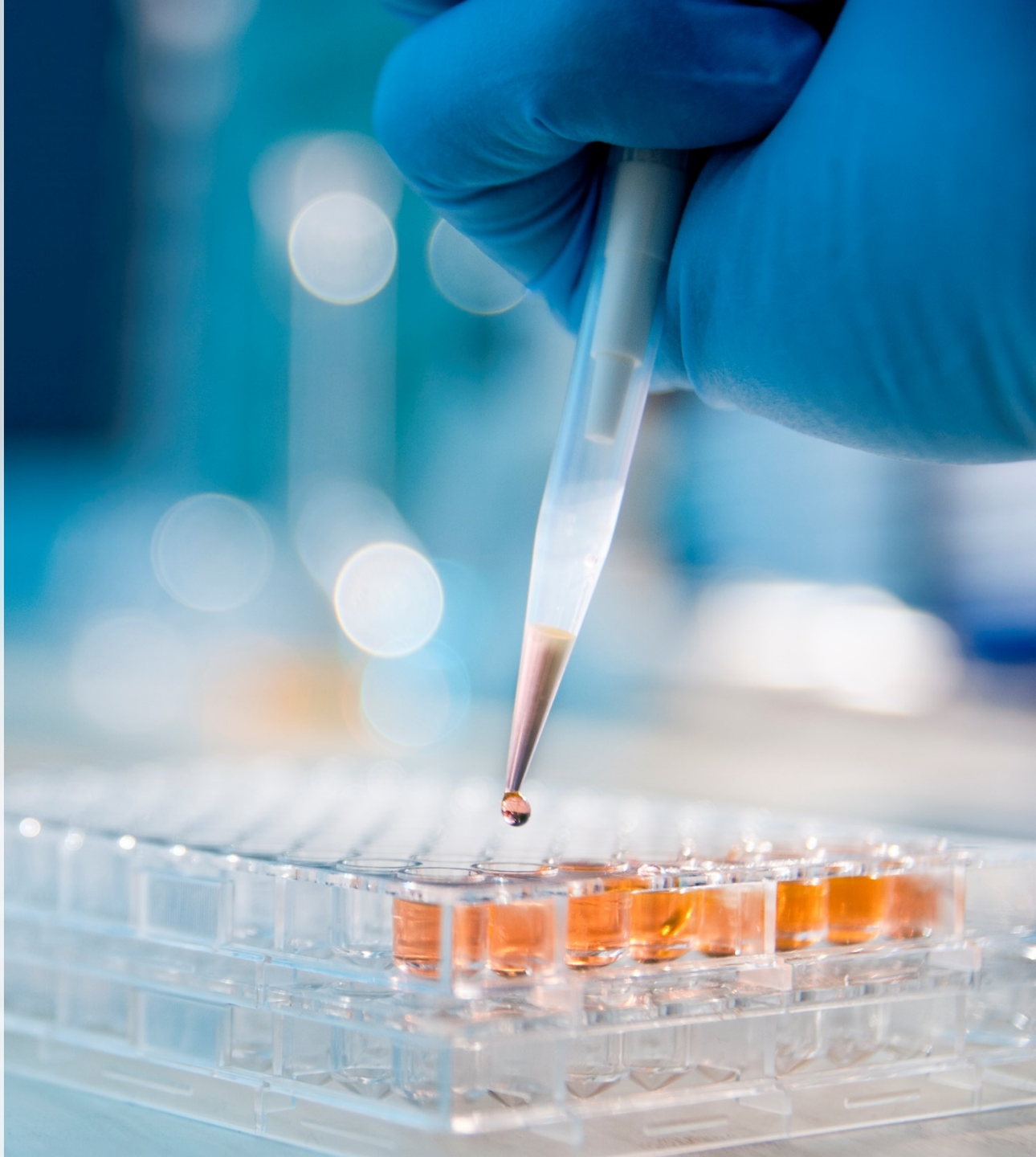
Univercells is developing **two innovative platforms** for cost-effective production of **viral vaccines and biologics**

Univercells platforms – Targets

	Viral Vaccine Platform	Recombinant platform for biologics	
	I. Viral vaccines	II. Monoclonal antibodies	III. Enzyme replacement for orphan diseases
 Objectives	Fully develop & demonstrate an automated viral vaccine manufacturing platform	Build a biosimilar portfolio to tech transfer as end-to-end manufacturing package incl. cell line, process equipment, characterization package	Leverage CHO-based platform at very small scale to develop manufacturing package for orphan drugs
 Scale	5-40 m doses/year	50-500 kg/year	>5 kg/year
 Products	Vaccines produced on Vero cells (e.g. sIPV, Salk IPV, Rotavirus, Rabies, Yellow Fever, Influenza)	Monoclonal antibodies from recent & upcoming biologics LoE ¹⁾ (e.g. Adalimumab, Rituximab)	Enzyme replacement therapies to Lysosomal Storage Disorders (e.g. Gaucher disease)
 Targets	> CAPEX: EUR ~10 m > COGS: <0.15 EUR/dose	> CAPEX: EUR ~10 m > COGS: <75 EUR/g	> CAPEX: < EUR 10 m > COGS: <i>scale-dependent</i>

1) Loss of exclusivity

Univercells innovative
technology for viral
manufacturing





Collaborative development supported by the **Bill & Melinda Gates Foundation**

BILL & MELINDA
GATES foundation

- > The development of the platform was supported by a 12M\$ grant from the Bill & Melinda Gates Foundation



- > Consortium integrator, coordinator and responsible party
- > Integrated continuous manufacturing technologies
- > High cell density bioreactor



- > High capacity / high flow purification membranes
- > High efficiency affinity ligands



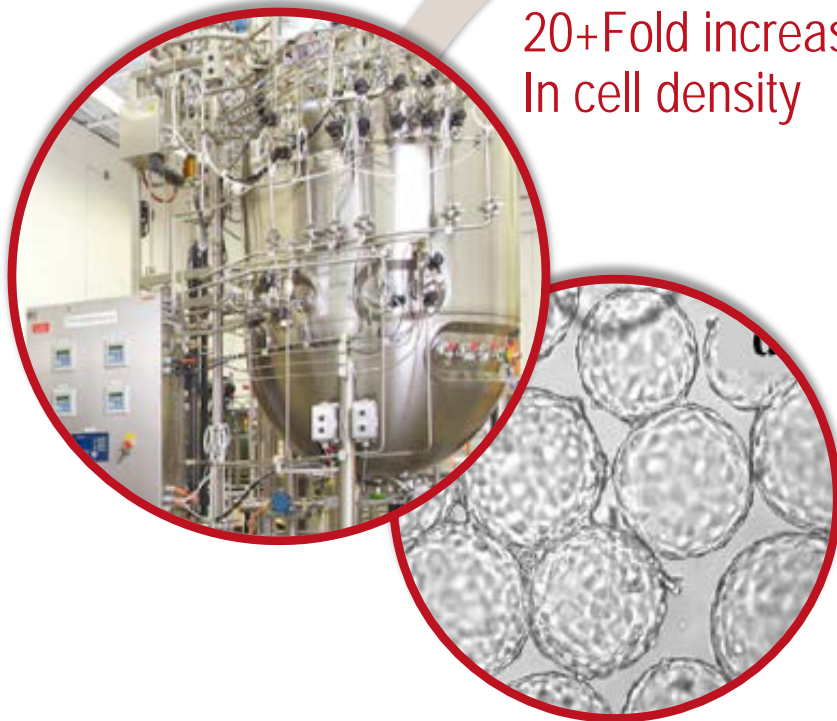
- > Viral vaccine process development & manufacturing
- > Cell line development



We have already achieved a remarkable increase in yields driven by our proprietary high cell density, small footprint, single-use bioreactor

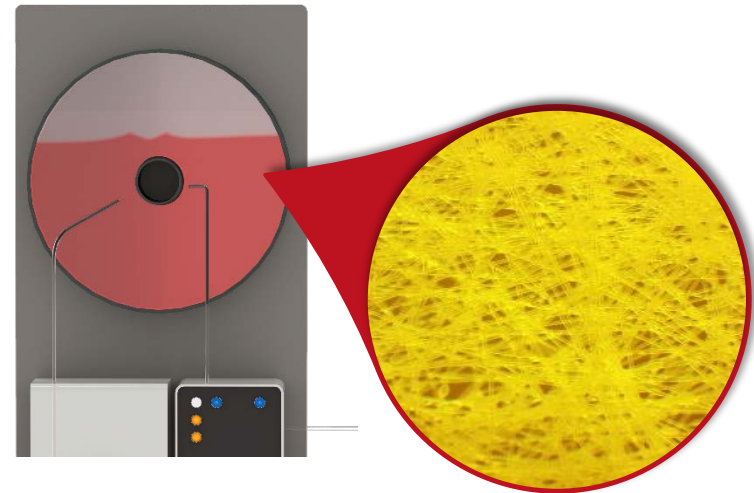
Evaluation of microfiber technology – structured fixed bed with multiple embodiments

Conventional reactor
+ Microcarriers



20+ Fold increase
In cell density

Microfiber-based fixed bed bioreactor



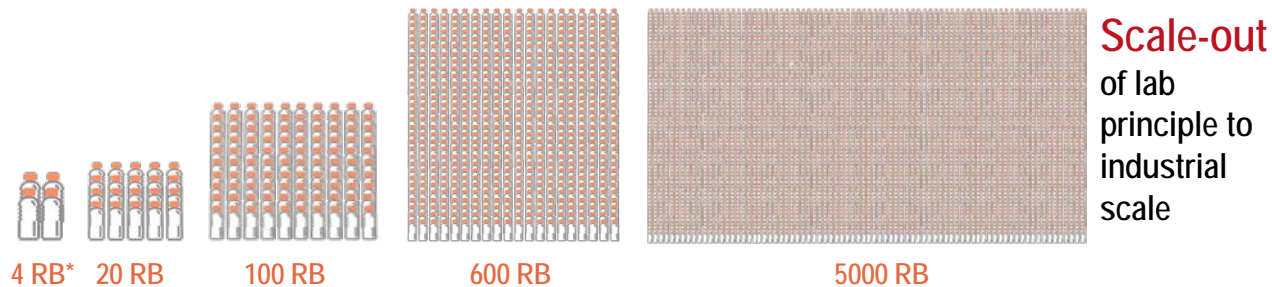
- > Microcarriers replaced by microfibers
- > High cell density - up to 200M cells/ml (20-fold increase compared to microcarriers)
- > Reduced CAPEX & OPEX, small footprint
- > “Integratable” into isolators



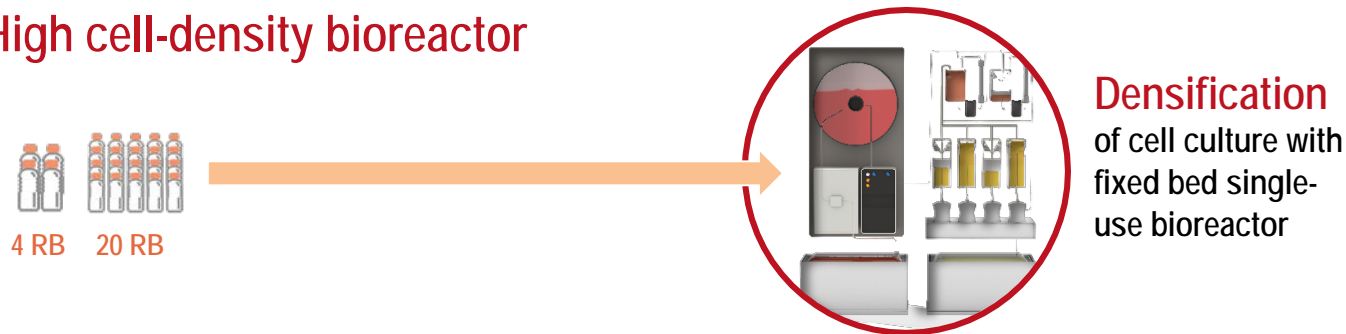
Cell culture is performed in a **bioreactor** to significantly increase cell-density, as a way to replace traditional manufacturing process

Increase efficiency in cell culture – Single-use fixed-bed Bioreactor

Traditional manufacturing



High cell-density bioreactor



*Roller bottle

- > **Limited innovation in current vaccine manufacturing**
 - Over 80% of viral vaccines are still manufactured by the scaling out of lab-scale systems
- > **A fixed-bed bioreactor significantly increases cell density**
 - Allows low seeding density and biomass multiplication by up to 500x
 - Offers 500m² of surface in <50L bioreactor



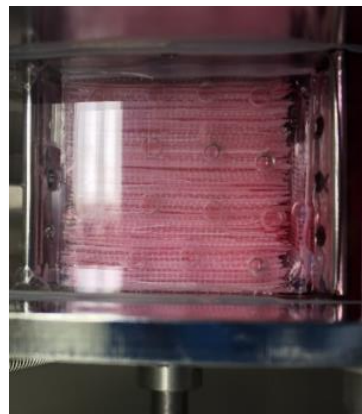
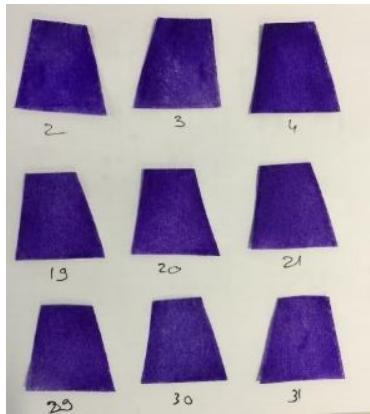
We have already achieved a remarkable increase in yields driven by our proprietary high cell density, small footprint, single-use bioreactor

Evaluation of microfiber technology – structured fixed bed with multiple embodiments

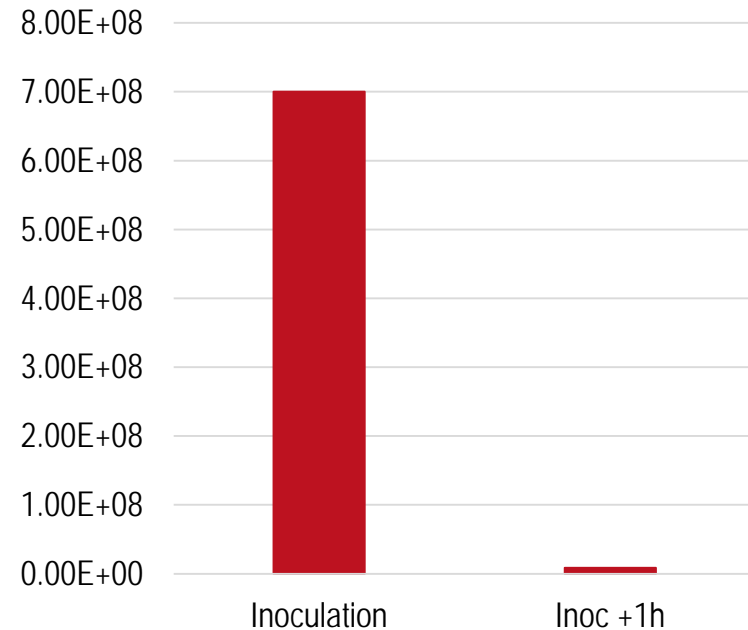


Benefits of a structured bed

- > Homogeneity – scale up virtually non limited
- > Fast cells entrapment/attachment
- > Easier to fabricate – cost effective
- > Compatible with multiple bioreactors



Cell Entrapment Kinetics

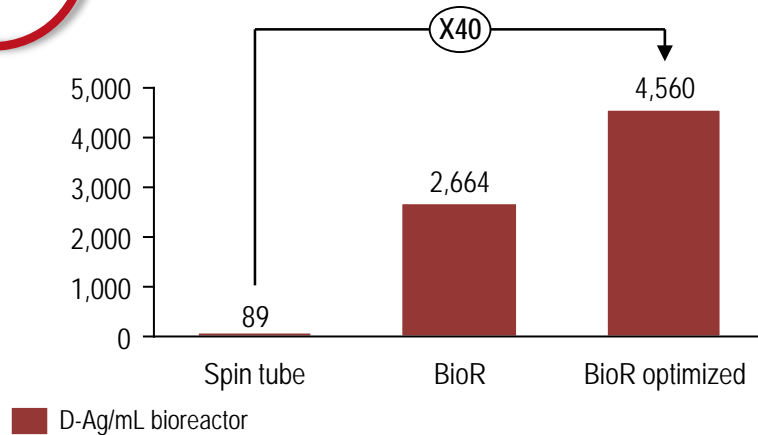




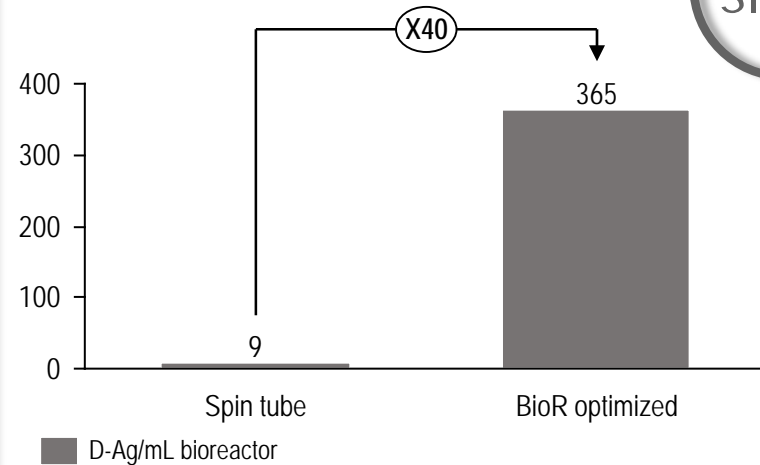
High cell densities and virus yields have been achieved in Univercells high-density, fixed bed bioreactor

Optimisation of Process development

SIPV3



SIPV2



Improvements

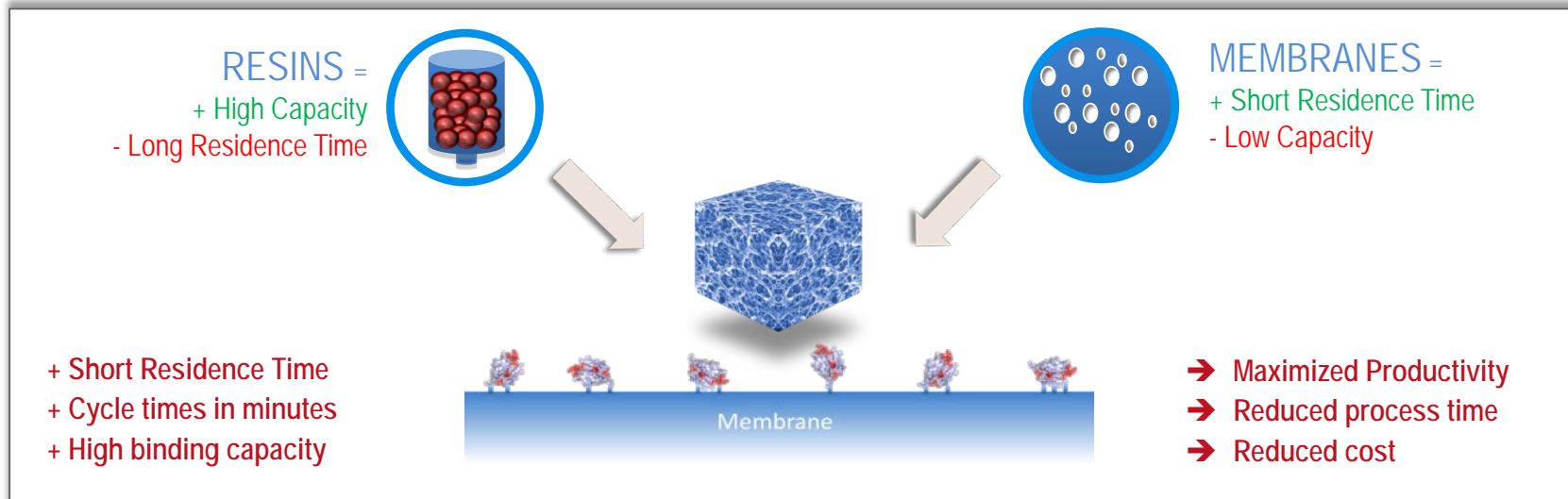


- > With current small scale yields and parental cell line, **Univercells process would yield:**
 - @500m² / 37L FB and 2x250L medium in perfusion, ~650DU/mL in 250L
 - ~4.2M doses/run in crude harvest

- > With current small scale yields and parental cell line, **Univercells process would yield:**
 - @500m² / 37L FB and 2x250L medium in perfusion, 52DU/mL in 250L
 - ~0.7M doses/run in crude harvest



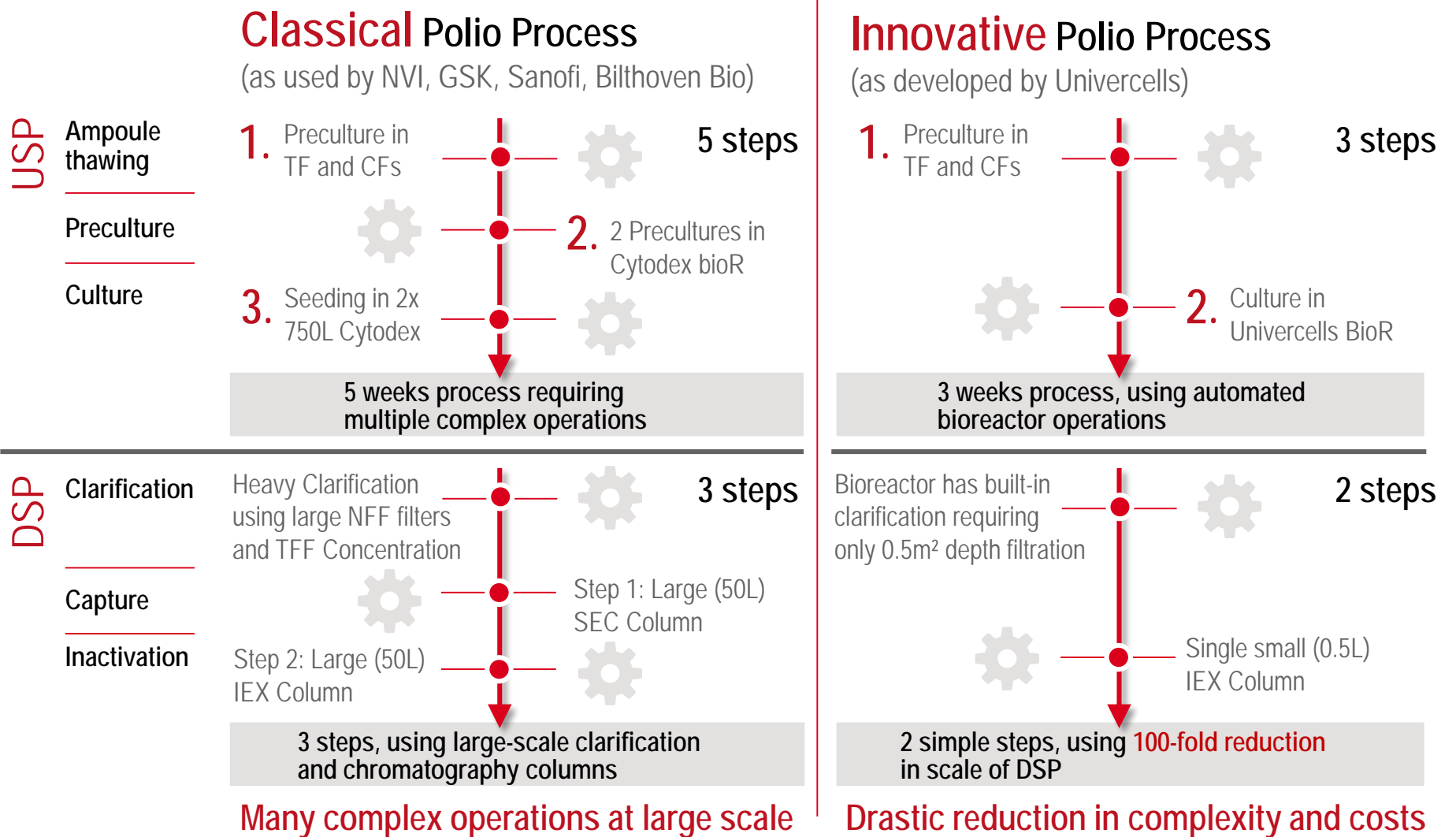
High capacity purification membranes drive a drastic reduction of clarification footprint and cost



> Affinity membranes drive >3-fold productivity over traditional resins
 > Membranes introduced in 2013, accepted for GMP manufacturing

High binding capacity	>50 000DU/mL Mb	Recovery	94%	ug HCP/DU	<0.04
Good HCP clearance	<0.1µg HCP/DU	Mass Balance	95%	DNA LRV	Pending
High yield	>90%	HCP LRV	1.6	ng DNA/DU	Pending

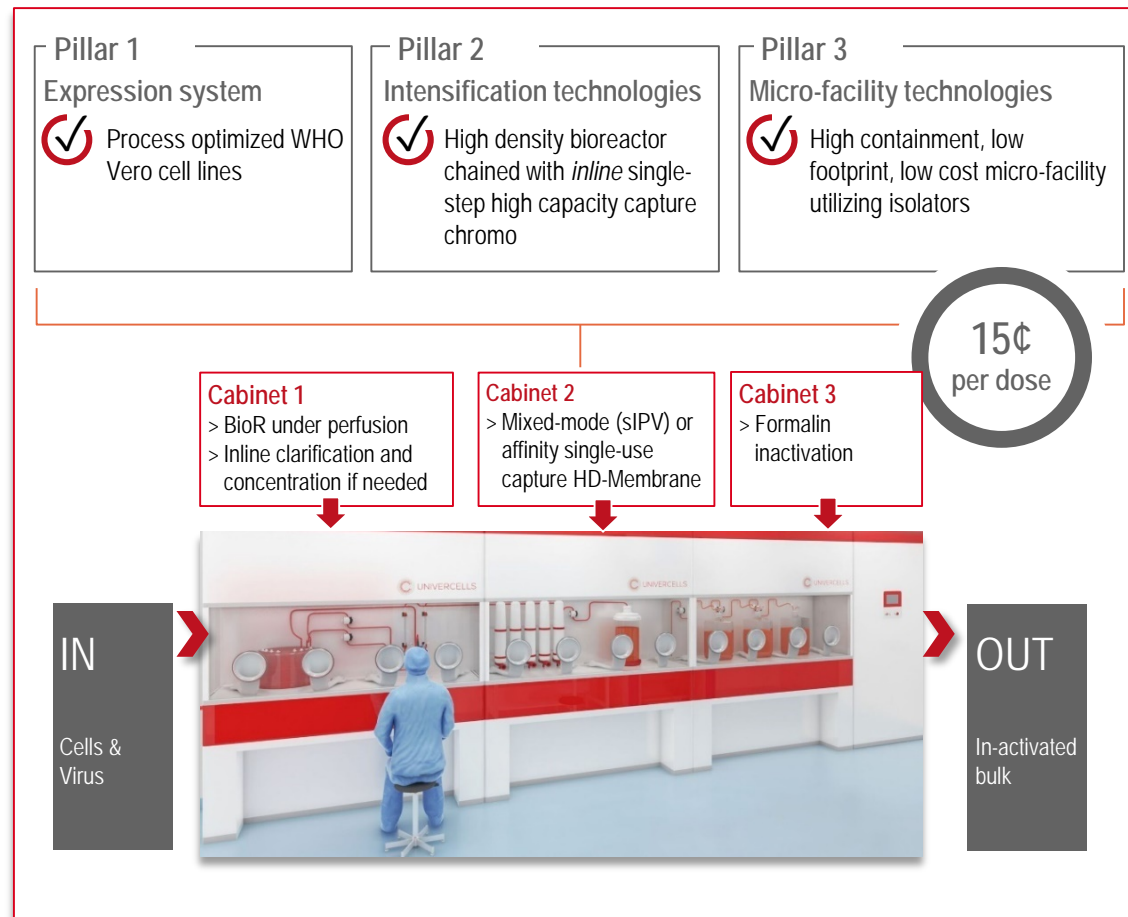
Global Process Comparison (USP and DSP)





The sIPV viral platform will produce **40M doses/year** in a **lab-scale micro-facility** at a cost of **USD 0.15/dose**

Univercells sIPV platform



Key benefits

- > **Industrial production at lab scale**
 - Highly intensified process allows miniaturization of manufacturing
 - Isolator-based micro-facility for simplified infrastructure, **high containment & safety**
- > **Delivering low CoGs**
 - Trivalent sIPV at **\$0.15 per dose**
 - Broadly applicable to viral vaccines
- > **Rapid implementation**
 - **Building footprint: <1600m²**
 - **CAPEX: ~€10M**
 - Factory operational in a few months
 - Implemented in new or existing facilities
 - Plug & Play system: rapidly deployed in-country-for country manufacture



The production platforms fits in a small facility, enabling **industrial production at lab scale**

Vaccine manufacturing at laboratory scale

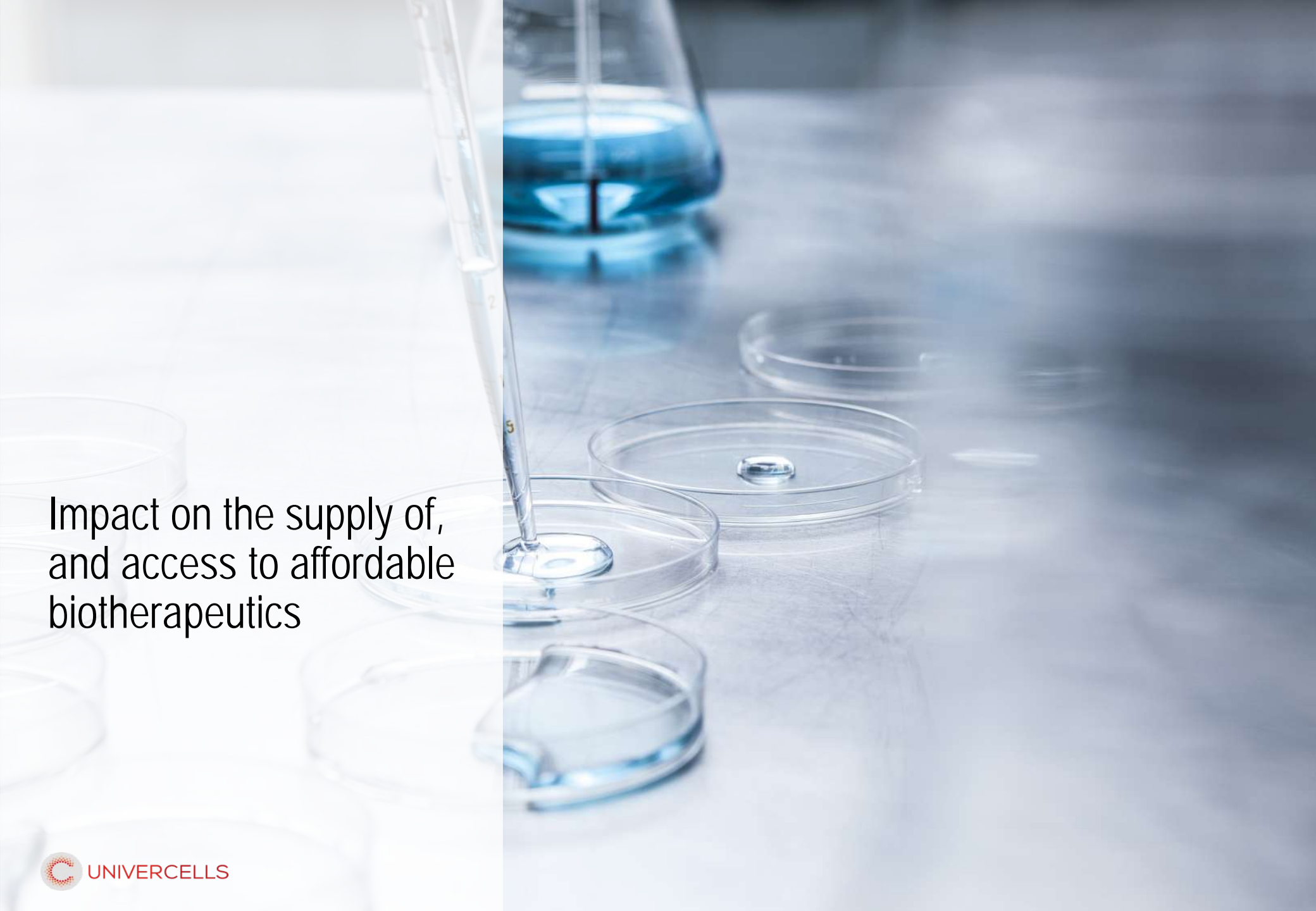


> ~ 1,600 m² flexible facility with 4 "Micro-facility" skids

> Objective : CAPEX **EUR 10-15M** capable of delivering **40M doses** trivalent IPV vaccine / year

> FTE's

- Management, Logistic, QA: 10 - 15
- Technicians, QC: 15 - 40



Impact on the supply of,
and access to affordable
biotherapeutics



Univercells viral platform enables **high production capacity at reduced costs** as an answer to current production limitations

Summary of platform and concept

**Technology
take-aways**

- 1 Industrial production at lab scale
- 2 Delivers Low COGs
- 3 Significant reduction of CAPEX, making factories affordable
- 4 Broadly applicable to viral vaccines
- 5 High Containment and safety

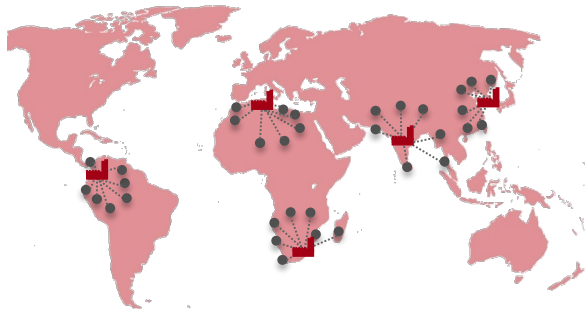


Univercells cost-effective local production platforms will transform the biopharmaceutical industry, maximizing local supply of biologics

Biologics for all – Industry paradigm shift

New paradigm

Distributed manufacturing for local markets
(e.g. Asia, Africa, Latin America)



Local production & supply of high-quality vaccines

- > High productivity addressing the global increase in demand
- > Regulatory acceptability of technologies
- > Adapted to Low & Middle-Income Countries (LMICs)
- > Increase of availability & affordability of biologics

Technology adaptable to other unmet needs

- > Rapid response to epidemics & global threats
- > Applicable to a range of biologics: gene therapy, veterinary vaccines... and recombinant proteins (mAbs, enzyme replacement therapies)



Biologics available to all !

Benjamin **DAMIEN**

Director of Business Development



+32 2 319 56 68



b.damien@univercells.com