



Novel End-to-end Platform for Scalable and Efficient Manufacturing of Extracellular Vesicles

EVscale™ - Extracellular *V*esicles *at scale*

Phoenestra GmbH
February 2024

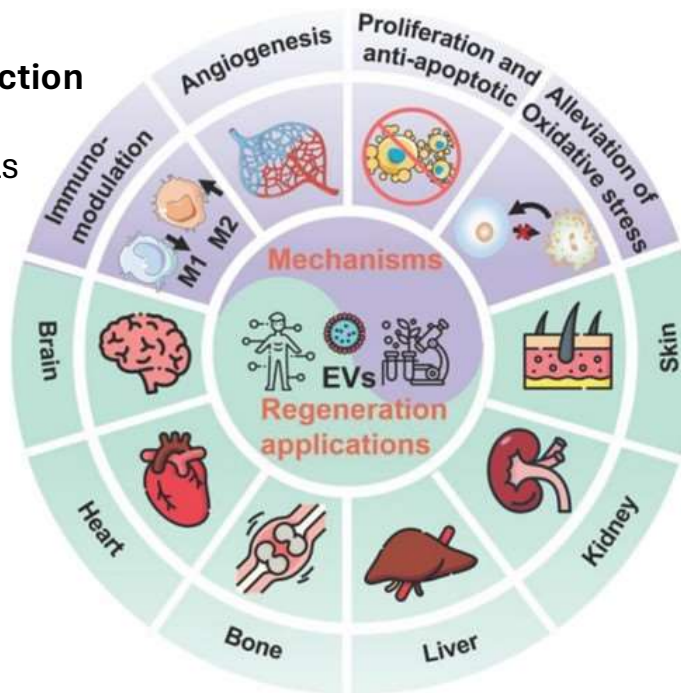
The Case for Extracellular Vesicles

Extracellular Vesicles (EV) are **natural and universal ‘cargo ships’** between cells in all organisms and tissues

Biologically relevant mechanisms of action

e.g. for Mesenchymal Stem/Stromal Cells (MSC)

- Anti-inflammation
- Anti-fibrosis
- Tissue-protection
- Pro-angiogenesis
- Macrophage polarization



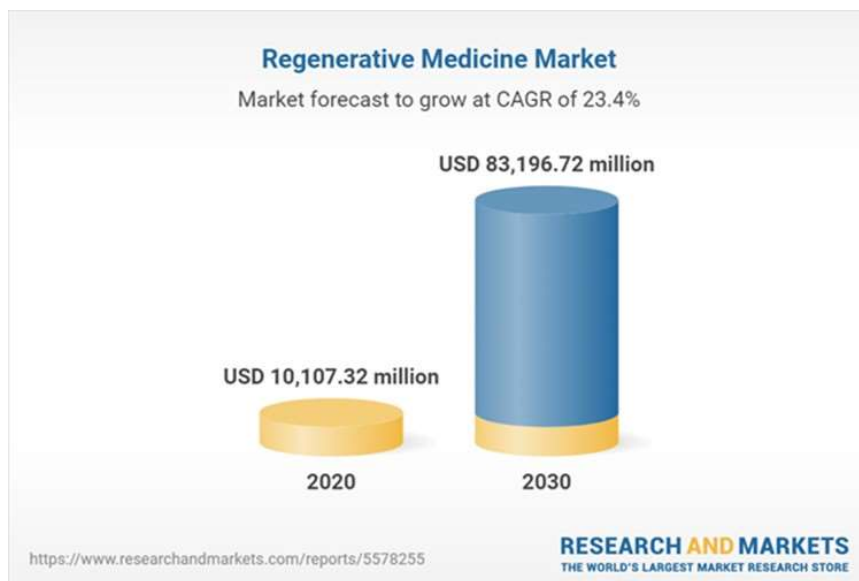
Broad Therapeutic potential in Regenerative Medicine

Conditions linked to overshooting or chronic inflammatory conditions and fibrosis

- Acute Lung Inflammation
- Lung Fibrosis
- Liver Fibrosis
- Heart fibrosis
- Kidney Fibrosis
- Brain and Peripheral Nerve Injury
- CNS Inflammation and Neurodegeneration

Li M, Fang F, Sun M, Zhang Y, Hu M, Zhang J. Extracellular vesicles as bioactive nanotherapeutics: An emerging paradigm for regenerative medicine. *Theranostics*. 2022 Jun 21;12(11):4879-4903. doi: 10.7150/thno.72812. PMID:35836815; PMCID: PMC9274746.

Market Potential for EV-based Therapies



EV market size 2022-2032 Trend Analysis Report

2022: USD 0.25 billion

2032: USD 3.2 billion (CAGR 29.7%)

Thereof ca. 50% diagnostics (Driver: Cancer)

USD 150 million in 2022 for therapeutics

Ca. 55% of Global Market in US

It is expected that EV-based therapeutics may capture a very significant portion of the projected Regenerative Medicine Market

Update Nov 2023:

2022 ... USD 12.2 billion (actuals)

2027 ... USD 40.6 billion (projected, CAGR 27.2%)

[Regenerative Medicine Market Size, Share, Trends and Revenue Forecast \[Latest\] \(marketsandmarkets.com\)](https://marketsandmarkets.com)

[Exosomes Market Size & Share – Trends Analysis Report, 2032 \(gminsights.com\)](https://gminsights.com)

Current Main Issues for EV-based Therapeutics

Topic	Current Issues
Cell Lines	<ul style="list-style-type: none">• Mostly primary cells are used for EV production• Donor-to-donor variability• Variable quality of cells and cell products
Manufacturing	<ul style="list-style-type: none">• Scaling difficulties• Variable process performance• Inconsistent quality between batches• Isolation and purification technology (DSP) still underdeveloped
Potency	<ul style="list-style-type: none">• Robust potency assays or• a surrogate assay for clinical efficacy are often missing
Analytics	<ul style="list-style-type: none">• EV are complex entities• Present in heterogenous mixtures• Unclear composition function relationship

Key Issues

Batch-to-batch
variability

Scalability and supply
issues

Prohibitive Cost of
Manufacturing


Phoenestra Provides Solutions for Current Issues - Introducing EVscale™




Topics	Value Proposition of EVscale™
Stable Cell Lines (MSC/TERT*)	<ul style="list-style-type: none"> • Consistent growth profile • Tiered Cell Banking Concept (Master Cell Bank (MCB)/Working Cell Bank (WCB) instead of donor variability • Fully documented (GMP-ready)
Scalable and Consistent Manufacturing	<ul style="list-style-type: none"> • Continuous manufacturing for high productivity • Consistent EV composition and quality • Scalable and easy to transfer into the GMP environment • GMP manufacturing services (from 2024)
Bioassays / Potency*	<ul style="list-style-type: none"> • Many relevant biological functionalities are covered • Link to (pre-)clinical translation
Extended Characterization*/**	<ul style="list-style-type: none"> • Linking RNA profiles and protein, lipid composition to biological functionalities • Composition-function relationships
Biomarker Development **	<ul style="list-style-type: none"> • Supportive tools and data for product development and clinical development

With **EVscale™**, Phoenestra provides a leading end-to-end approach for **cell-derived EV product candidates** which opens ample opportunities for a 'pipeline from a Technology Platform'

- Batch-to-batch consistency
- Scalability
- Leading Cost of Manufacturing

*in collaboration with  **GO EVERCYTE**
forever is just enough.

in collaboration with  **TAMIRNA
stability for life.

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EVscale™ from Different Telomerized MSC Lines

End-to-end Approach



Cryovial

Seed train

MSC/TERT from different human tissues (see below)
Fully documented and characterized
Tiered cell banking possible
GMP-ready

Bioreactor-based expansion**

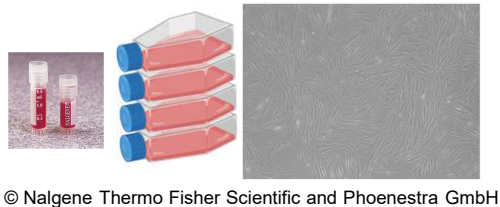
Fully controlled bioreactor-based cultivation
Consistent EV quality
Tunable biological functionalities
Productive and scalable
Fast translation into GMP

Downstream processing

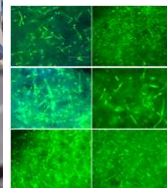
Gentle membrane methods (TFF)
Chromatographic separation
Scalable and GMP-ready unit operations

EV characterization

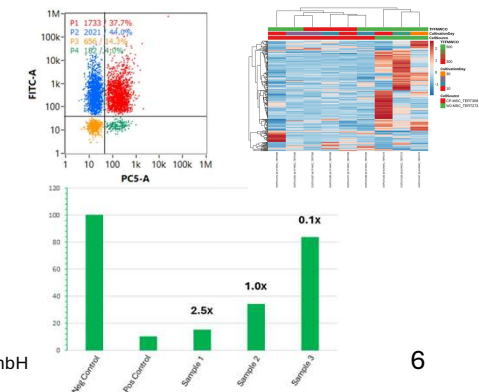
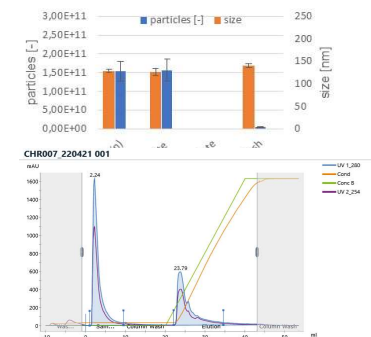
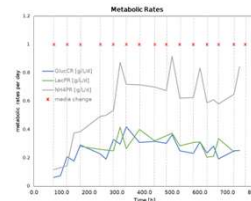
Standard methods
NanoFCM
RNA sequencing
Potency assays
Composition-function relationships



**Patent pending



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MSC/TERT lines licensed from Evercyte GmbH
EV characterization in collaboration with Evercyte and TamiRNA GmbH



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The Proprietary EVscale™ Cultivation Platform



Patent Pending

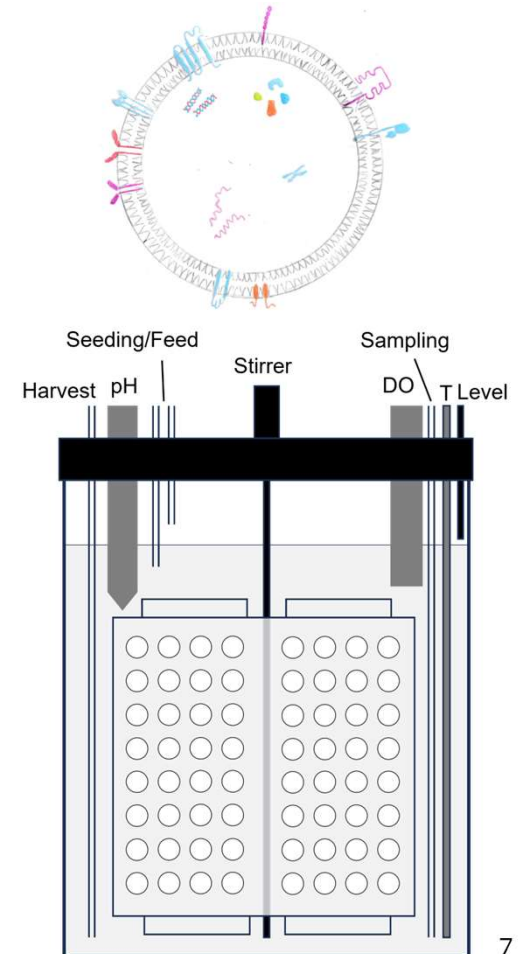


Main Design Features

- Simple, scalable
- Sanitary, easy to clean
- Bioreactor brand agnostic
- Adherent cells are within a well perfused basket system
- May be used with a wide range of cell carriers

Key Performance Data for MSC/TERT in a 250 mL DASbox bioreactor unit (Eppendorf AG)

- High specific surface area
- High cell densities even for difficult-to-grow cells, such as MSC/TERT from different tissues
- High volumetric productivity feasible

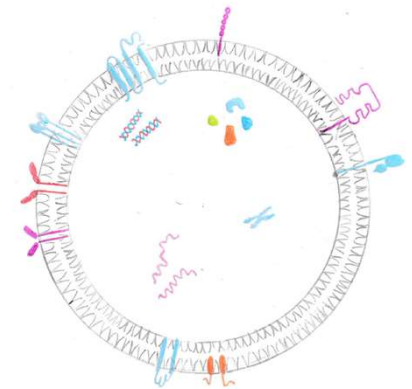


Phoenestra is the Best Partner for Your EV Project



EVscale™ - One-stop shop and End-to-end approach for Extracellular Vesicles from MSC

- Broad range of fully characterized and documented MSC lines from different donors/tissues
 - Bone Marrow, Adipose tissue, Wharton´s Jelly, Placenta, Chorionic Plate, Reflected Amnion, Endometrial or
 - Custom-made
- Scalable platform process for straight forward process development
- Different Downstream processing options available
- In-depth analytical characterization methods are well established
- Including functional bioassays for process and product analysis and definition
- GMP cell banking and processing (from Q4 2024)
- Experienced project management – single face to the customer



Get in touch and let's talk about your needs!



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