ASX ANNOUNCEMENT & MEDIA RELEASE

EXOPHARM TO PRESENT AT KEY EXOSOME INDUSTRY EVENT

11 November 2020

Melbourne, Australia: Australian exosome medicine company Exopharm Limited (ASX: EX1) announces that Chief Commercial Officer, Dr Chris Baldwin, will present to the *Exosome Based Therapeutic Development Digital Summit* on 11 November (9:00 AM US Eastern Time, 1.00 AM AEDT), the first day of the two-day event.

Dr Baldwin's presentation entitled "*Producing EVs at the Clinical Scale*" (see attached) will cover its current PLEXOVAL II study. PLEXOVAL II is Exopharm's world-first Phase I study using a cell-free, allogeneic (unmatched) platelet-derived exosome product, called Plexaris™. The presentation also highlights Exopharm's proprietary Ligand-based Exosome Affinity Purification (LEAP™) technology.

The PLEXOVAL II study is testing Plexaris for safety and benefits in wound healing. This is Exopharm's second human clinical trial using extracellular vesicles (EVs) isolated from human platelets and further highlights Exopharm's leadership position in the exosome therapeutics field. PLEXOVAL II is on track to complete by the end of 2020: Exopharm is the first company to initiate first exosome dosing in two separate human trials.

The Exosome TX event, subtitled "*Advancing and Scaling Exosome-Based Products into a Reality*", is the key international industry-dedicated exosome meeting. The focus of the meeting is clinical and commercial advancements, manufacturing, mechanisms of action, clinical progress partnerships and regulation.

Dr Baldwin's presentation is in a prime slot on the first day of Exosome TX. Partnering and other discussions are part of the Summit.

A copy of Dr Baldwin's PowerPoint presentation is attached.

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ABOUT EXOPHARM

Exopharm Limited (ASX:EX1) is a clinical-stage Australian exosome medicine company developing naive exosome products for regenerative medicine and engineered exosomes for new precision medicines.

Exosomes (or EVs) are small particles naturally produced by cells, which deliver therapeutic 'cargoes' to other cells to reduce inflammation and promote regeneration. EVs are plentiful in our youth but decline with age. Recent research points to naïve EV medicines as a way to extend the number of healthy, functional years. EVs secreted by stem cells could be used instead of stem-cell therapy with equal or greater benefit, without the problems associate with stem-cell therapies.

Engineered EVs (EEVs) are the most significant emerging technology for precision medicine. By altering proteins on the surface of EVs and adding custom cargoes such as RNA and small molecules, EEVs hold promise in a variety of untreatable diseases. This promise has led to a number of major development deals within the small community of EEV capable companies such as Exopharm.

While trillions of EVs are produced by stem cells, the technology has been hampered by the challenge of purifying EVs into drug products. Exopharm owns a purification technology called Ligand-based Exosome Affinity Purification (LEAP). LEAP technology and associated know-how places Exopharm at the forefront of this emerging field worldwide. Exopharm is at clinical stage with pending and current trials for wound healing, hearing loss and osteoporosis.

FORWARD LOOKING STATEMENTS

This announcement contains forward-looking statements which incorporate an element of uncertainty or risk, such as 'intends', 'may', 'could', 'believes', 'estimates', 'targets', 'aims', 'plans' or 'expects'. These statements are based on an evaluation of current corporate estimates, economic and operating conditions, as well as assumptions regarding future events. These events are, as at the date of this announcement, expected to take place, but there cannot be any guarantee that such events will occur as anticipated or at all given that many of the events are outside of Exopharm's control or subject to the success of the Development Program. Furthermore, the Company is subject to several risks as disclosed in the Prospectus dated 6 November 2018.

INHERENT RISKS OF INVESTMENT IN BIOTECHNOLOGY COMPANIES

There are a number of inherent risks associated with the development of biopharmaceutical products to a marketable stage. The lengthy clinical trial process is designed to assess the safety and efficacy of a drug prior to commercialisation and a significant proportion of drugs fail one or both of these criteria. Other risks include uncertainty of patent protection and proprietary rights, whether patent applications and issued patents will offer adequate protection to enable product development, the obtaining of necessary drug regulatory authority approvals and difficulties caused by the rapid advancements in technology. Companies such as Exopharm are dependent on the success of their research and development projects and on the ability to attract funding to support these activities. Investment in research and development projects cannot be assessed on the same fundamentals as trading and manufacturing enterprises. Therefore, investment in companies specialising in drug development must be regarded as highly speculative. Exopharm strongly recommends that professional investment advice be sought prior to such investments.

Producing EVs at the Clinical Scale

Exosome TX Conference 11 November 2020

Chris Baldwin, PhD
Chief Commercial Officer

IMPORTANT INFORMATION

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Exopharm Ltd – Summary

An “exosome first” clinical-stage biotech entirely focused on building a complete platform for producing EV medicines

39 staff (50% PhD)
in Melbourne, Australia

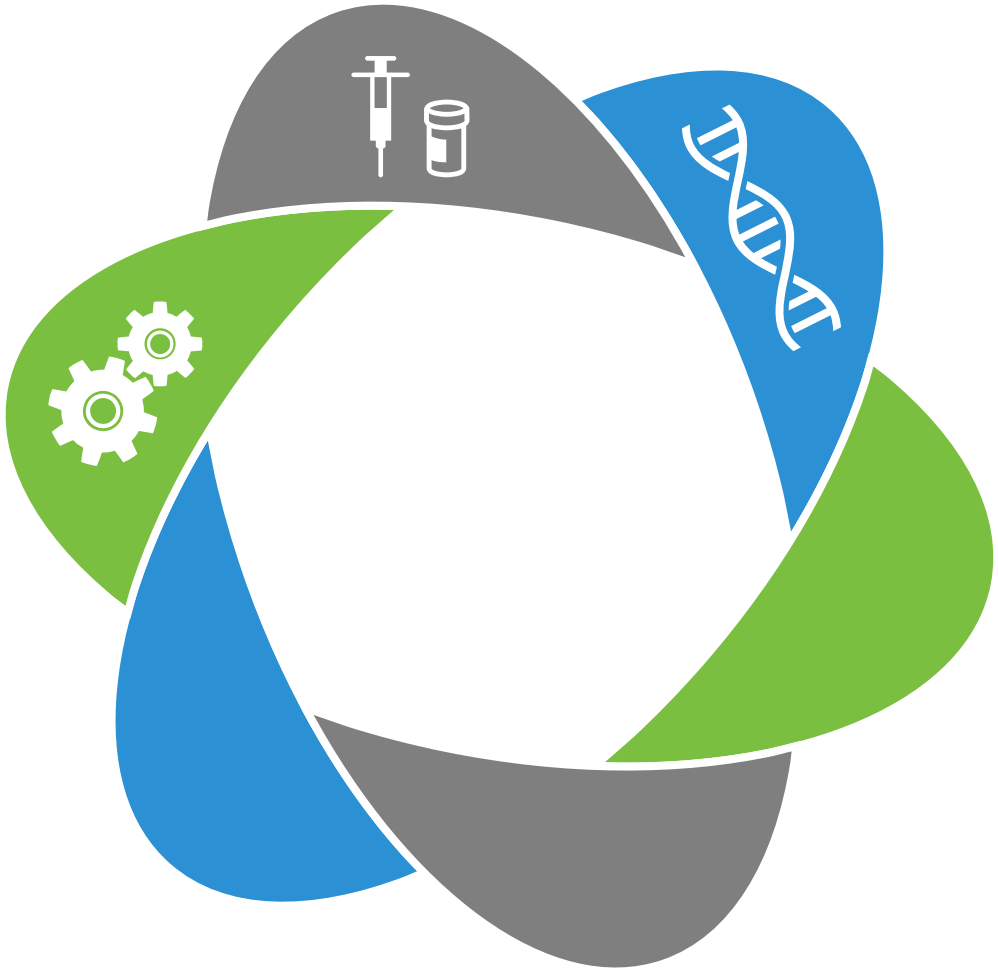
Publicly-traded on the ASX (ASX:EX1) (listed Dec 2018)

Three Interconnecting Programs

1 **Technology** – Designing economical, scalable, and consistent processes for EV medicines **from Day 1**

2 **Naïve EVs** – Producing EVs from existing cell types (platelets, MSCs) for repair and regeneration

3 **Engineered EVs** – Customized EVs for delivering precision medicines for untreatable diseases



Manufacturing Program: Key Assets

LEAP

Purification of EVs at Scale


(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)
(19) World Intellectual Property Organization
International Bureau
(43) International Publication Date
26 December 2019 (26.12.2019)
WIPO | PCT
(10) International Publication Number
WO 2019/241836 A1

- Developed internally
- Comprehensive application to EVs
- Family of resins and potential resins await development

LOAD

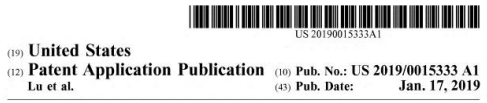
Addition of nucleic acids to EV Payloads


(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)
(19) World Intellectual Property Organization
International Bureau
(43) International Publication Date
15 November 2018 (15.11.2018)
WIPO | PCT
(10) International Publication Number
WO 2018/209182 A3

- Global, exclusive in-licensing agreement (2020)
- Comprehensive application for Engineered EVs

EVPS

Addition of proteins to EV Surfaces


US 20190015333A1
(19) United States
(12) Patent Application Publication
Lu et al.
(10) Pub. No.: US 2019/0015333 A1
(43) Pub. Date: Jan. 17, 2019

- Global, exclusive in-licensing agreement (2020)
- Comprehensive application for Engineered EVs

Starting with the End in Mind

Founding Vision	Requirements
EV medicines become a major modality for delivering precision and regenerative medicines	• **Uniquely efficacious** • **Safe** • **Economical** • **Scalable**

Typical Product Approach
- Identify the indication
- Determine efficacy
- Develop product capabilities
- *Solve the engineering later*

Exopharm's Process First Approach
- Learn from the experience of stem cell companies
- Create **general, scalable, economical** process first
- Process must scale all the way from the lab bench to product manufacturing
- *Select therapeutic applications later*

Presentation Overview

Company at a Glance

LEAP Purification

Reaching the Clinical Scale

Closing Comments

Bench (< 1L) to Production Scale (1,000L+) Process Design Requirements

Technology	Mode Of Separation	Generality	Cost	Scalable
UC	DENSITY			**No**
PEG + UC	DENSITY, SOLUBILITY			**No**
SEC	SIZE			**No**
TFF/Filtration	SIZE			
Ion Exchange	ELECTROSTATIC			
Immunoaffinity	AFFINITY	**No**	**HIGH**	

TFF/Filtration

- **Necessary but not sufficient**
- Other contaminating particles within the size of interest (protein aggregates, cellular debris, etc)

Ion Exchange

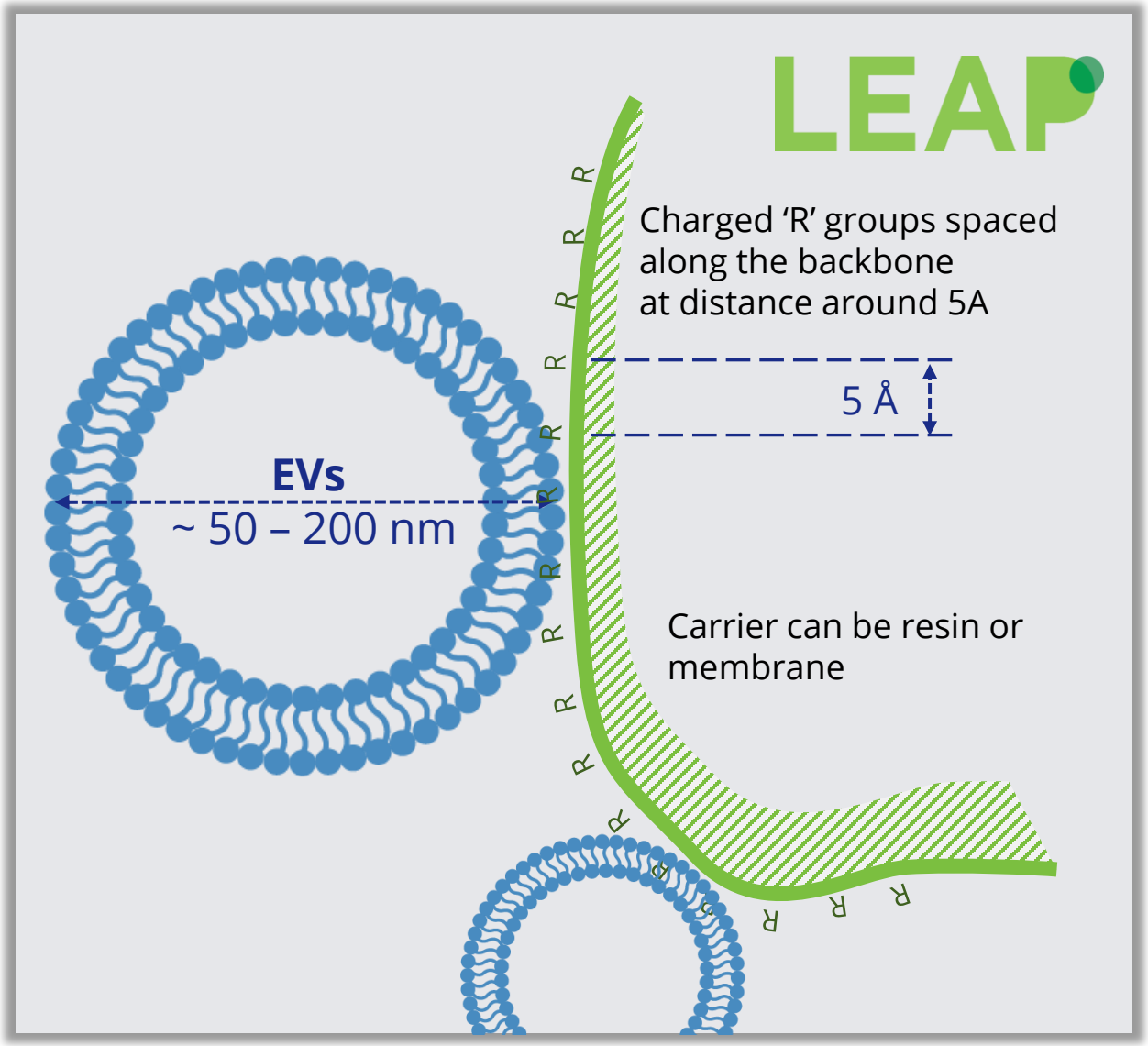
- Fully scalable technology
- **Variety of parameters available to explore**

LEAP – *Cation* Exchange Process

Discovery (2016)

Although EVs have a **net** negative surface charge, **local positive surface charges allow for EVs to be reversibly bound** using cation exchangers with unique ligand geometries

This discovery applies to an entire class of ion exchangers, including some commercially available resins

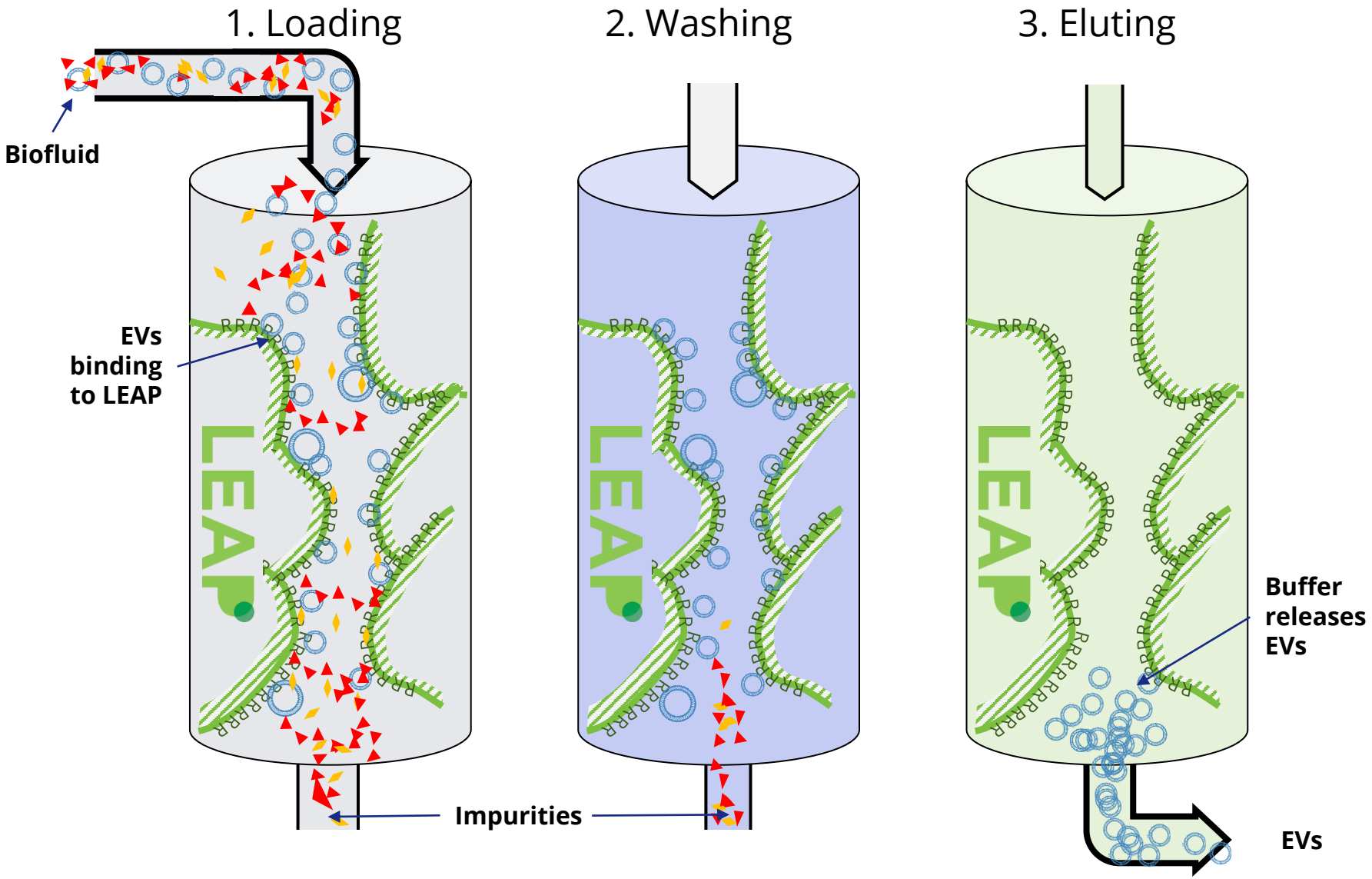


LEAP In Action: 1 – 2 – 3

1. **Loading** – Biofluid is added to LEAP affinity chromatography column
   - EVs bind to the LEAP matrix
   - Most impurities fail to bind to the LEAP matrix and pass through
2. **Washing** – EVs are retained while residual impurities are washed out
3. **Eluting** – Simple buffer releases EV binding from LEAP ligand

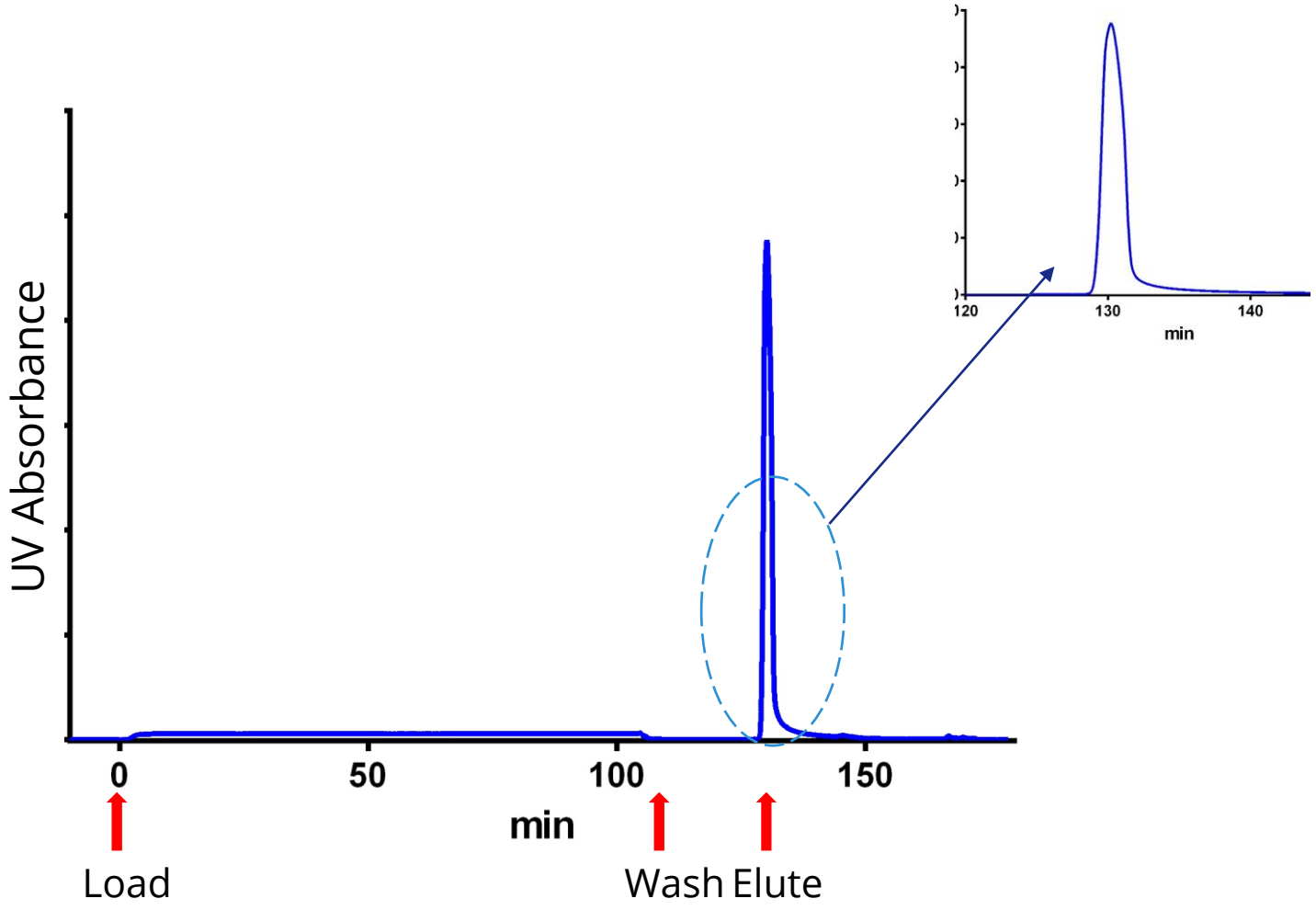
- EVs are now ready for formulation

Column is re-sterilized and prepared for next batch



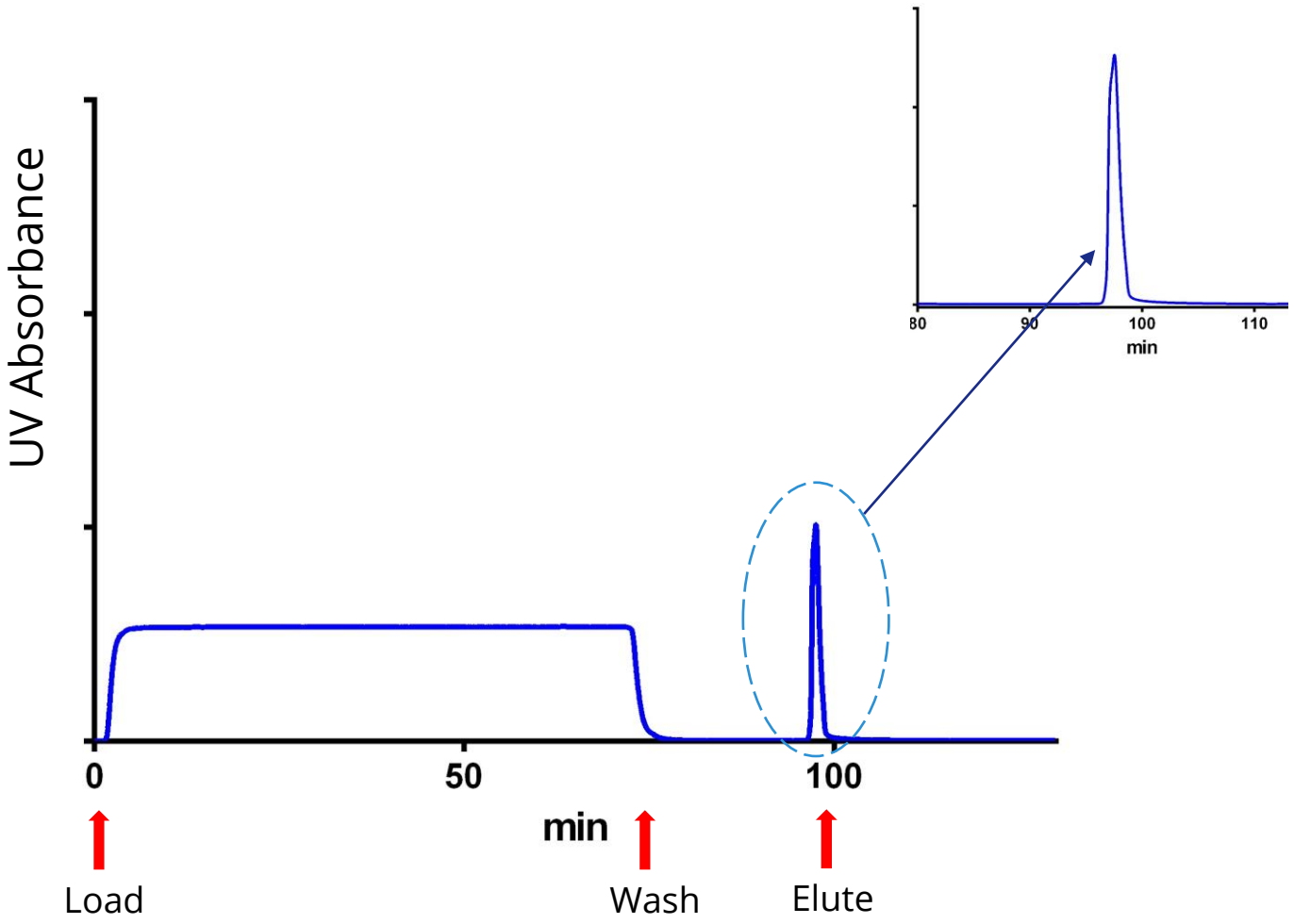
Not to scale

LEAP Process Monitoring (Platelet-EVs)



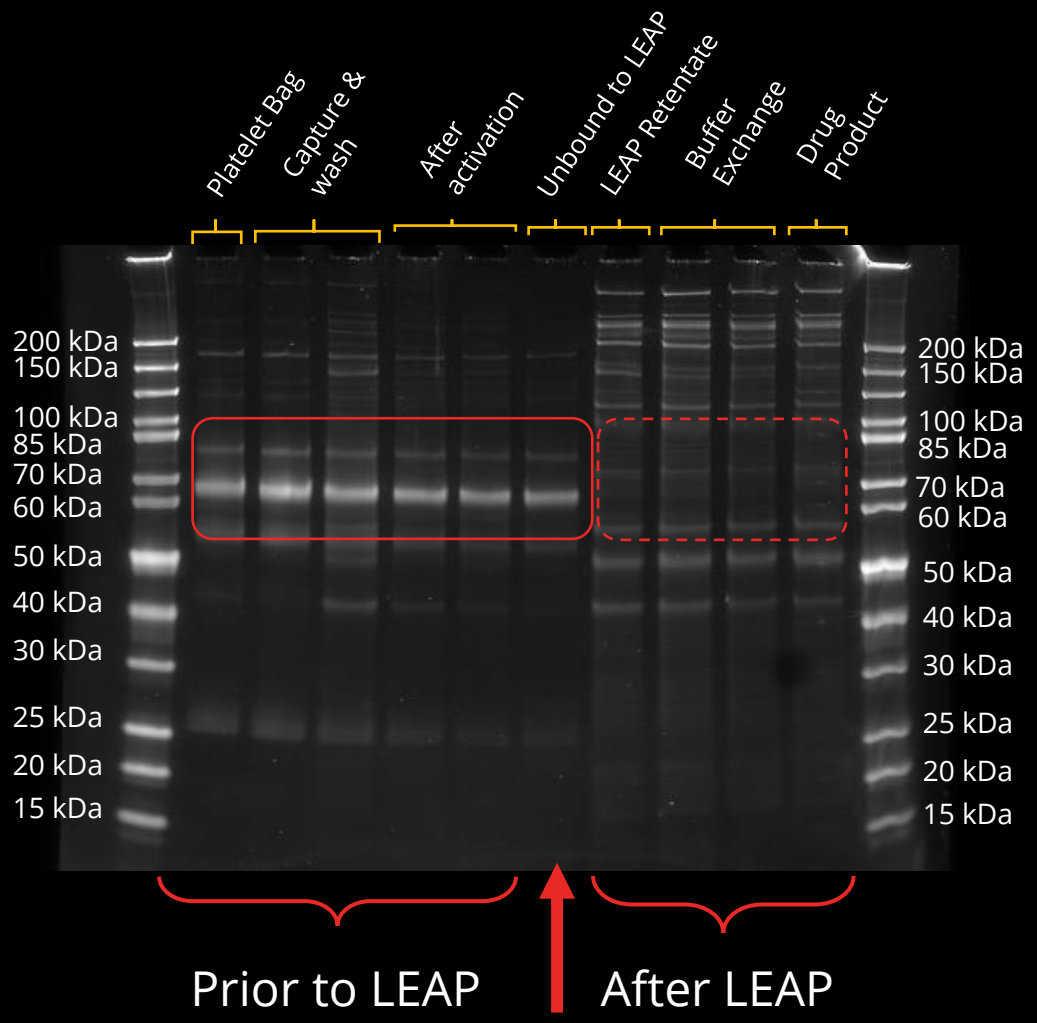
- LEAP columns can be sanitized and reused
- Concentration factor ~ 70x

LEAP Process Monitoring (MSC-EVs)



- Starting cultured media more dilute than platelets
- Concentration factor ~ 100x
- So far, all EV-containing biofluids can be separated via LEAP

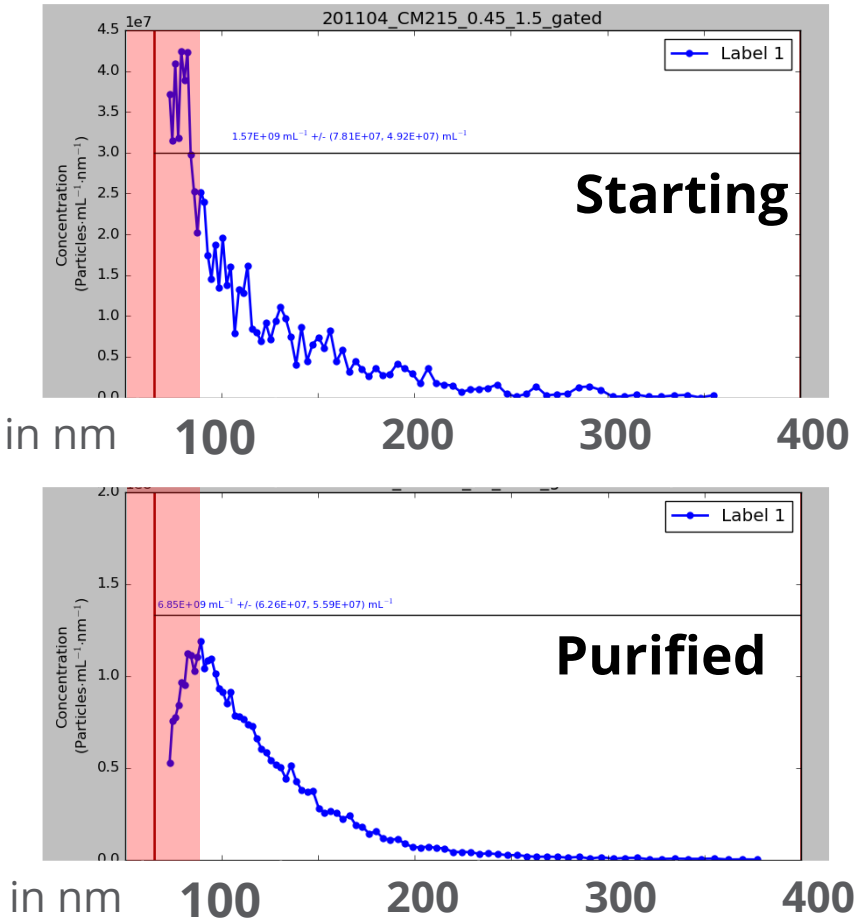
Protein Elimination (PLT-EVs)



- SDS-PAGE performed on equal protein load at every step
- Major contaminating proteins virtually eliminated
- Similar results for all tested biofluids

Particle Counting Challenge: Mistaking Purification for Efficiency

Particle Size Distribution



Total particle retention ~ 40 – 70%, depending on biofluid

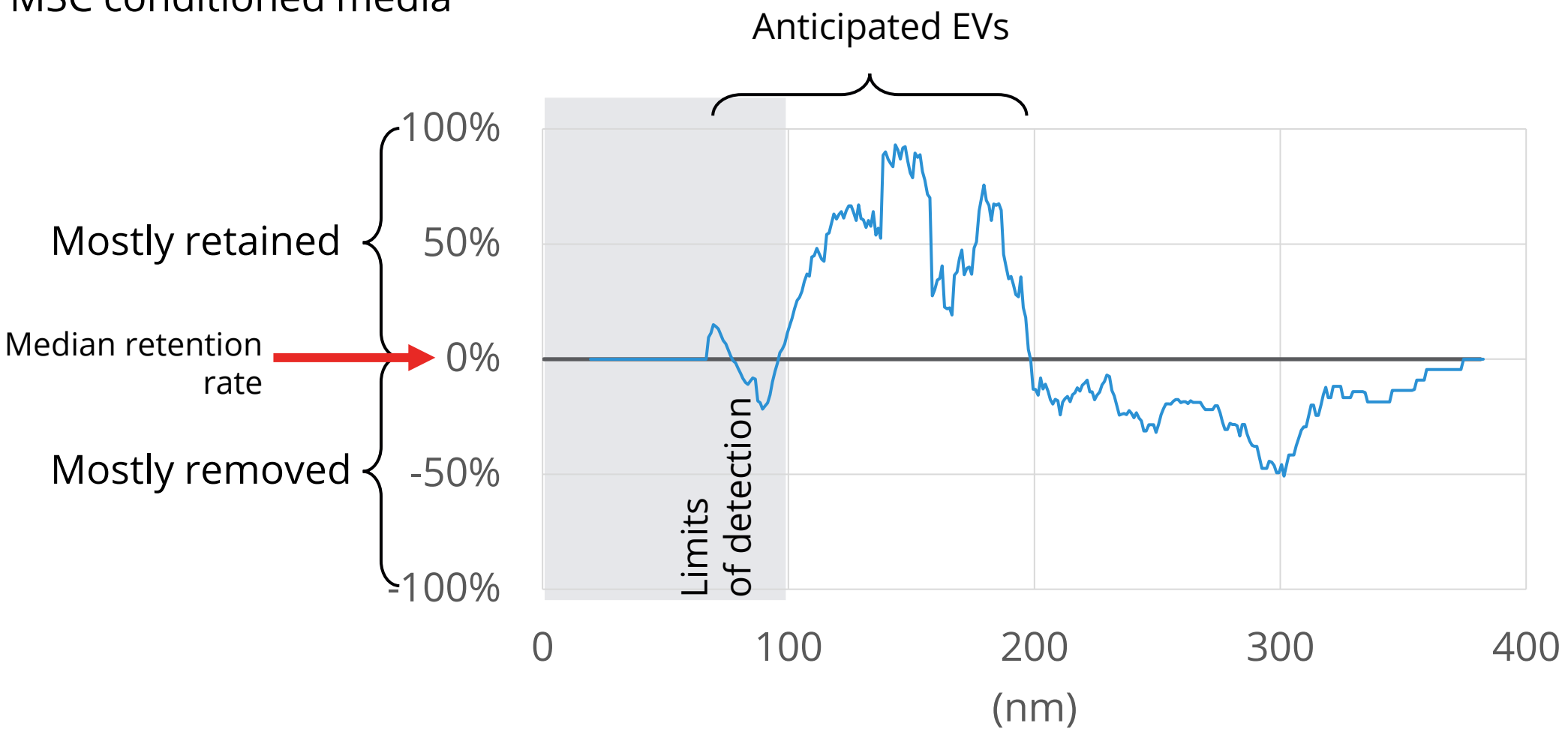
But particles include:

- Protein aggregates
- Cellular debris
- HDLs/LDLs, etc

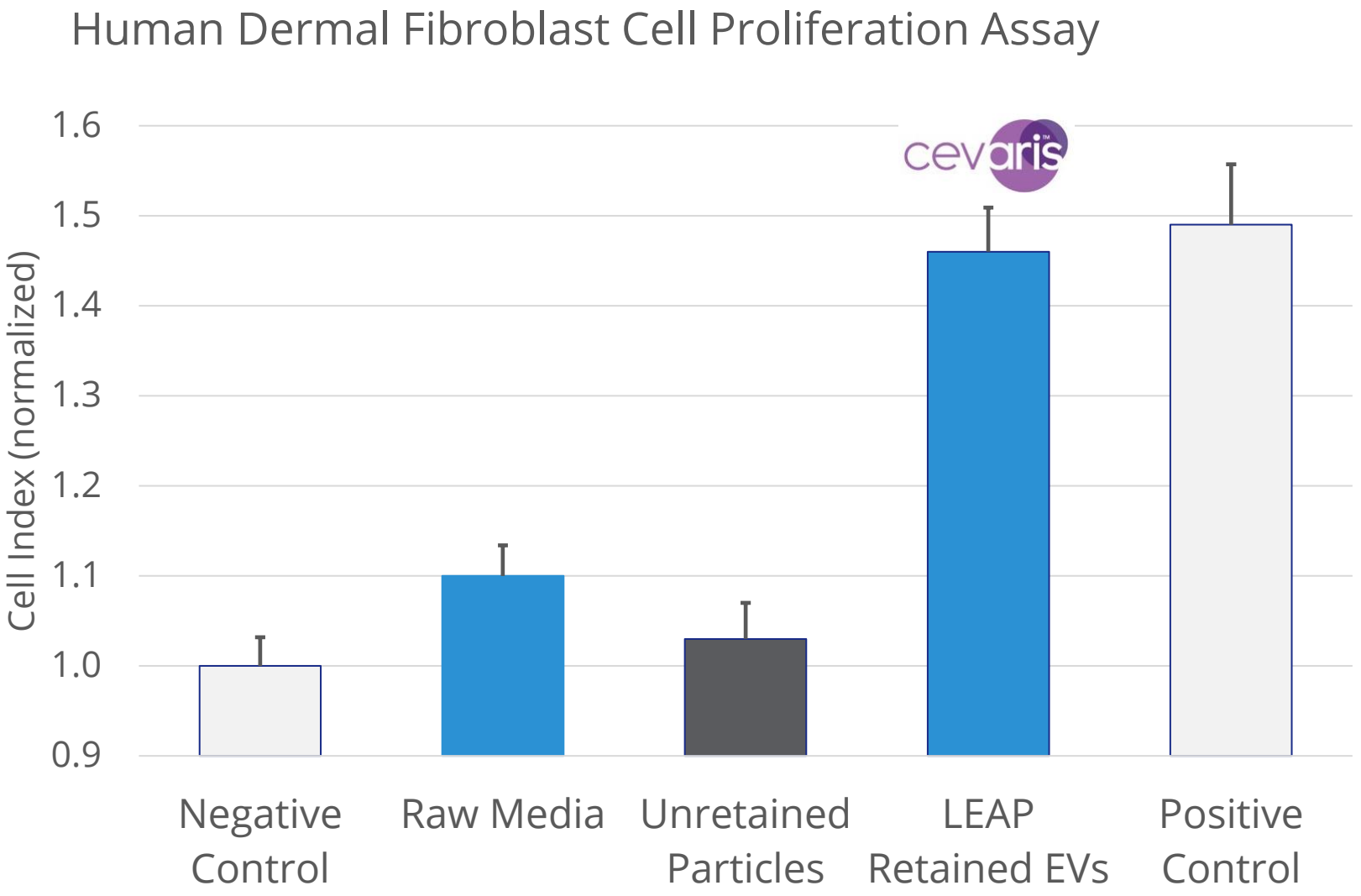
So did LEAP keep the EVs?!?!

Particle Counting: Capture vs Purification

Particle retention as a function of size
MSC conditioned media



LEAP Captures Active Particles



LEAP-captured EVs demonstrate higher activity than raw media

Non-retained particles activity not distinguishable from negative control

LEAP is purifying active particles from inactive ones

LEAP EVs from Various Sources Meet MISEV Definition

A) Particles detected by MRPS were 65 to 250nm in size. Thus, EVs isolated by LEAP are a heterogenous population containing small, medium and large EVs

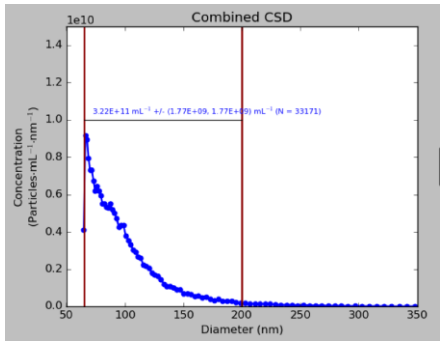
B) Morphology was as expected with vesicles being spherical in shape with a distinct lipid bilayer and proteins embedded on the surface indicating that EVs were intact post-purification

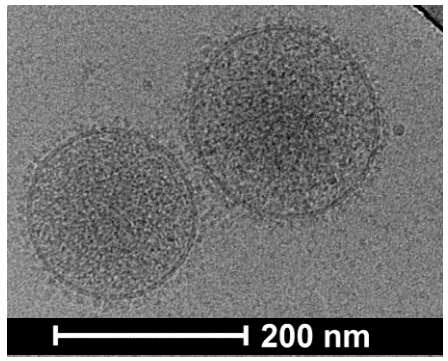
C) Positive for the presence of markers found characteristically within EVs

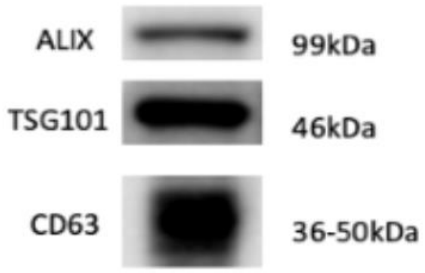
MISEV 2018 guidelines*

* Théry et al. 2018

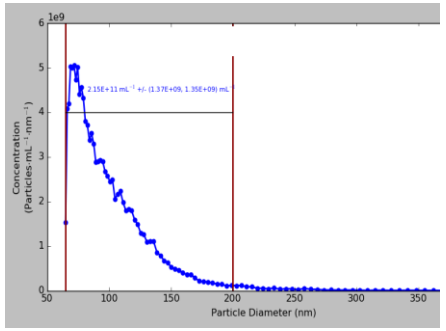
PLT-EVs

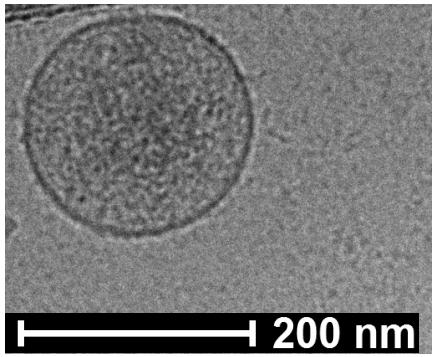


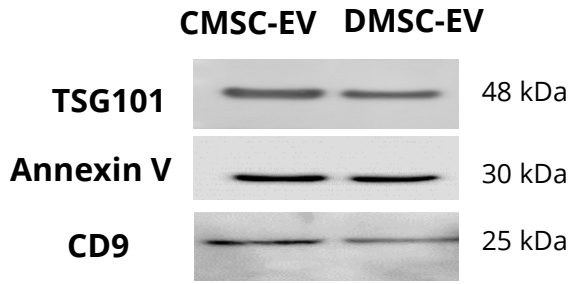




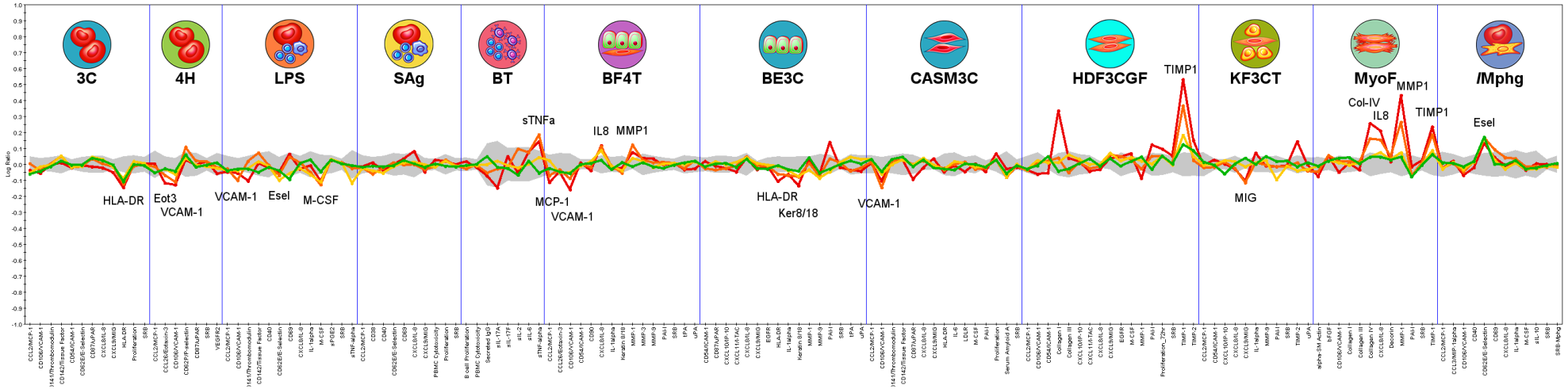
MSC-EVs







Cevaris Strongly Associated with Immunomodulation, Tissue Remodelling



- Cevaris contains numerous factors that have been associated with immunomodulatory activities. Cevaris was not cytotoxic and did not cause antiproliferative effects at the concentrations tested
- The BioMAP assay demonstrated Cevaris was active in modulating multiple types of protein biomarkers including cytokines, chemokines, cell adhesion molecules, MHC class II receptors, extracellular proteins, proteases and inhibitors associated with inflammatory, immunomodulatory and tissue remodelling activities

Presentation Overview

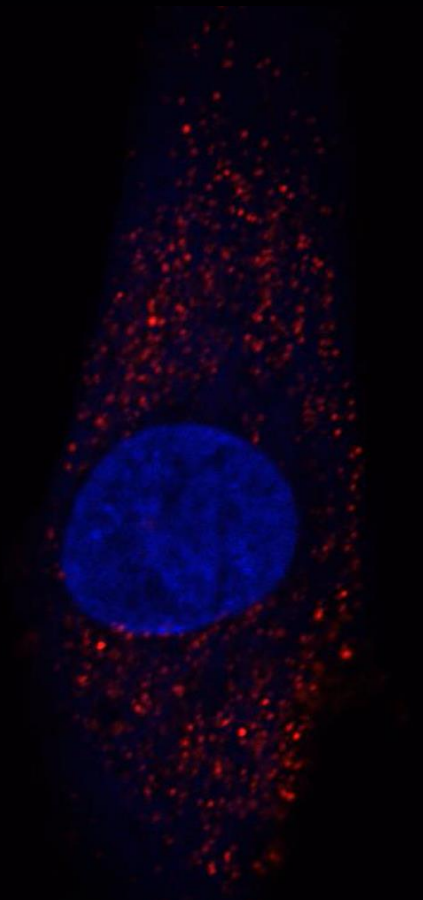
Company at a Glance

LEAP Purification

Reaching the Clinical Scale

Closing Comments

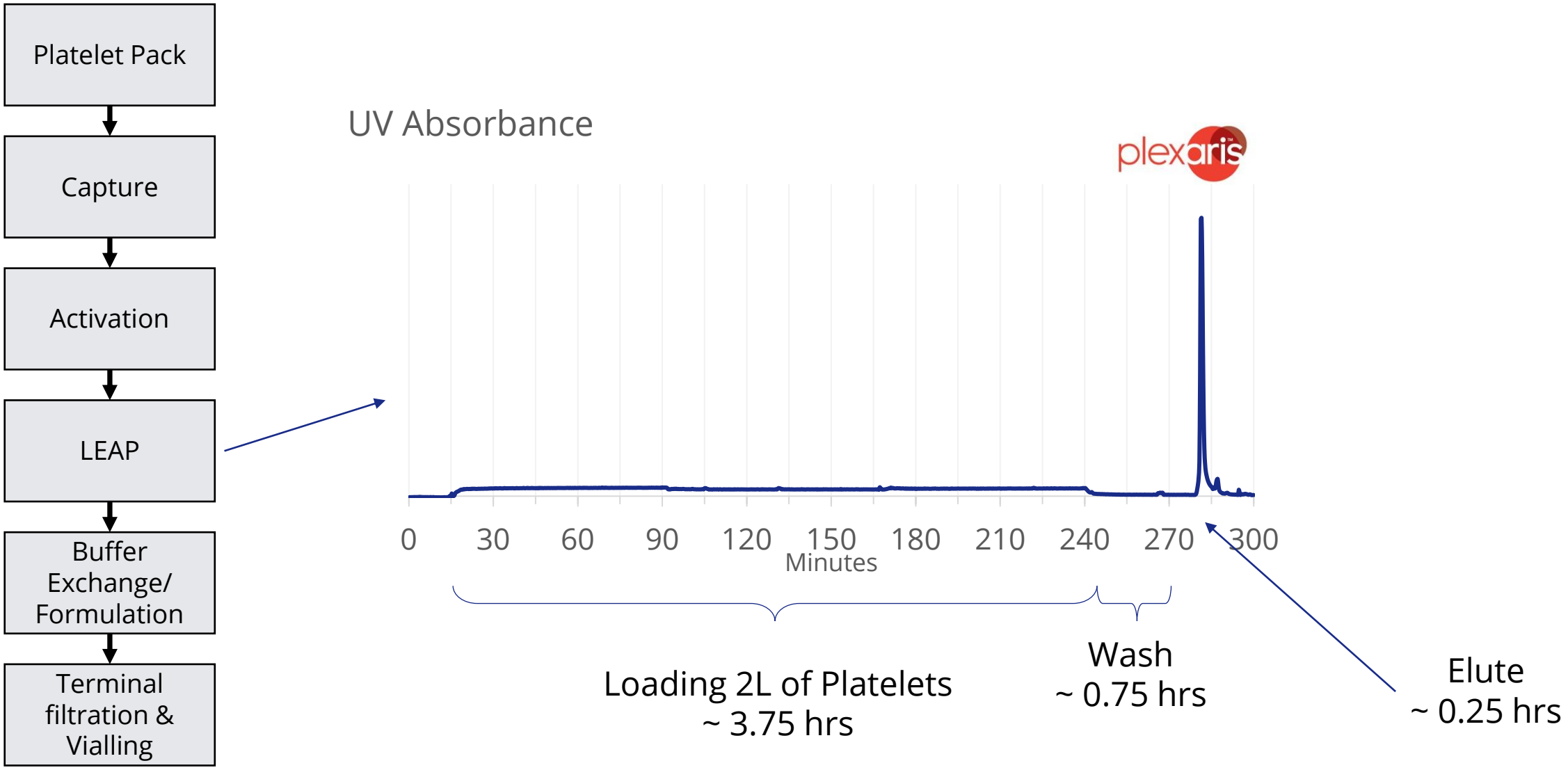
PLEXOVAL II Study: Platelet EVs



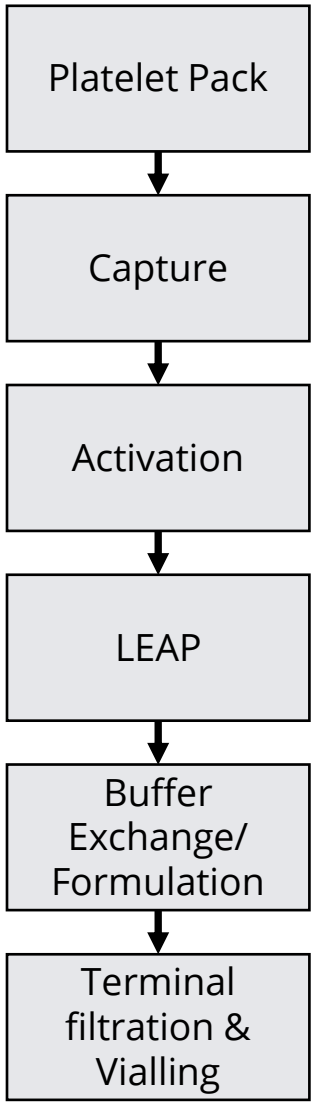
"A prospective, randomised, **double blind, placebo controlled**, single dose, single site **phase I study to assess the safety and biological activity** of a Human non-autologous platelet derived **extracellular vesicle therapy** vs placebo on **wound healing** rate following skin punch biopsy in healthy volunteer adults" (Trial registration number CT-2020-CTN-01678-1)

Target final dosing by Dec 2020

LEAP: Standard Chromatography



Phase II/III Manufacturing Process



<u>Given the Phase I Study (PLEXOVAL II) …</u>

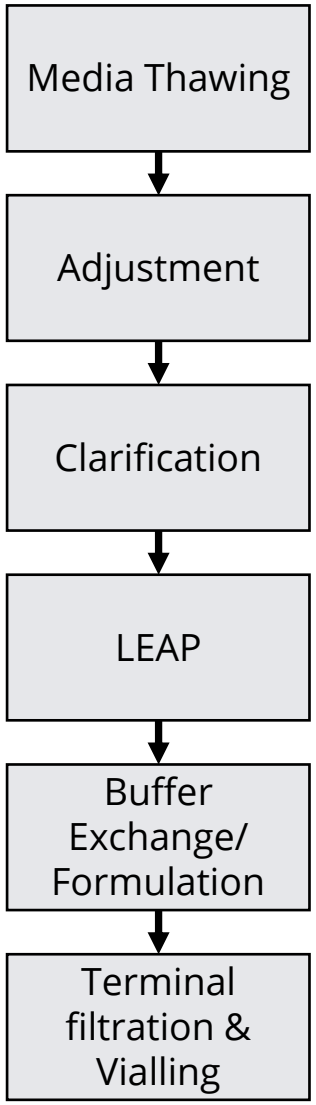
- 2 L platelets (8 packs)
- 2 operators, 8 hr from LEAP to final product
- 40 doses of Plexaris product

<u>Then …</u>

- Producing 400 doses would require bigger equipment, but ***only the vial filling would require more labor***

- Producing 4,000 doses would require bigger equipment, **and the vial filling would be automated**

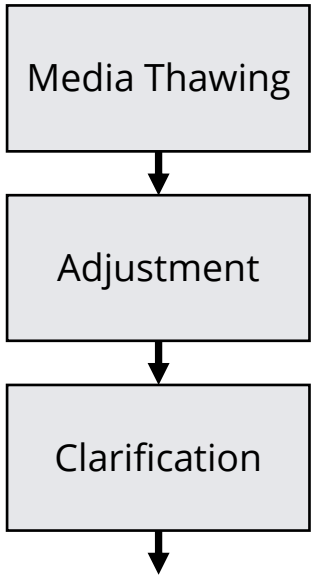
LEAP Manufacturing Process (400L)



Future Clinical Study

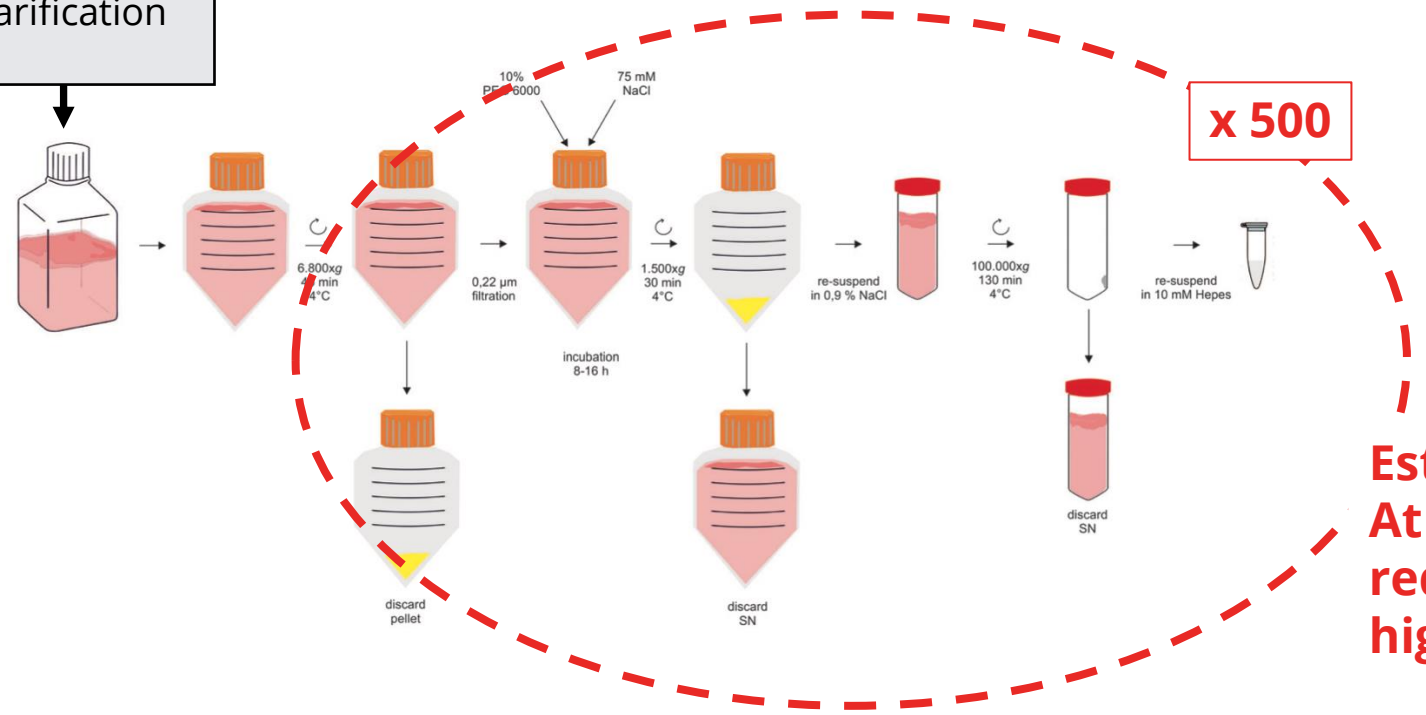
- 400 L of conditional media
- 2 operators, 8 hr from LEAP to final product

PEG/UC Manufacturing Process (400L)



Börger, V., Staubach, S., Dittrich, R., Stambouli, O., & Giebel, B. (2020). Scaled isolation of mesenchymal stem/stromal cell-derived extracellular vesicles
Current Protocols in Stem Cell Biology, *55*, e128. doi: 10.1002/cpsc.128

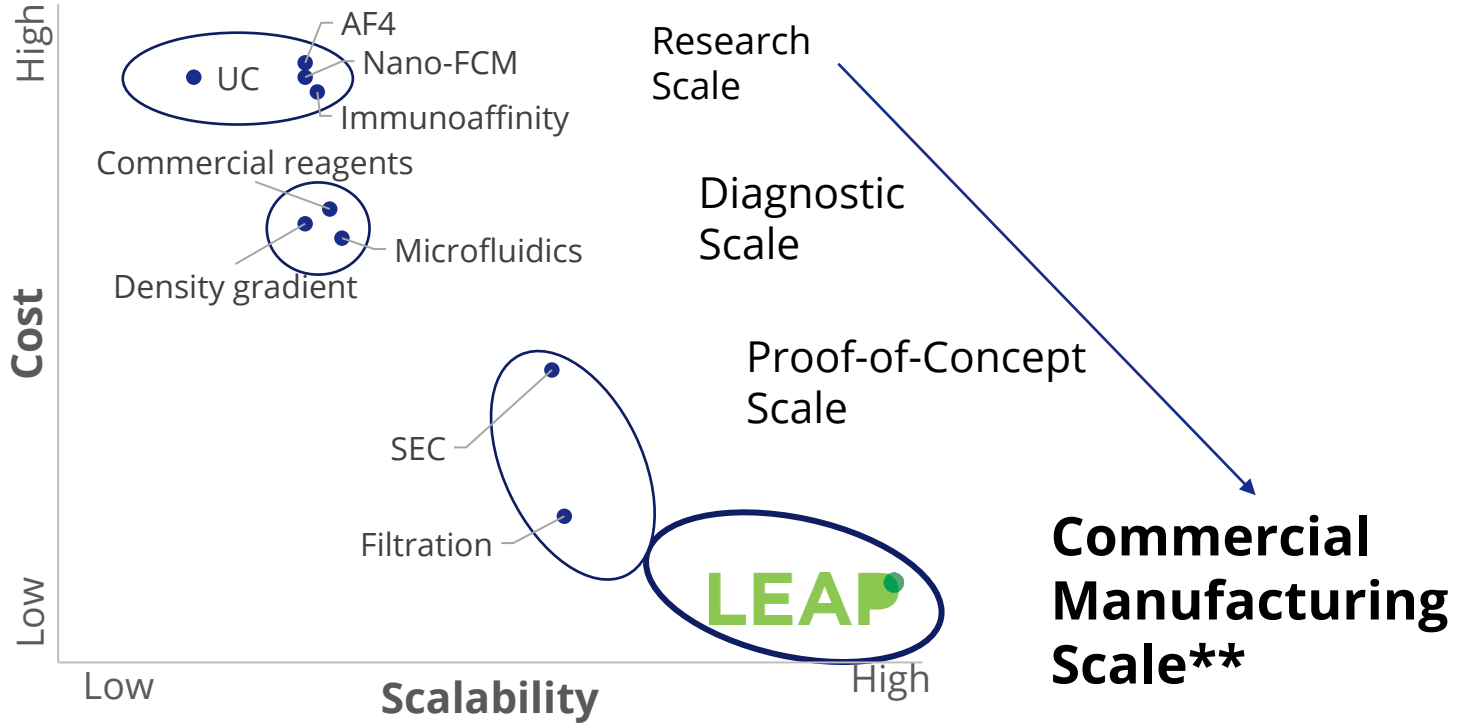
4L media using PEG/UC



Estimate:
At 400L, the labour requirement is >>100x higher than with LEAP

Commercial-scale EV Purification Technology

State of the Art, EV Purification as of June 2020*



Unlike all other alternatives, LEAP technology:

(i) is readily scaled over 1,000L,

(ii) uses industry-standard equipment and processes,

(iii) uses low-cost, reusable consumables (with validated sterilization process)

Technologies and Standardization in Research on Extracellular Vesicles

Srujan Gandham,[1,4] Xianyi Su,[2,4] Jacqueline Wood,[2,4] Angela L. Nocera,[1] Sarath Chandra Alli,[2,3] Lara Milane,[1] Alan Zimmerman,[2] Mansoor Amiji,[1] and Alexander R. Ivanov[2,*]

* Adapted from https://doi.org/10.1016/j.tibtech.2020.05.012

** LEAP assessment from Exopharm, based on industrial use to date; LEAP Patents processing through National phases at present

Presentation Overview

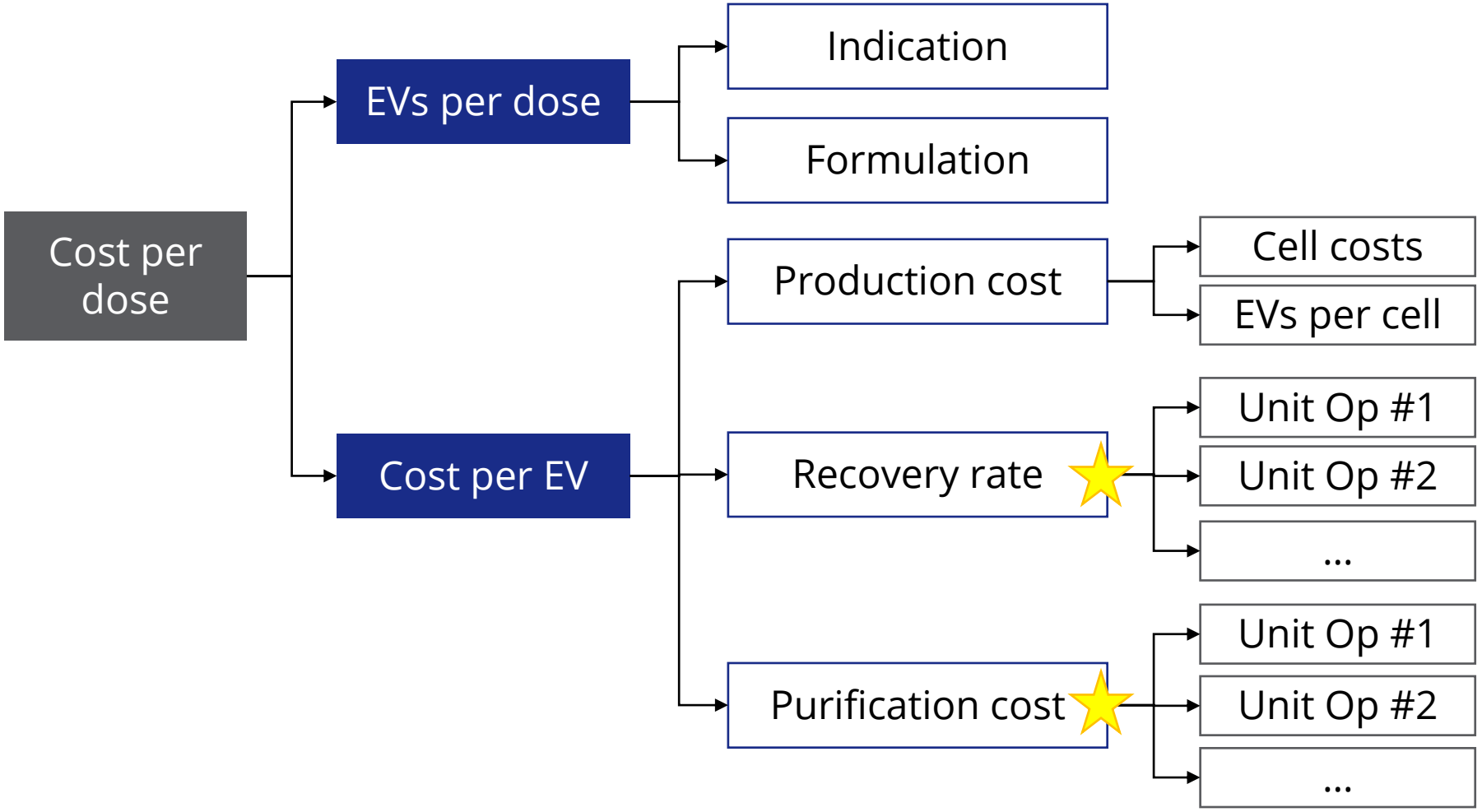
Company at a Glance

LEAP Purification

Reaching the Clinical Scale

Closing Comments

Observation 1: COGS Matters Most



Benefits of LEAP

- Fewer Unit Ops
- Reduction in purification cost
- Increase in recovery rate

Observation 1: COGS Targeting

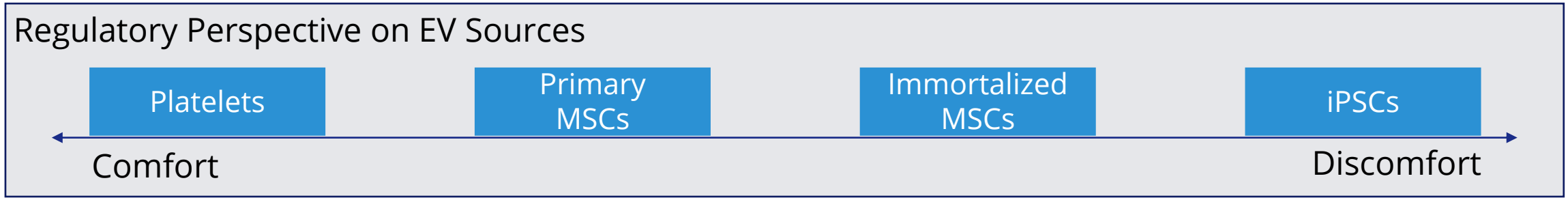
For emerging exosome TX applications, COGS is what will determine if we succeed with large indications or must focus on rare diseases.

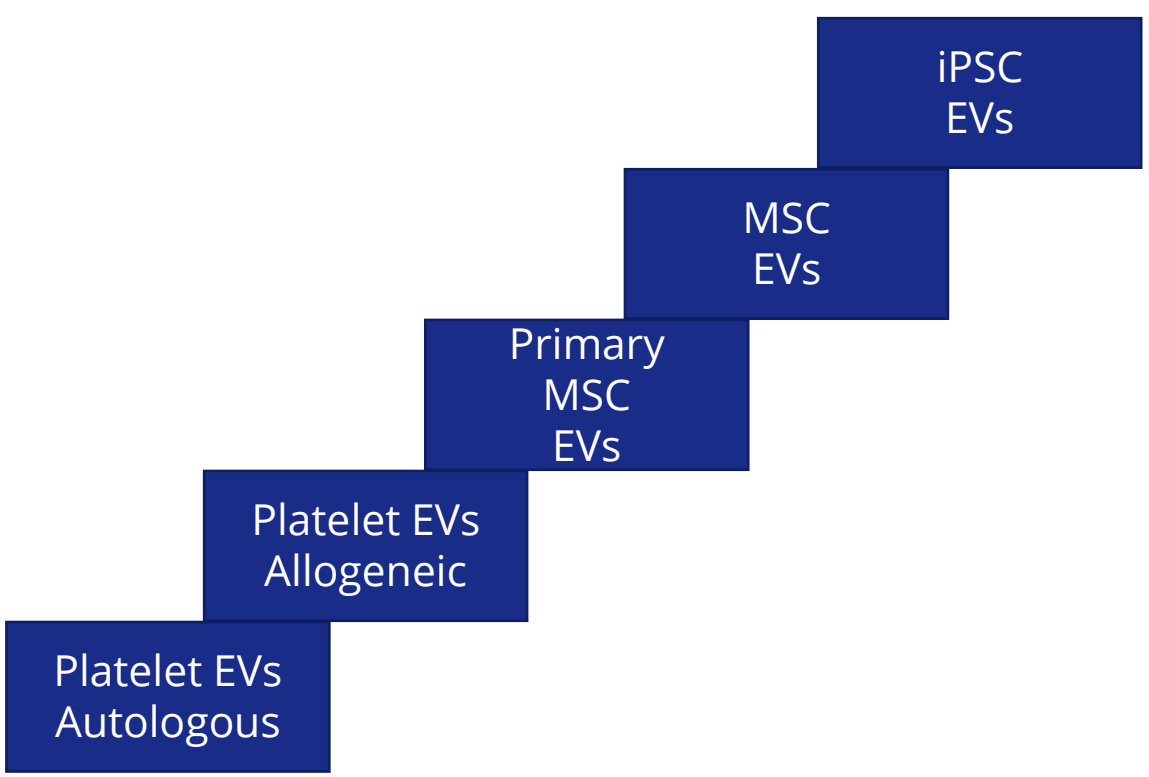
LEAP at bench scale (today) ~ $10 per billion EVs

- With further optimization → x 0.1
- With continuous harvest → x 0.5
- With recycled cell media → x 0.1
- With scale-up → x 0.2

Target: Less than $0.05 per billion EVs

Observation 2:
Scalable Processes Support Regulatory Progress





Step-wise progression to **regulatory acceptance** of EV medicines possible due to **consistent process**

Observation 2:
Scalable Processes Support Regulatory Progress

AKTA pure 25

Proof-of-
Concept Scale

Scale-up,
Clinical Trials

AKTA*ready*™

Commercial
Manufacture

AKTA*process*™

Observation 3: Winning Together

Production Team on Clinical Manufacture Day

Educating regulatory agencies step-wise is our collective responsibility

Exopharm believes that every successful Clinical Study for an EV medicine benefits the industry

Exopharm is eager to work with our peers:

- Creating an exosome TX industry body to promote safe, science-based advancement
- Collaborating to produce EV medicines efficiently at scale

Going Big, Together

Exopharm seeks partners to combine IP, know-how to make the most of an amazing opportunity; in other words, we have desire to go big … together!

Exopharm is open to partnerships now:

- Out-licensing of existing IP for wider use
- Collaborative extension of IP to new uses, efficiency improvements, adjacent processing techniques, etc

Thank you

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Refreshing Medicine, Today