UNIVERCELLS Technologies

A disruptive vaccine manufacturing platform enabling rapid response to disease outbreaks

Webinar presentation

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The next evolution of biomanufacturing

Univercells Technologies was launched at the initiative of two global groups to deliver intensified and integrated platforms enabling access to life-saving therapies

Univercells Technologies' genesis

Univercells
Biologics for all

Making biologics **affordable and available to all**

gamma biosciences

Enabling the promise of **Advanced Therapies**

2020

UNIVERCELLS Technologies

Designing and delivering the next evolution of **biomanufacturing**

Global provider of innovative biomanufacturing technologies to achieve cost-effective advanced therapies production from R&D to commercial scales

Source: Univercells Technologies

Next-generation bioprocessing solutions: a coordinated offering across the discovery and manufacturing pipeline

Gamma Biosciences | Overview

From Discovery to Downstream Production, offering small bench scale to large manufacturing scale solutions

gamma biosciences

Coordinated commercial engine to offer entire Gamma portfolio through customer centric and key account approach

Cell Engineering & Delivery

Mirus, BIOMagnetic SOLUTIONS

VirusGEN for AAV and LV, TransIT transfection reagents and expression systems, FerroSelect cell selection

Bioproduction Systems

UNIVERCELLS Technologies, nirrin technologies

scale-X hydro, carbo and NevoLine Upstream continuous processing, RTA 2300 & CellStat in-line analytics

Bioseparations

Astrea Bioseparations, Nanopareil

Affinity and IEX/HIC chromatography resins, Evolve & SNAP columns, nanofiber chromatography membranes, RTA 1550

Discovery and Cell Line Development → *Upstream & Midstream Production* → *Downstream Production*

Data & Process Analytical Technologies

Source: Univercells Technologies

Rapid response to disease outbreaks – what are the challenges?

UNIVERCELLS Technologies

Most vaccine viruses are produced with traditional adherent-cell technologies that present challenges to responding rapidly to disease outbreaks

Traditional virus-producing technologies and their challenges for rapid vaccine manufacturing

Adherent technologies

Accessible

Easy adoption and process development

Suspension – STR

(microcarriers)

High capacity

Established technology

Seed train

Disease outbreak response **challenges:**

> **Capacity** constraints

> **Economies of scale**

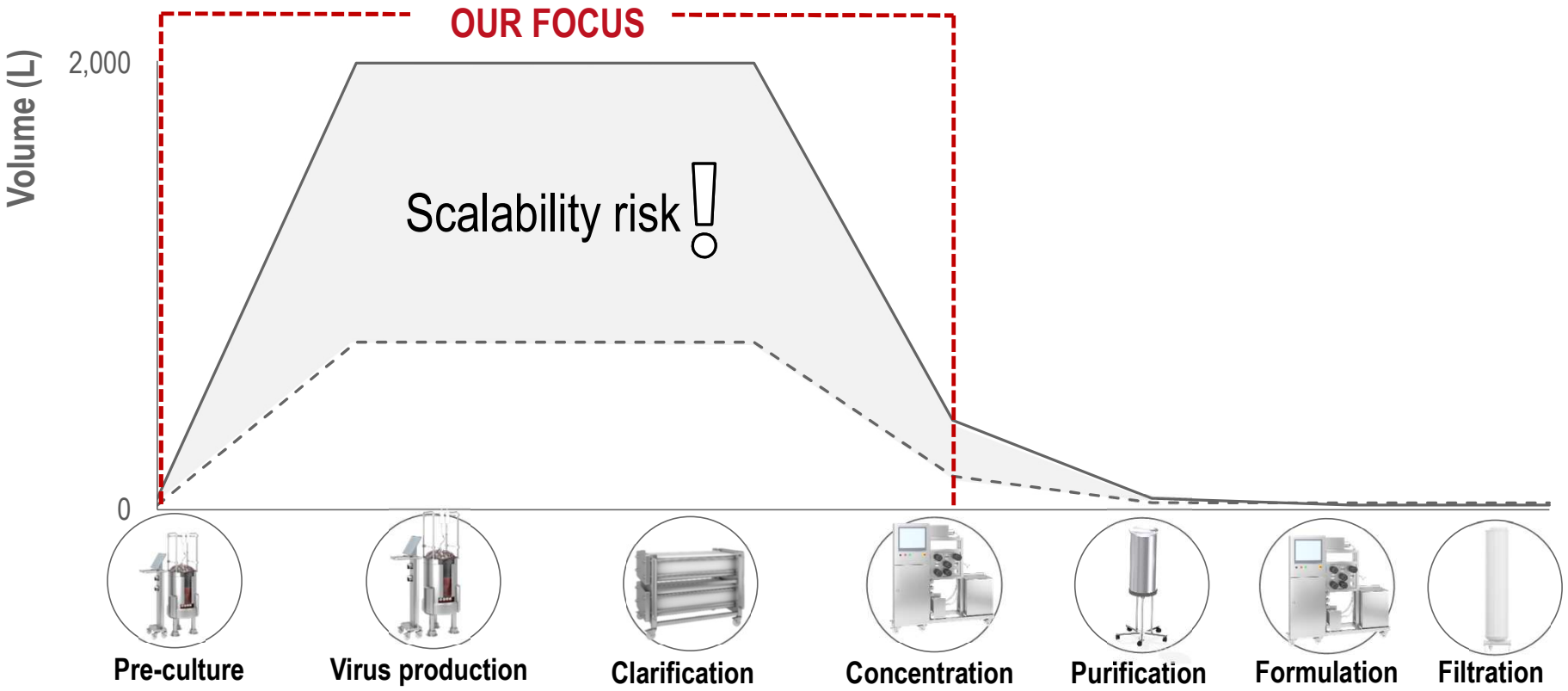
> Lack of **flexibility**

> Limited **scalability**

Source: Univercells Technologies

Large-scale viral production involves processing huge volumes and running multiple standalone operation units

Virus production process in stirred-tank bioreactors with microcarriers

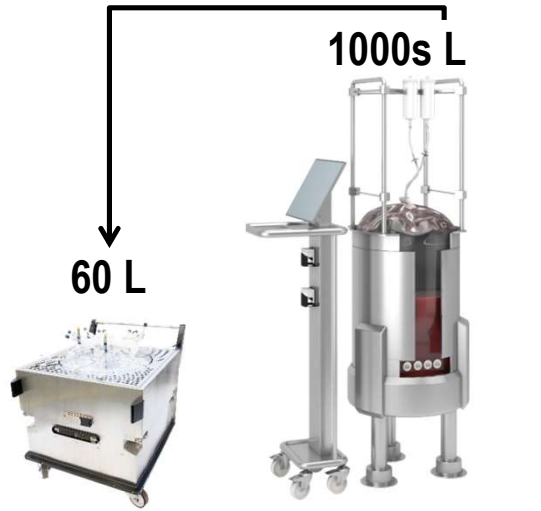


Source: Univercells Technologies

Tackling the cost, flexibility and scalability challenges to disease outbreak rapid response by applying the principles of process intensification and integration

The impact of process intensification and integration

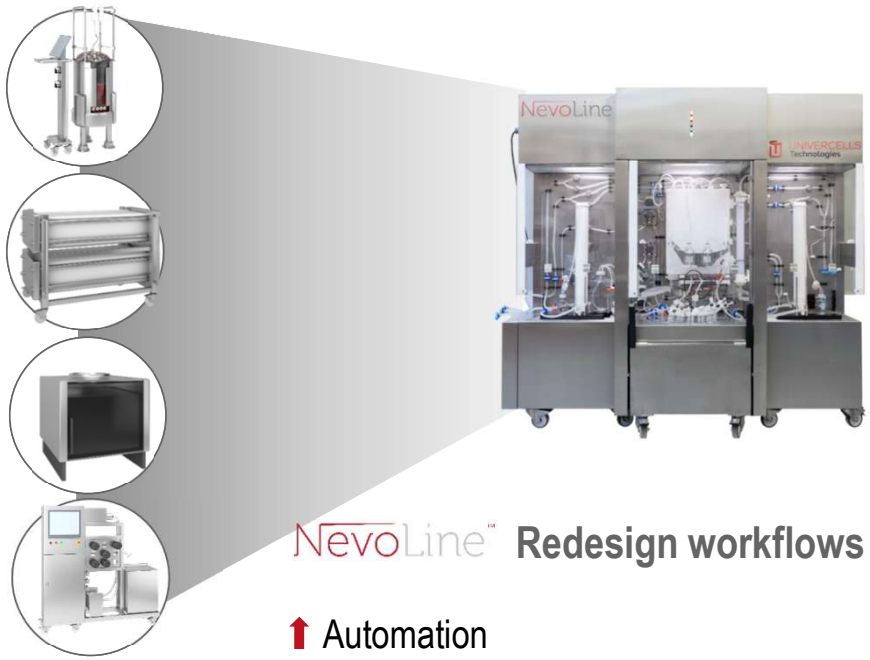
Process Intensification



scale-X™ **Redefine capacity**

- ⬆ Concentration and productivity
- ⬇ Volume

OUR APPROACH



Process Integration

NevoLine™ **Redesign workflows**

- ⬆ Automation
- ⬇ Footprint and consumable use

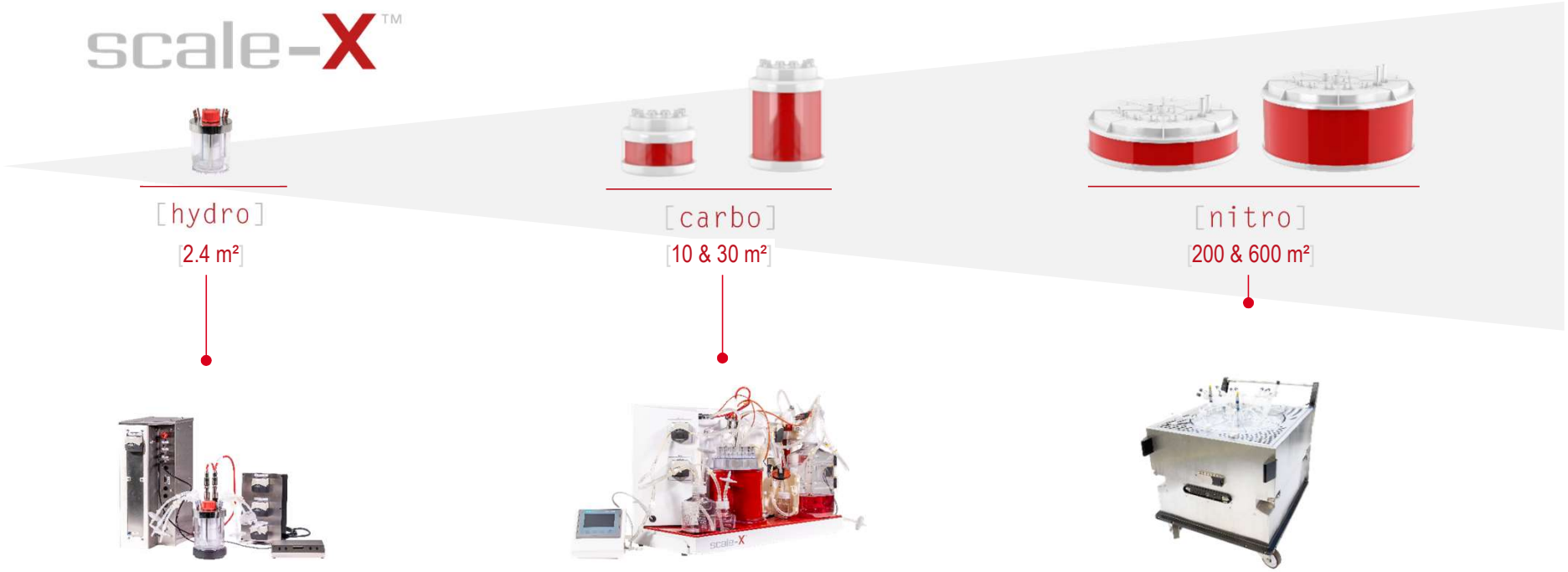
Source: Univercells Technologies

Intensifying viral production with novel technologies

UNIVERCELLS
Technologies

Univercells Technologies has designed the scale-X™ range of intensified bioreactors to tackle vaccine manufacturing challenges

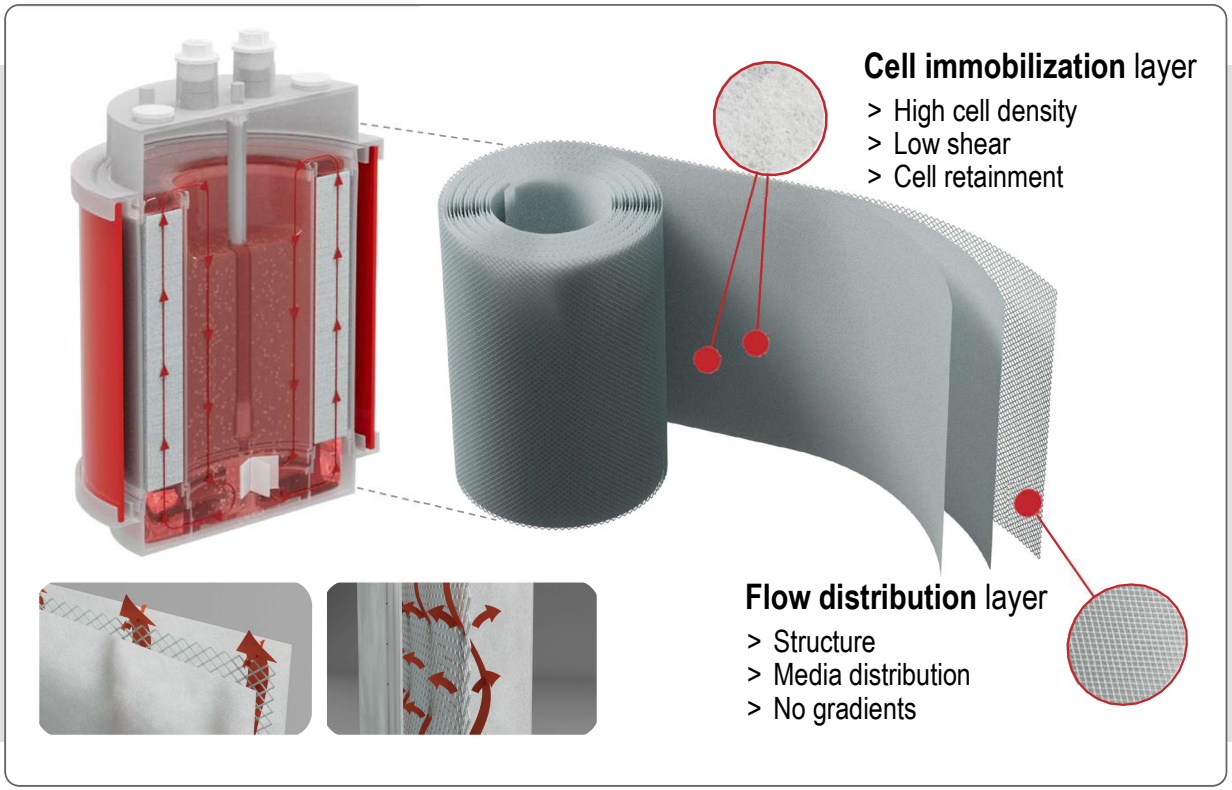
Bioreactor product range from development to commercial manufacturing



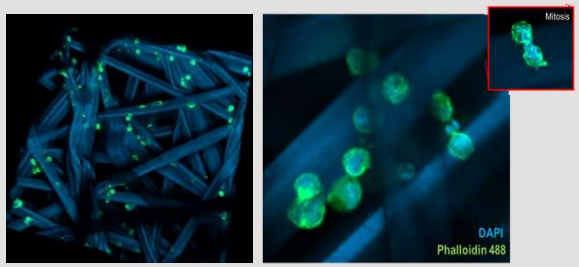
Source: Univercells Technologies

scale-X encompasses a unique dual layer design combining high cell density, low shear, homogeneity and reproducibility applied to adherent and suspension cells

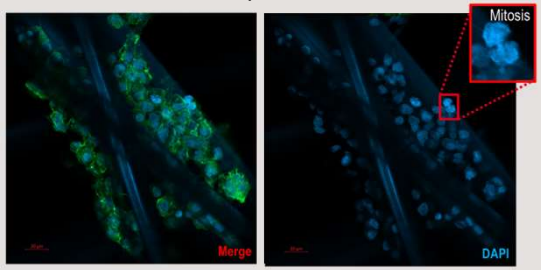
scale-X bioreactors | Redefining capacity



Suspension adapted cells (HEK293)



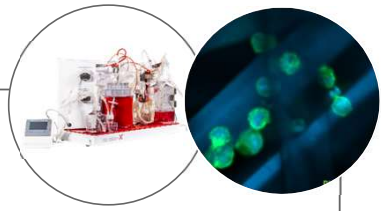
Adherent cells (HEK293)



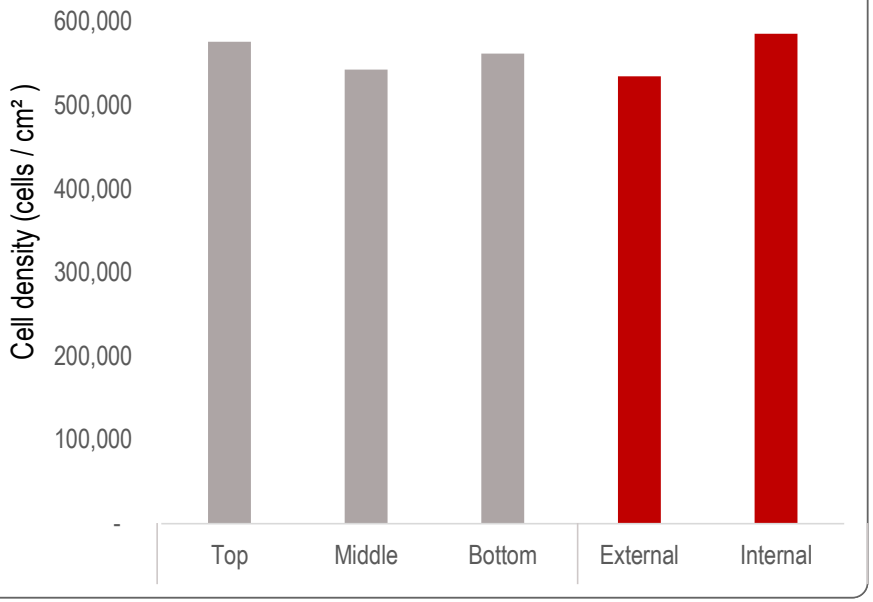
Source: Univercells Technologies

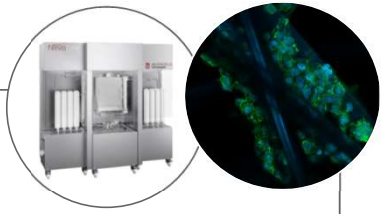
The fixed bed's homogeneous environment contributes to well characterized processing and predictably high performance

Cell distribution in scale-X

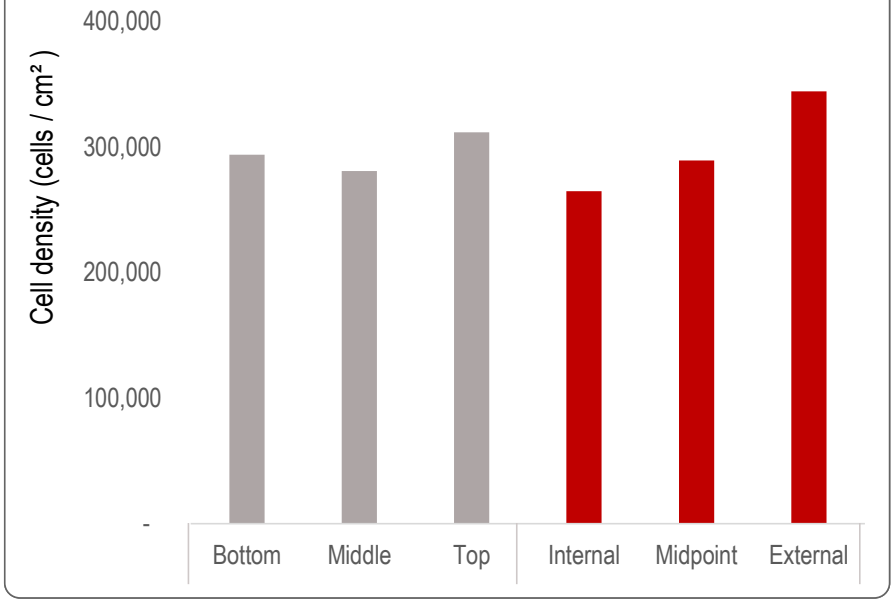


HEK293 cells in scale-X carbo 30





HEK293 cells in scale-X nitro 600



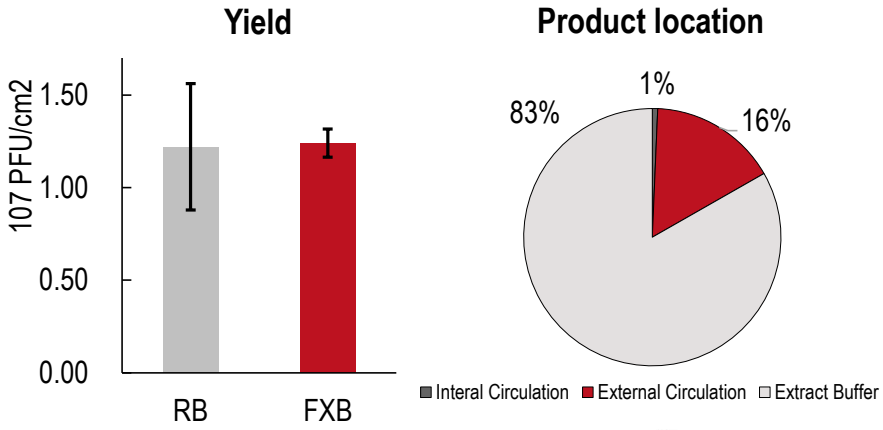
Source: Univercells Technologies (internal development)

Cell immobilization within the fixed-bed bioreactors positively affects the process impurity profile and harvesting volumes

Experimental results | HSV-based therapy produced in VERO cells

HSV vector produced in Vero cells

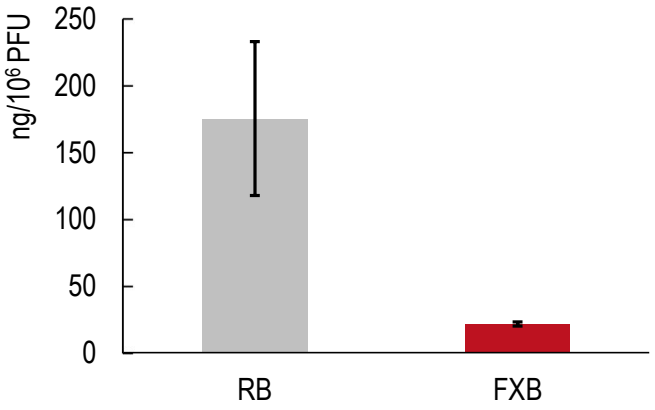
RB = roller bottle
FXB = scale-X



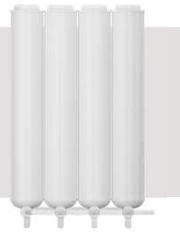
~60-100 L of harvest moved to DSP at scale

HPC content (96h post inoculation)

RB = roller bottle
FXB = scale-X

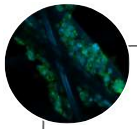


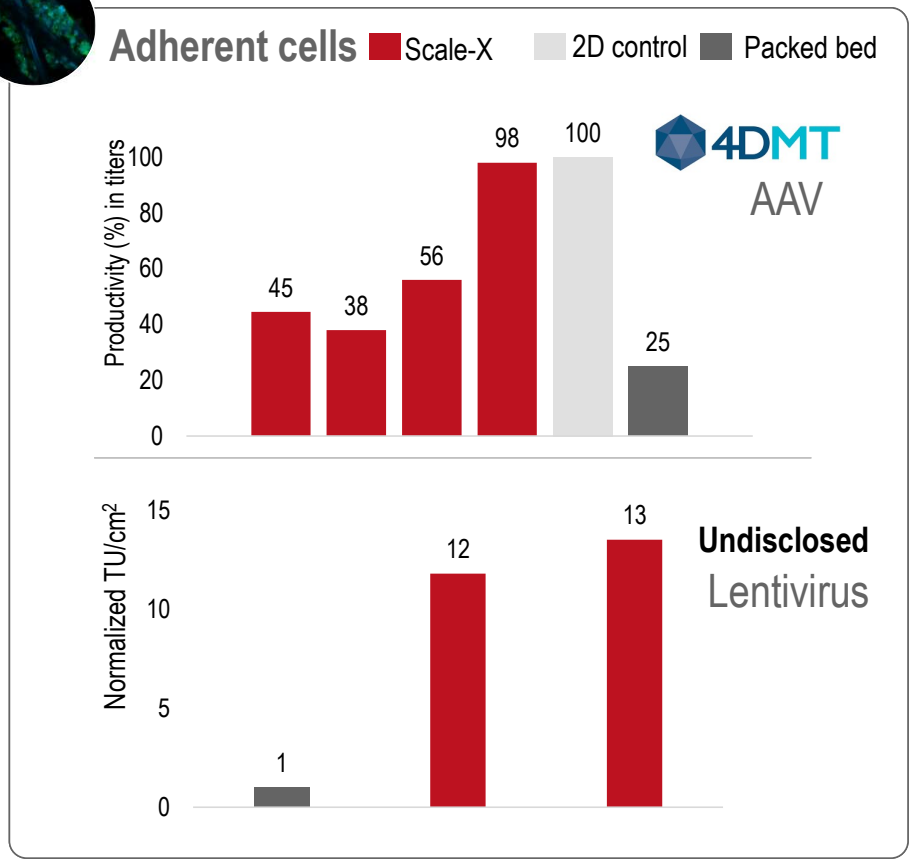
Reduction in filtration media usage

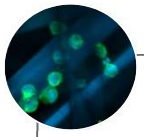


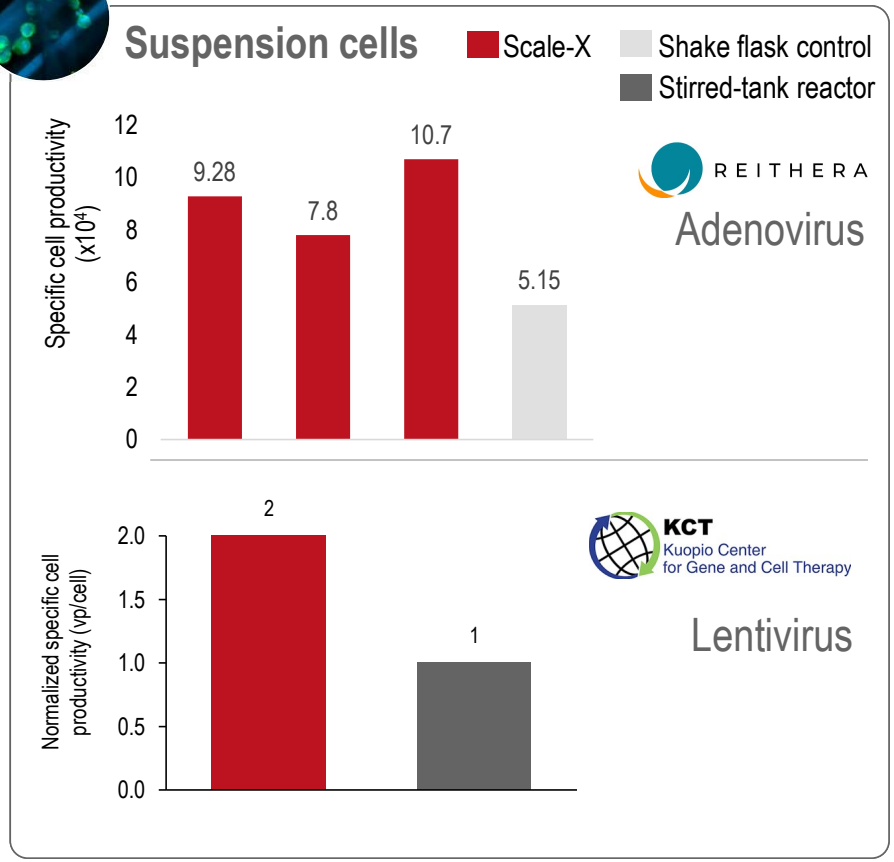
Source: Tang et al., ASGCT, 2022

scale-X bioreactors show higher productivities compared to alternative adherent and suspension platforms









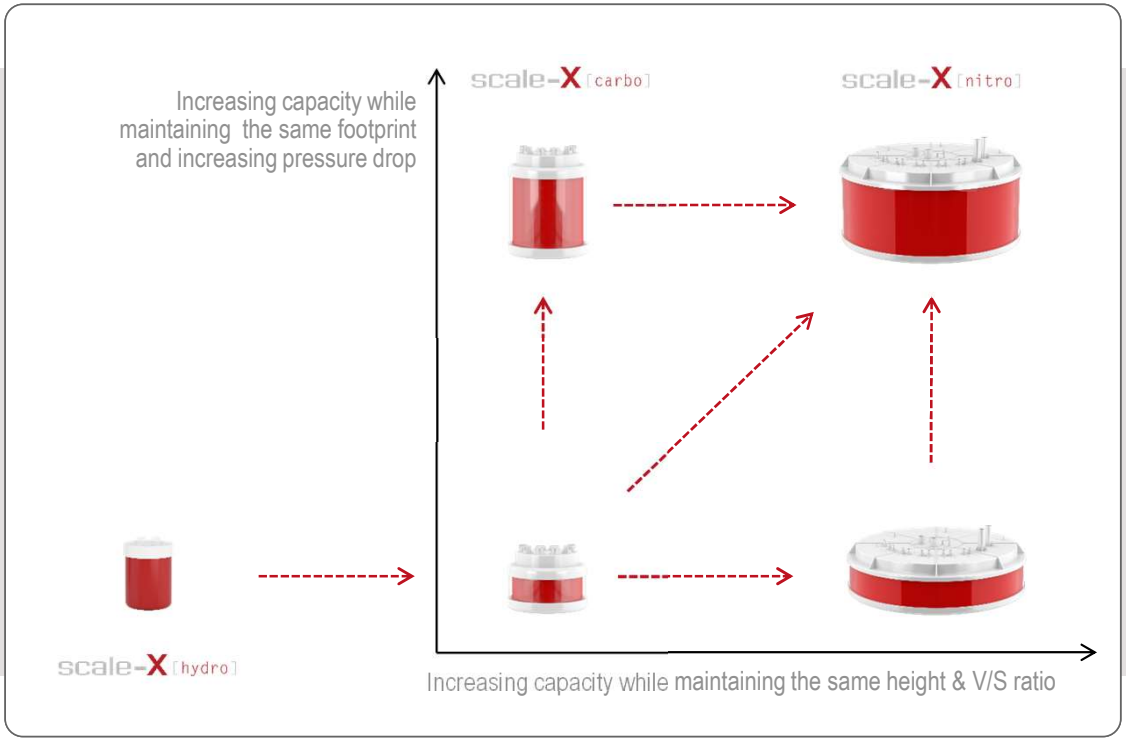
Source: Univercells Technologies

A truly scalable bioreactor portfolio can minimize development costs and timelines

Redefining scalability

Redefinition of scalability

SCALE-UP Parameters		
Design		
Geometrical similarity	H/DT & DT/Di	Volume/Surface FB height
Flow pattern/ characteristics	Impeller the shape	Pump housing design FB compaction
Control		
Mixing	P/V Re	Linear speed Tm
Shear	P/V kolmogorov number U_T	N/A N/A
Gas transfer	kLA, pCO_2, VVM	kLA, pCO_2

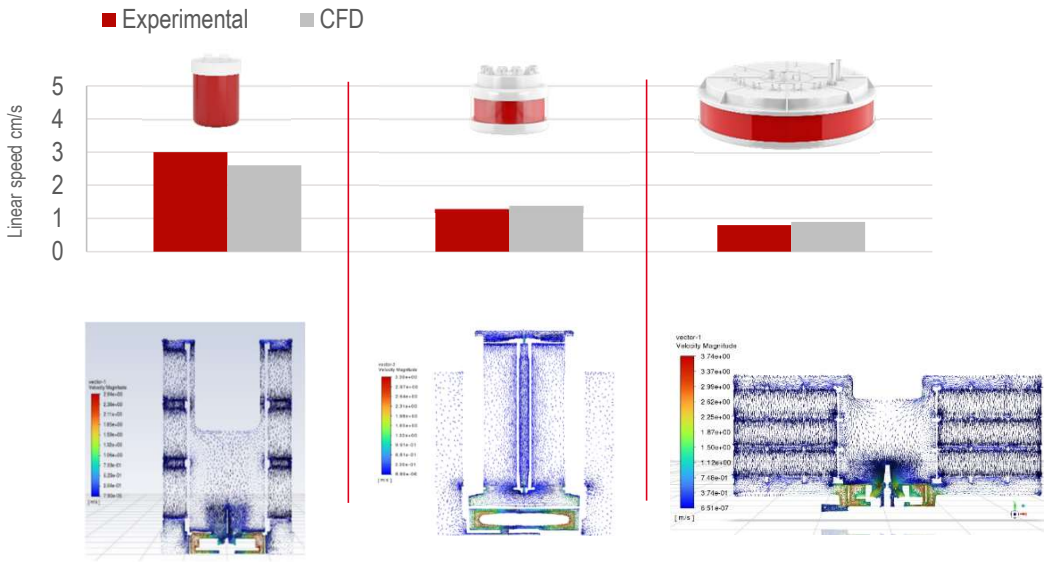


Source: Univercells Technologies

Similar linear speed and cell densities across scales enable predictive and scalable cell growth in scale-X bioreactor

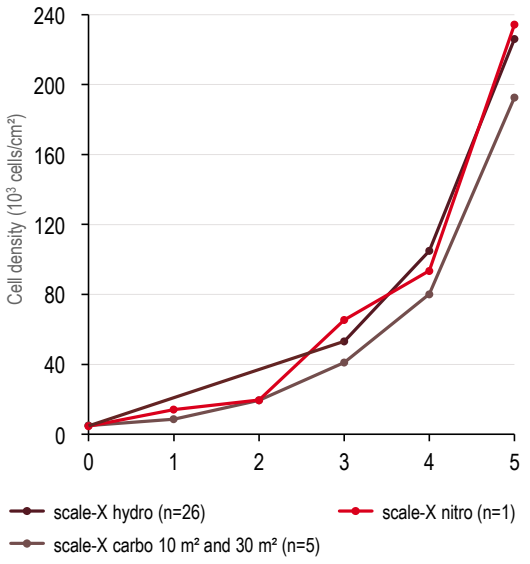
Proving scalability

Modelling and cold testing



scale-X hydro, carbo 10 m² and nitro 200 m² (left to right)

VERO cell growth in scale-X



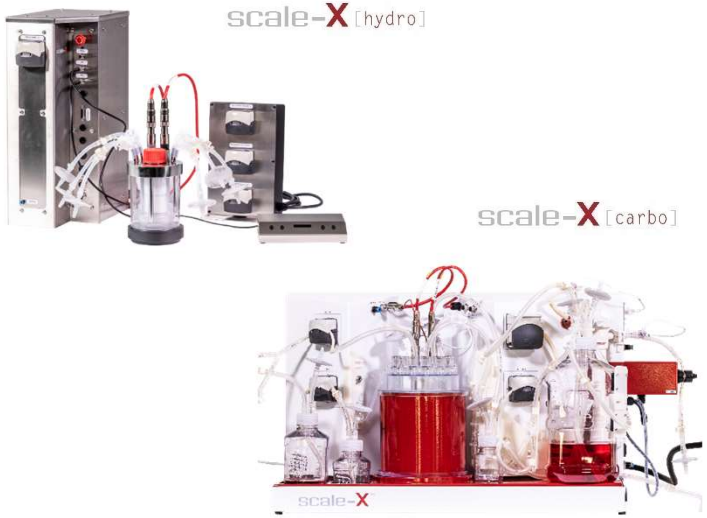
Source: Univercells Technologies

Production of Rubella in a scalable solution demonstrating faster viral production and comparable results across scales

MRC5 / Rubella | scale-X hydro (2.4 m^2) and carbo (10 m^2) viral production

Case study adherent cells

MRC5
Rubella



Highlights

Achieved target productivity
6 log Rubella titer achieved within 4 days

GMP compatible production process
Low-cost manufacture with rapid process transfer

Reliable scale-up
Consistency in viral productivity across scales

Source: Univercells Technologies

Scaling up from static T-flask to GMP ready scale-X carbo while optimizing the process and maintaining target productivity

Rubella (MRC-5) process scale-up from T-flask to scale-X carbo

Transfer from static to FB environment	T-flask > scale-X hydro
Simplify seed train	Reduce 10K > 5K cells/cm²
Optimize media consumption	Increase from 0.17 to 0.4 mL / cm²
From recirculation to perfusion	Maintain productivity

Moving away from serum during production phase	Maintain productivity
Scale-up from hydro to carbo 10 & 30	Maintain productivity achieved in hydro Optimize cell seeding step (recirc., vol., inoc. prep) Reach same cell growth as in carbo 10

Impact

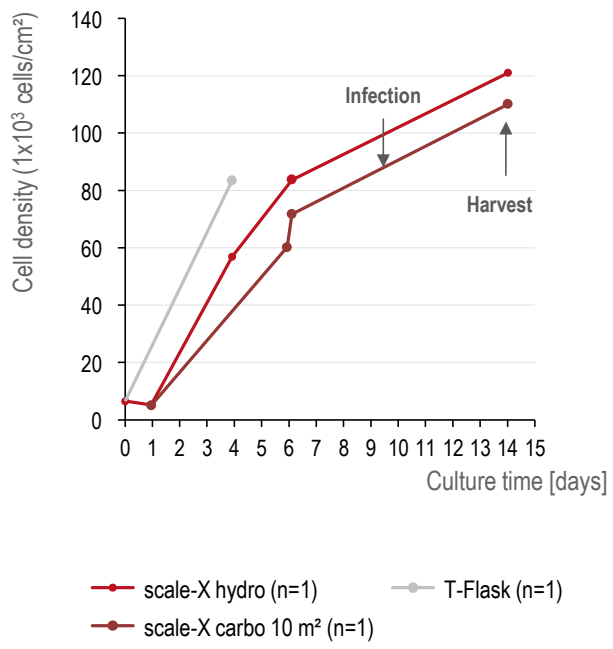
GMP compatible production process that meets target productivity for low-cost manufacture with rapid process transfer

Source: Univercells Technologies

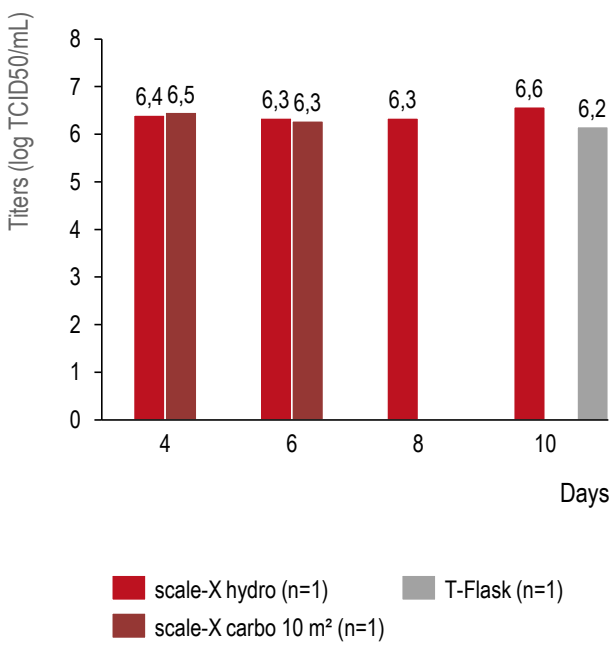
Production of Rubella in a scalable solution demonstrating faster viral production and comparable results across scales

MRC5 / Rubella | scale-X hydro (2.4 m²) and carbo (10 m²) viral production

Scalability of MRC5 cell growth in scale-X



Production of Rubella



Impact

> **Consistency** in viral productivity **across scale-X range** for a reliable scale-up

> **Projected productivity** in scale-X bioreactors:
- 3M doses/batch in scale-X carbo 30 m²
- 20M doses/batch in scale-X nitro 200 m²

Source: Univercells Technologies

We have successfully produced implement a PoC study for an adenovirus-based vaccine

Adenovirus production with HEK293 cells adapted to suspension | scale-X hydro

Case study suspension cells

HEK293 adapted to suspension
Adenovirus

Highlights

Achieved target productivity
Productivity was > 70 000 vp/cell

Achieved target cell entrapment
Cell entrapment achieved was >80%

Achieved target PDT
PDT at infection was 35 to 45 h

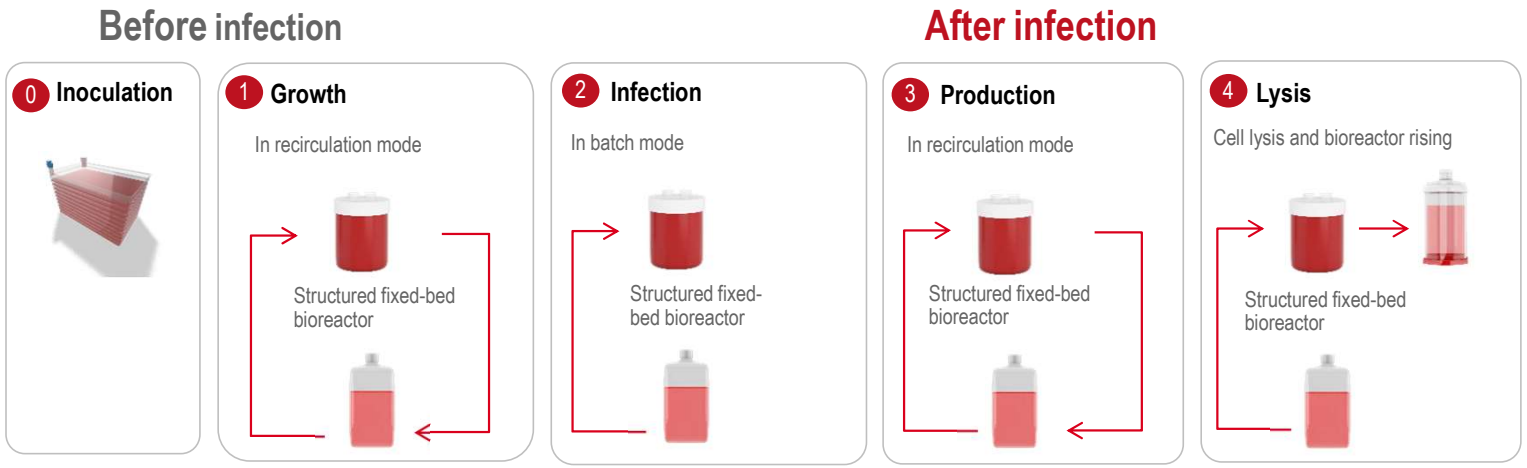
Source: Univercells Technologies

Three different process designs were assessed in the scale-X bioreactor during the PoC study

Materials and methods: scale-X experimental details

Control process

Working volume	250ml
Seeding density	$5x10^5$ cells/mL
Growth phase	3 days
MOI	Kept constant
Temp.	37°C
DO	50%
Ph	Kept constant
Production phase	3 days

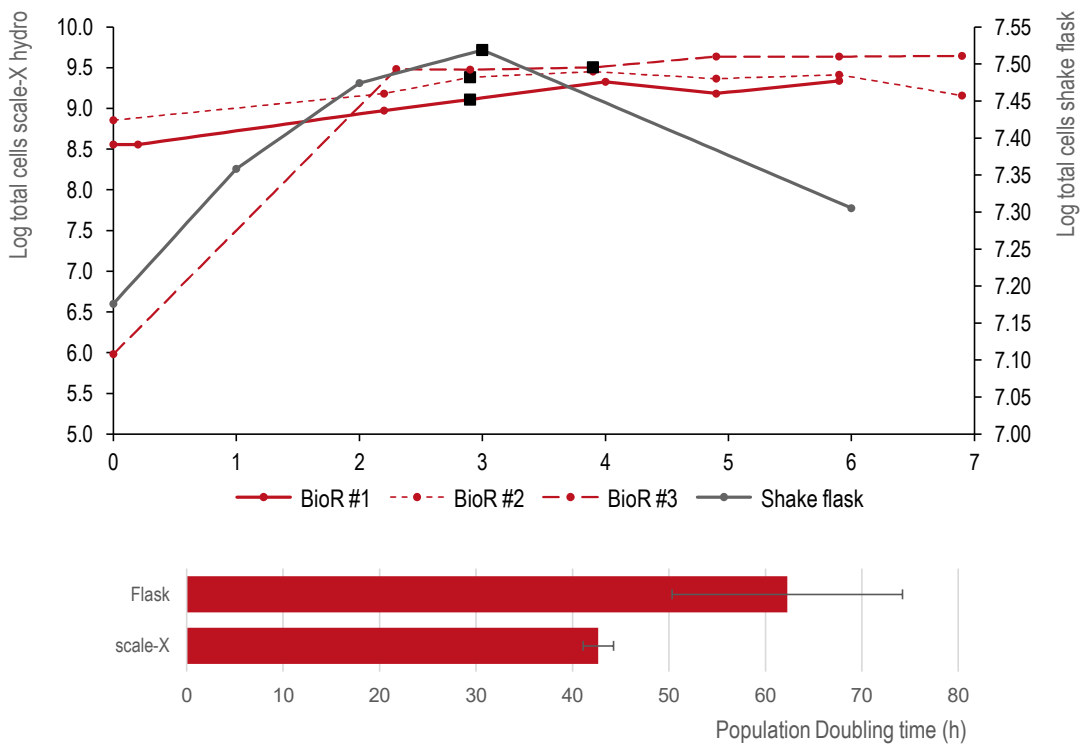


Bioreactor #1	Process transfer: Adjust the cell densities into the FB bioreactor and ensure satisfactory cell entrapment with PDT of 42±5h
Bioreactor #2	Increase in production phase: Assess whether the production phase can be extended past 3 days or the productivity plateaus after this period
Bioreactor #3	Increase cell density at infection: Assess whether the increasing the biomass at the point of infection has an impact on productivity

Source: Univercells Technologies

Reproducible PDT achieved at different inoculation densities, reaching cell densities of >5M cells/mL

Cell growth | scale-X hydro



Results

> Reproducible growth profile and doubling time changing to a controlled culture environment

> Adherence properties kept with higher cell density without major changes in process (medium formulation)

Less than 5% of the biomass in suspension during the runs

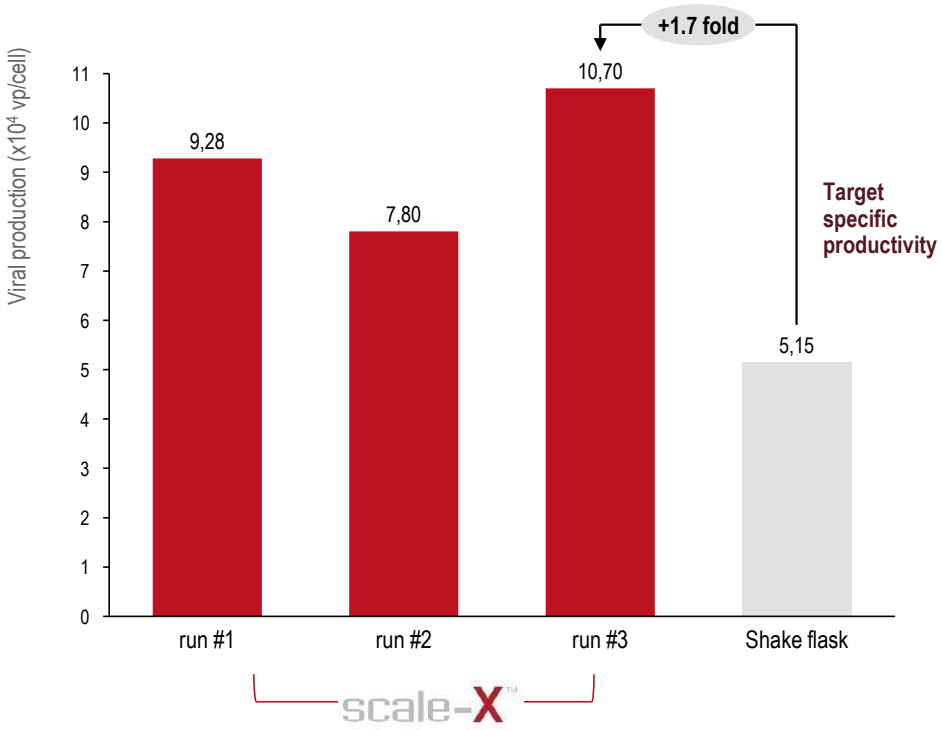
Impact

Successful adaptation of process parameters in scale-X technology without significant process changes

Source: Univercells Technologies

The productivity results shown that a process transfer without optimization enabled the target productivity to be achieved

Production of viral particle | scale-X hydro and expected 2000L bioreactor



Unit	nitro600	Control shake flask (extrapolated 2000L)
Vp/mL	4.8E+10	3.15 E+10
Vp/cm²	1.4E+10	N/A
Vp TOT	8.4E+16	6.3E+16
Total medium used	**1750L**	**2000L**

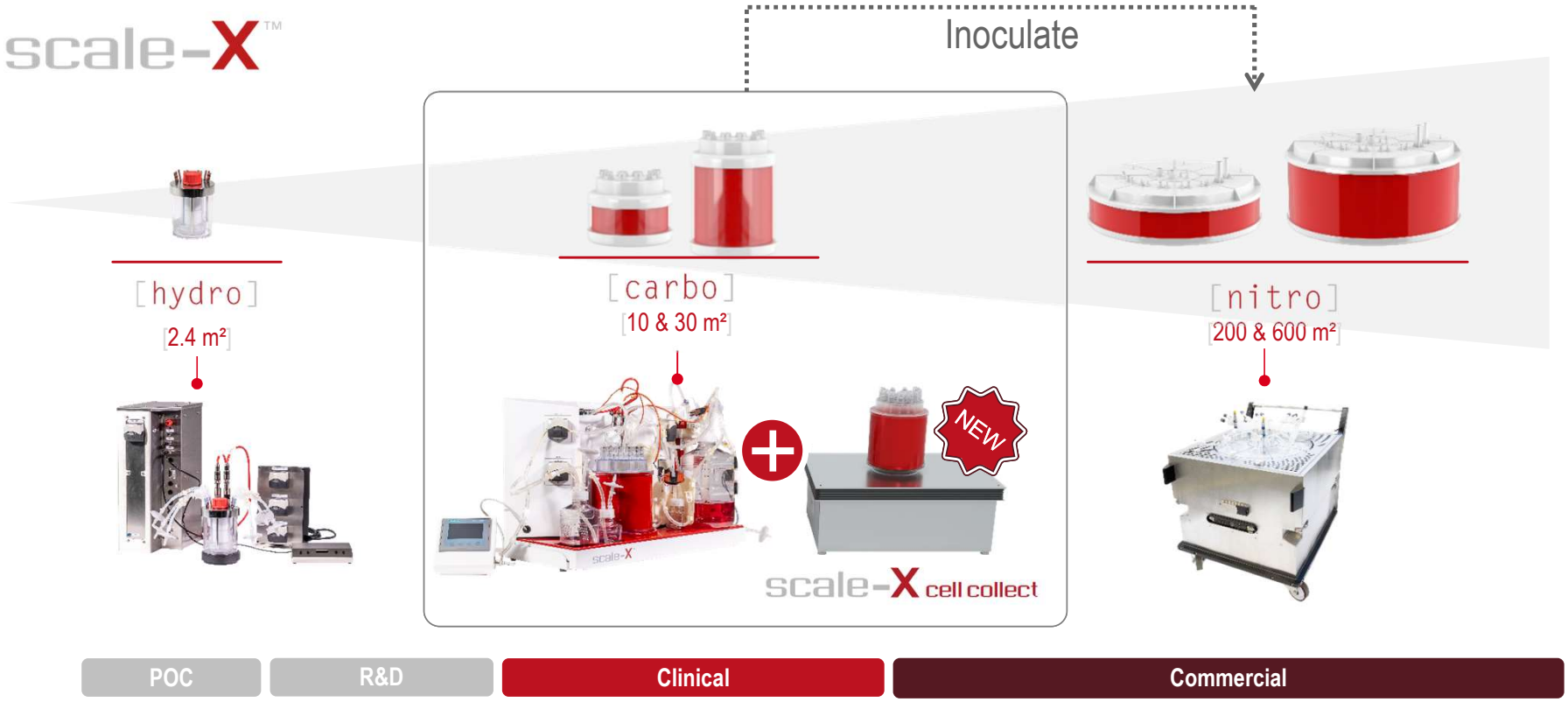
> With scale-X data, volumetric production halved compared to shaken process **with unoptimize process**

→ Possible to match volumetric titer with process parameter optimization

Source: Univercells Technologies

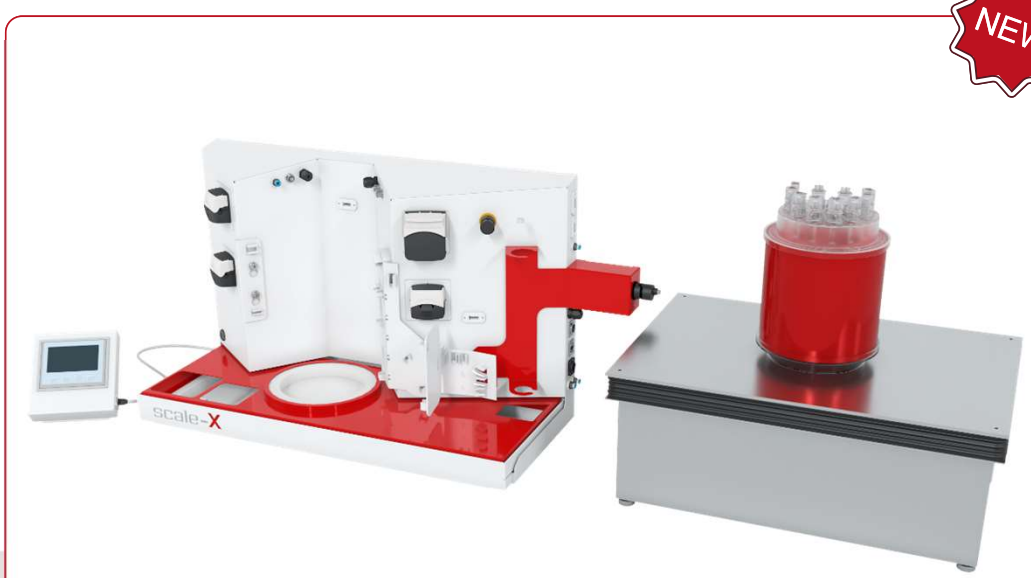
The scale-X range enables fixed-bed intensification as cells can be detached from the fixed bed using the scale-X cell collect module

scale-X product range



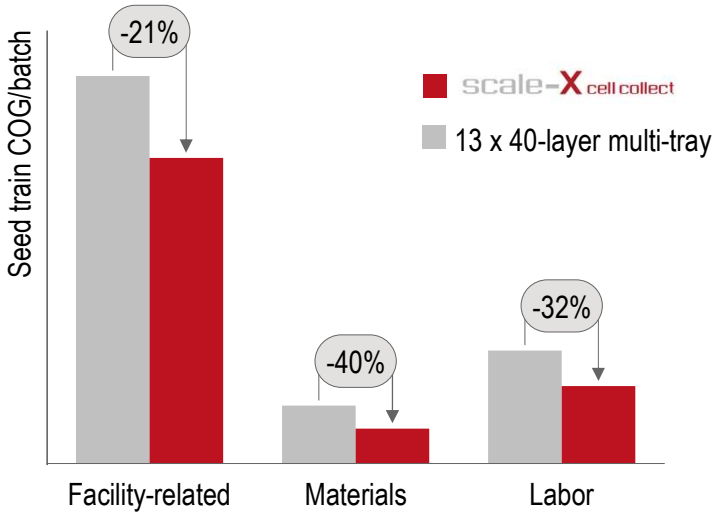
Source: Univercells Technologies

The scale-X cell collect system will intensify and automate seed train generation for large-scale applications using a benchtop system



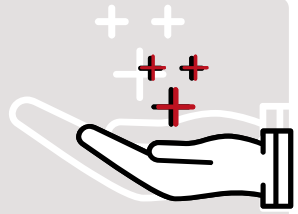
New module connected to an existing controller

Automated control & monitoring through a single interface



KEY BENEFITS

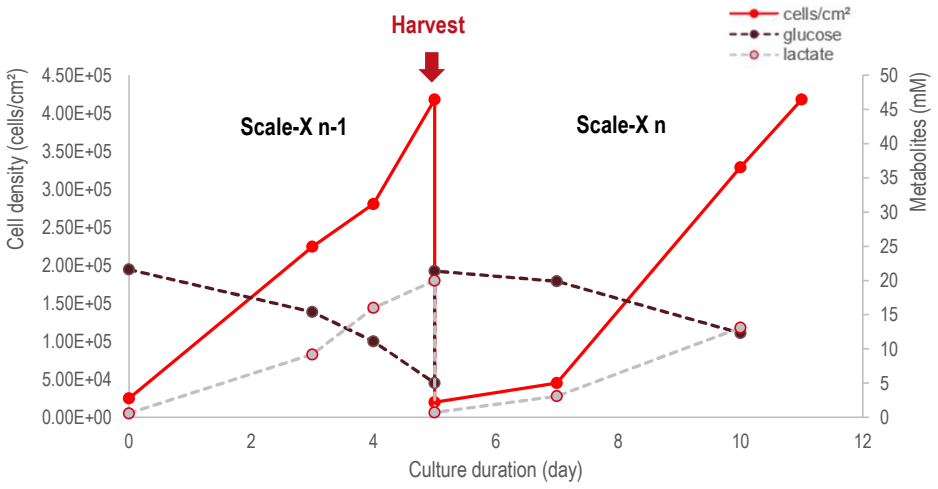
> Risk mitigation
> Reliability
> Cost savings

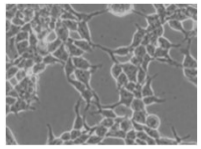


Source: Univercells Technologies

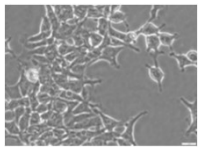
The scale-X™ cell collect achieves >98% cell detachment while maintaining cell viability and PDT from R&D to final scale

Cell growth



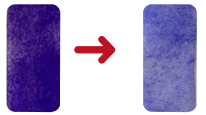


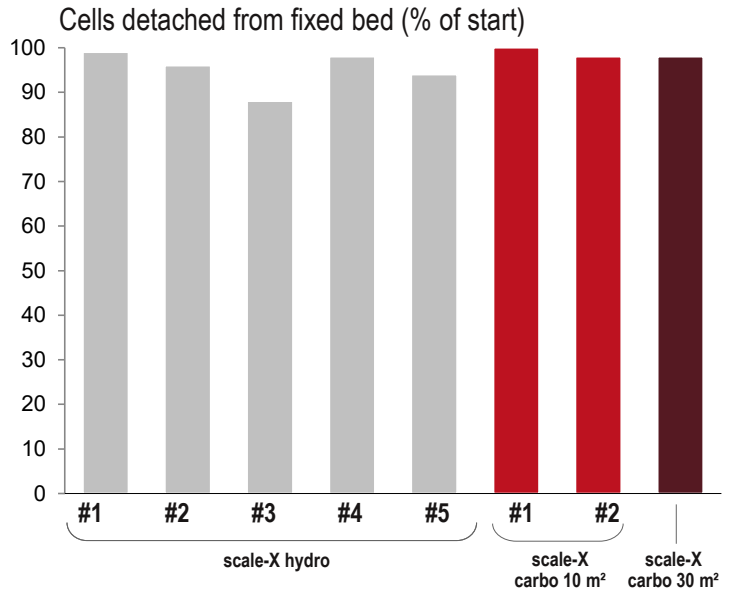
Harvested from fixed bed PDT 29-37h



Harvested from T-flask (control) PDT 29-39h

Detachment efficiency





Source: Univercells Technologies

Intensification and integration in a single platform

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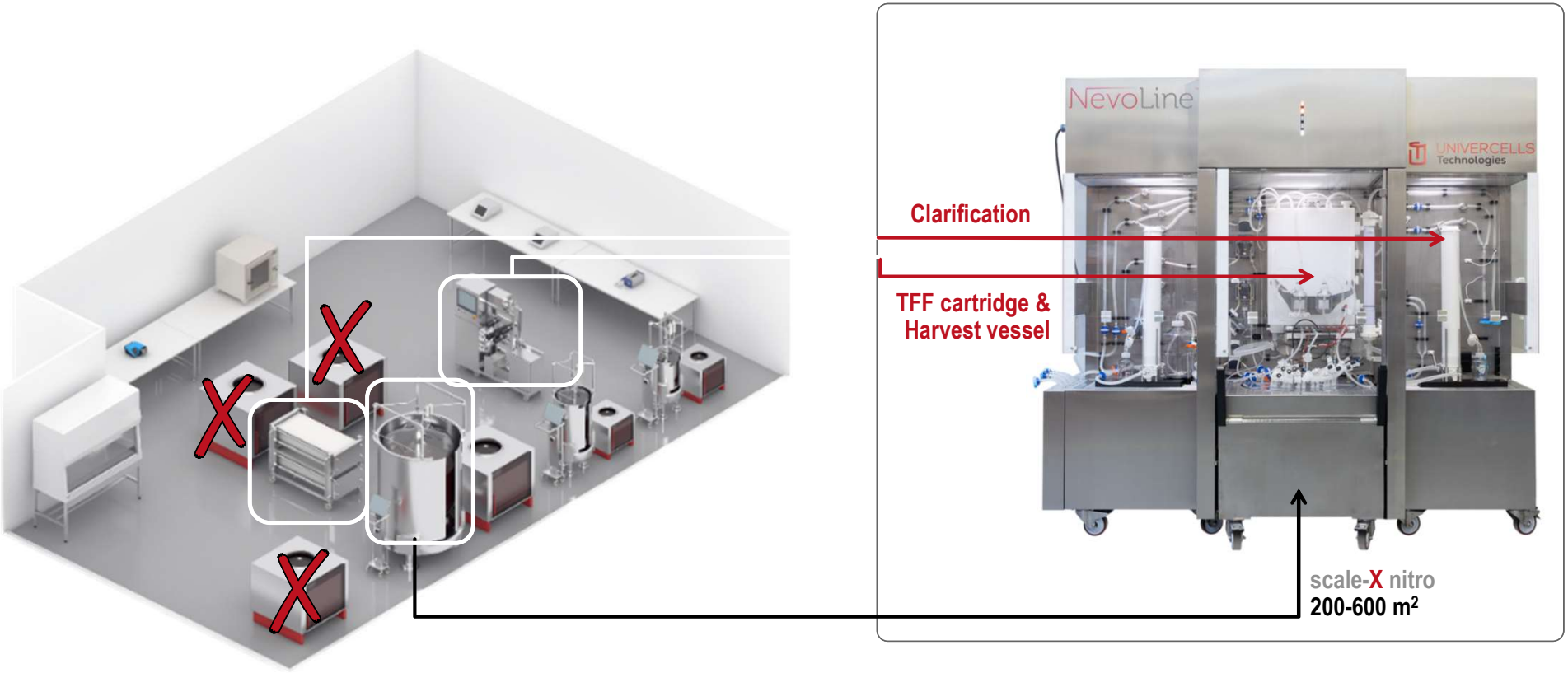
The next evolution of biomanufacturing

The NevoLine Upstream integrates multiple operation units in one platform along with an intensified scale-X fixed-bed bioreactor

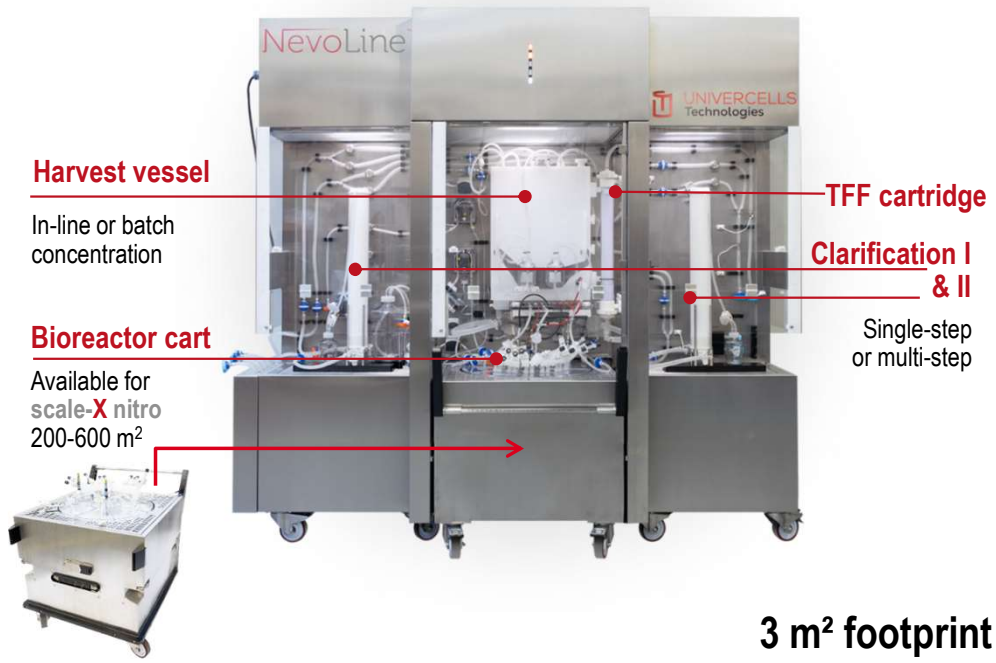
NevoLine Upstream platform's integration



Source: Univercells Technologies

All unit operations integrated into the NevoLine benefit from centralized process control and monitoring

Achieving integrated and continuous processing



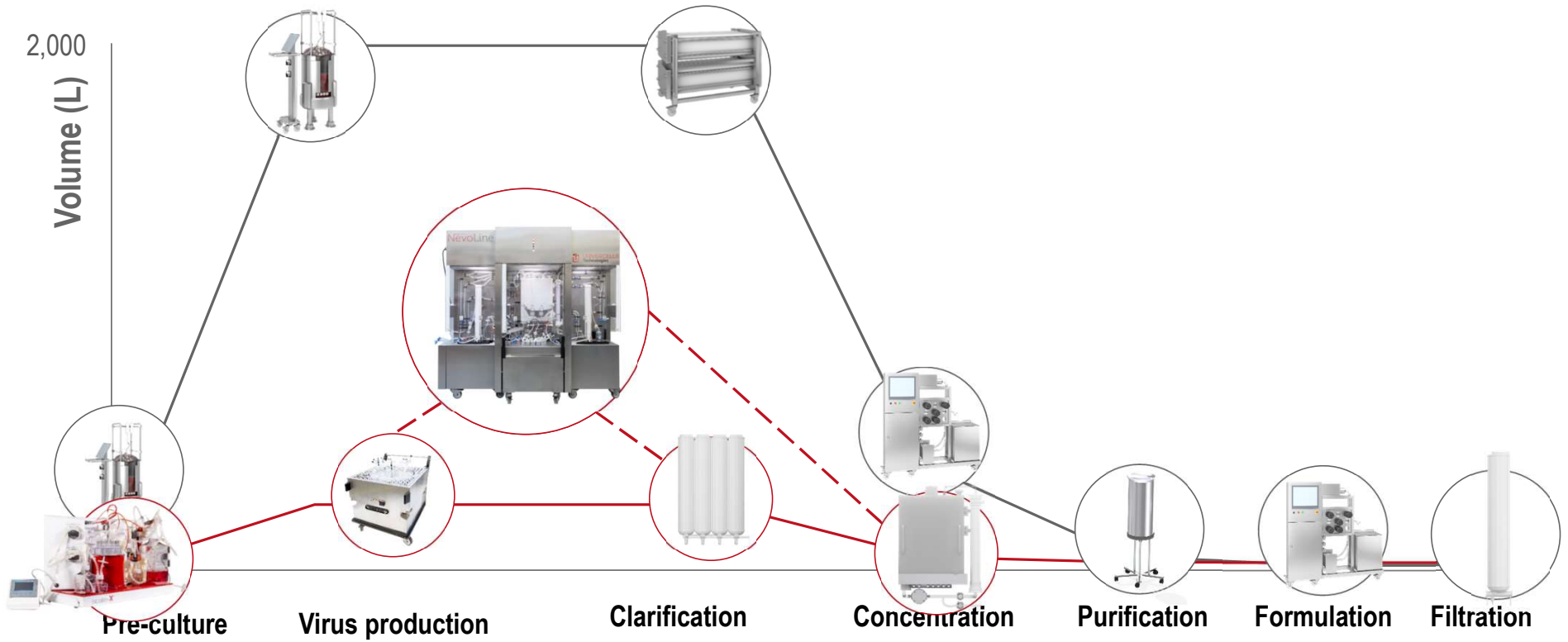
3 m² footprint

Single HMI

Centralized control and monitoring

Source: Univercells Technologies

The scale-X combined with the NevoLine Upstream platform enable high capacity while maintaining low volumes throughout the manufacturing process



Source: Univercells Technologies

The NevoLine Upstream platform enables high performance in vaccine manufacture, reaching millions of doses per year

Vaccine production in the NevoLine Upstream platform

NevoLine™ Upstream

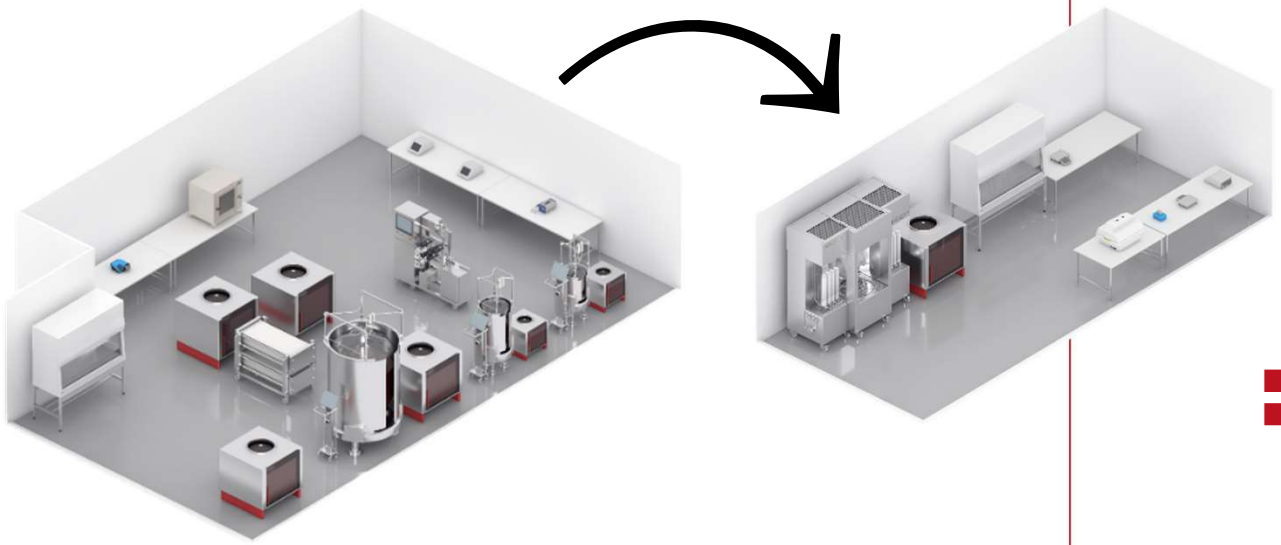
scale-X™ [nitro]

	Dose size	Unit	Doses/batch 200 m²	Doses/batch 600 m²	Doses/year 200 m²	Doses/year 600 m²
rVSV- LASV	2.00E+07	PFU	>11M	>34M	228M	684M
sIPV	58.00	DU (trivalent)	>150k	>0.5M	>3.5M	>11M
VSV- Ebola	2.00E+07	PFU	>100k	>300k	>2M	>6M
nOPV	2.00E+05	TCID50	85M	255M	>1,5B	>5B

Source: Univercells Technologies

The NevoLine Upstream platform is an intensified and integrated solution that tackles all challenges to rapid response vaccine manufacturing to disease outbreaks

Stand alone unit operations with volume-based capacity



Intensified and integrated

- Volumetric **Productivity**
- Product **Quality**
- Process **Flexibility**
- Development **resources**
- **Consumables** & **Reagents** usage
- **Labour** requirements

Enable disease outbreak rapid response vaccine manufacturing

Source: Univercells Technologies

UNIVERCELLS
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Thank you
for your attention

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