



CustomEX™ - A NEW STEM CELL-DERIVED DRUG DELIVERY PLATFORM

....TARGETING TISSUES OF INTEREST AND DELIVERING PAYLOADS OF CHOICE

Randolph Corteling, PhD
Chief Scientific Officer

Disclaimer

THIS PRESENTATION MAY NOT BE COPIED OR REPRODUCED IN ANY FORM, FURTHER DISTRIBUTED OR PASSED ON, DIRECTLY OR INDIRECTLY, TO ANY OTHER PERSON OR PUBLISHED, IN WHOLE OR IN PART, FOR ANY PURPOSE. IN PARTICULAR THIS PRESENTATION AND ITS CONTENTS ARE STRICTLY CONFIDENTIAL AND ARE NOT FOR RELEASE, PUBLICATION OR DISTRIBUTION, IN WHOLE OR IN PART, DIRECTLY OR INDIRECTLY, IN OR INTO THE UNITED STATES OF AMERICA, AUSTRALIA, NEW ZEALAND, CANADA, JAPAN, THE REPUBLIC OF SOUTH AFRICA OR TO ANY RESIDENT THEREOF, OR ANY OTHER JURISDICTION WHERE SUCH DISTRIBUTION IS UNLAWFUL.

The information contained in this document and communicated during the presentation of these slides, including the talks given by presenters, any question and answer session and any documents or other materials distributed at or in connection with the presentation (together, this “Presentation”) is strictly confidential, and is supplied on the understanding that it will be held in confidence, and not copied, reproduced, recorded, distributed, published or disclosed to third parties. This Presentation has been prepared and issued by and is the sole responsibility of ReNeuron Group plc (the “Company”) solely in connection with the proposed placing, subscription and retail offer of new ordinary shares in the capital of the Company and the proposed admission of such shares to trading on AIM, the market operated by London Stock Exchange plc (the “Fundraising”).

This Presentation does not constitute a prospectus or offering memorandum or an offer in respect of any securities and is not intended to provide the basis for any investment decision and should not be considered as a recommendation that any investor should subscribe for or purchase any securities. No prospectus or offering document has been or will be prepared in connection with the Fundraising. Any investment decision to buy securities in connection with the Fundraising must be made solely on the basis of publicly available information. This Presentation has not been approved by the Financial Conduct Authority (the “FCA”) under the Prospectus Regulation Rules (made under Part VI of the Financial Services and Markets Act 2000, as amended) or otherwise, or by London Stock Exchange plc.

This Presentation does not constitute or form part of, and should not be construed as, any offer, invitation or recommendation to purchase, sell or subscribe for any securities of the Company in any jurisdiction and neither the issue of this Presentation nor anything contained herein shall form the basis of or be relied upon in connection with, or act as an inducement to enter into, any investment activity. This Presentation does not purport to contain all of the information that may be required to evaluate any investment in the Company or any of its securities and should not be relied upon to form the basis of, or be relied on in connection with, any contract or commitment or investment decision whatsoever. This Presentation is intended to present background information on the Company, its business and the industry in which it operates and is not intended to provide complete disclosure upon which an investment decision could be made. The merit and suitability of an investment in the Company should be independently evaluated and any person considering such an investment in the Company is advised to obtain independent advice as to the legal, tax, accounting, financial, credit and other related advice prior to making an investment.

This Presentation is only being made, supplied or directed at (A) in member states of the European Economic Area, persons who are “qualified investors” within the meaning of Article 2(1)(e) of the Regulation (EU) 2017/1129; and (B) in the United Kingdom persons that are “qualified investors” as defined in Article 2(e) of the UK version of Regulation (EU) 2017/1129 which forms part of UK law by virtue of the European Union (Withdrawal) Act 2018 (as amended) and are persons that (i) have professional experience in matters relating to investments who fall within the definition of “investment professionals” in Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the “Order”), or (ii) fall within Article 49(2) (High Net Worth Companies, etc.) of, the Order, or (iii) to whom it may otherwise lawfully be communicated (all such persons together being referred to as a “Relevant Person”). No other person should act or rely on this presentation and persons distributing this presentation must satisfy themselves that it is lawful to do so. Any person who is not a Relevant Person should not act or rely on this Presentation or any of its contents. If you have received this presentation and you are not a Relevant Person, you must return this presentation immediately to the Company.

The Company’s securities have not been and will not be registered under the U.S. Securities Act of 1933, as amended (the “Securities Act”), or under the securities laws of any state or other jurisdiction of the United States (within the meaning of Regulation S under the Securities Act), and such securities may not be offered or sold into or within the United States absent registration under the Securities Act or pursuant to an exemption from, or in a transaction not subject to, the registration requirements of the Securities Act. Neither the United States Securities and Exchange Commission nor any securities regulatory authority of any state or other jurisdiction of the United States has approved or disapproved of an investment in the securities of the Company or passed on the accuracy or adequacy of the contents of this presentation. Any representation to the contrary is a criminal offence in the United States.

Neither this presentation nor any copy of it may be taken, transmitted or distributed, directly or indirectly, in or into the United States, Australia, New Zealand Canada, Japan or the Republic of South Africa or to any resident thereof, or to any other jurisdiction where such distribution is unlawful, except in compliance with applicable securities laws. The distribution of this document in other jurisdictions may be restricted by law and the persons into whose possession this document comes should inform themselves about, and observe, any such restrictions. Any failure to comply with these restrictions may constitute a violation of the securities laws or the laws of any such jurisdiction.

No representation, warranty or undertaking or other assurance, express or implied, is made or given by or on behalf of the Company, Liberum Capital Limited (“Liberum”) or their respective subsidiary or subsidiary undertakings, or any of their respective directors, officers, partners, employees, agents, affiliates or advisers as to the accuracy, completeness, fairness or sufficiency of the information or opinions contained or expressed in this Presentation and none of the information contained in this Presentation has been independently verified by any person. Save in the case of fraud, no responsibility or liability whatsoever (whether in negligence or otherwise) is accepted by any person for any loss, cost or damage suffered or incurred directly or indirectly as a result of use of, or reliance on this Presentation nor for any errors, omissions or inaccuracies in the information or opinions contained therein. No duty of care or otherwise is owed by any such person to recipients of the Presentation or any other person in relation to the Presentation. All information in this Presentation is subject to verification, correction, completion and change without notice. None of the Company, Liberum or their respective subsidiary or subsidiary undertakings, or any of their respective directors, officers, partners, employees, agents, affiliates or advisers, undertakes any obligation to amend, correct or update this Presentation.

To the extent available, the data contained in this Presentation has come from official or third party sources. Third party industry publications, studies and surveys generally state that the data contained therein have been obtained from sources believed to be reliable, but that there is no guarantee of the accuracy or completeness of such data. While the Company believes that each of these publications, studies and surveys has been prepared by a reputable source, the Company has not independently verified the data contained therein. In addition, certain of the data contained in this Presentation come from the Company’s own internal research and estimates based on the knowledge and experience of the Company’s management in the market in which the Company operates. While the Company believes that such research and estimates are reasonable and reliable, they, and their underlying methodology and assumptions, have not been verified by any independent source for accuracy or completeness and are subject to change without notice.

The information contained in the Presentation is confidential and may constitute inside information for the purposes of the Criminal Justice Act 1993 and Regulation (2014/596/EU) (as it forms part of UK domestic law by virtue of the European Union (Withdrawal) Act 2018, as amended) (“UK MAR”). You should not use inside information as a basis for your behaviour in relation to any financial instruments (as defined in MAR), as to do so could amount to market abuse for the purposes of UK MAR. Dealing in shares in the Company prior to publication of an announcement by the Company in relation to the Fundraising could also constitute insider dealing for the purposes of the Criminal Justice Act 1993 and UK MAR.

Certain information contained in this Presentation constitutes “forward-looking statements”, which can be identified by the use of terms such as “may”, “will”, “should”, “expect”, “anticipate”, “project”, “estimate”, “intend”, “continue”, “target” or “believe” (or the negatives thereof) or other variations thereon or comparable terminology, many of which are based upon various assumptions including, without limitation, management’s intentions going forward, projects or product development that is underway or may be undertaken or management’s examination of historical operating trends, data contained in the Company’s records and other data available from third parties. Due to various risks and uncertainties, actual events or results or actual performance of the Company may differ materially from any opinions, forecasts or estimates reflected or contemplated in this Presentation. There can be no assurance that future results or events will be consistent with any such opinions, forecasts or estimates. Potential investors should not rely on such forward-looking statements in making their investment decisions. No representation or warranty is made as to the achievement or reasonableness of, and no reliance should be placed on, such forward looking statements. The past performance of the Company is not a reliable indication of the future performance of the Company. No statement in this Presentation is intended to be nor may it be construed as a profit forecast. Neither the Company, Liberum or their respective subsidiary or subsidiary undertakings, or any of their respective directors, officers, partners, employees, agents, affiliates or advisers intend or have any duty or obligation to supplement, amend, update or revise any of the opinions, forward-looking statements or estimates contained in this Presentation.

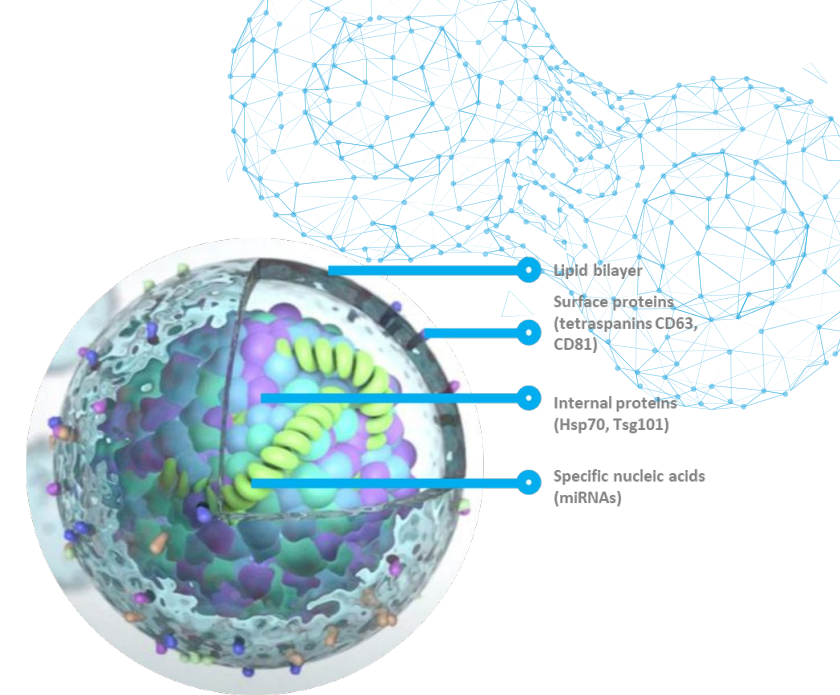
Liberum is regulated in the United Kingdom by the FCA and is acting only for the Company in connection with the proposed Fundraising and is not acting for or advising any other person, or treating any other person as its client, in relation thereto and will not be responsible for providing the regulatory protection afforded to clients of Liberum or advice to any other person in relation to the proposed Fundraising or the contents of this Presentation. Any other person attending the Presentation should seek their own independent legal, investment and tax advice as they see fit.

By accepting receipt of or electronically accessing this Presentation, or attending any presentation or delivery of this Presentation, you agree to be bound by the above conditions and limitations and, in particular, will be taken to have represented, warranted, undertaken and acknowledged to each of the Company and Liberum, that: (i) you have read and agree to comply with the foregoing limitations and restrictions including, without limitation, the obligation to keep permanently confidential the information contained in this Presentation or made available in connection with further enquiries to the extent such information is not made publicly available (otherwise than through a breach by you of this provision); (ii) you are able to receive this Presentation without contravention of any applicable legal or regulatory restrictions; (iii) you are a Relevant Person (as defined above); (iv) you will not rely on this Presentation for the purposes of any involvement in the Fundraising; and (v) you will not record, distribute, copy, reproduce, publish, store in a retrieval system, transmit or pass on this Presentation, directly or indirectly, in whole or in part.

Why stem cell exosomes?

⦿ Limitations around current delivery platforms

- **Safety** - Viral vectors have been plagued by side effect issues. Viral vectors and LNP's, both have immunogenetic properties that are problematic
- **Efficiency of loading and delivery** - Limitations on the type, size of cargo and the efficient delivery of therapeutic dose (endosomal escape)
- **Tissue/cell targeting** - Lipid Nanoparticles & HEK derived exosome have no natural tropism with delivery mainly to the liver.

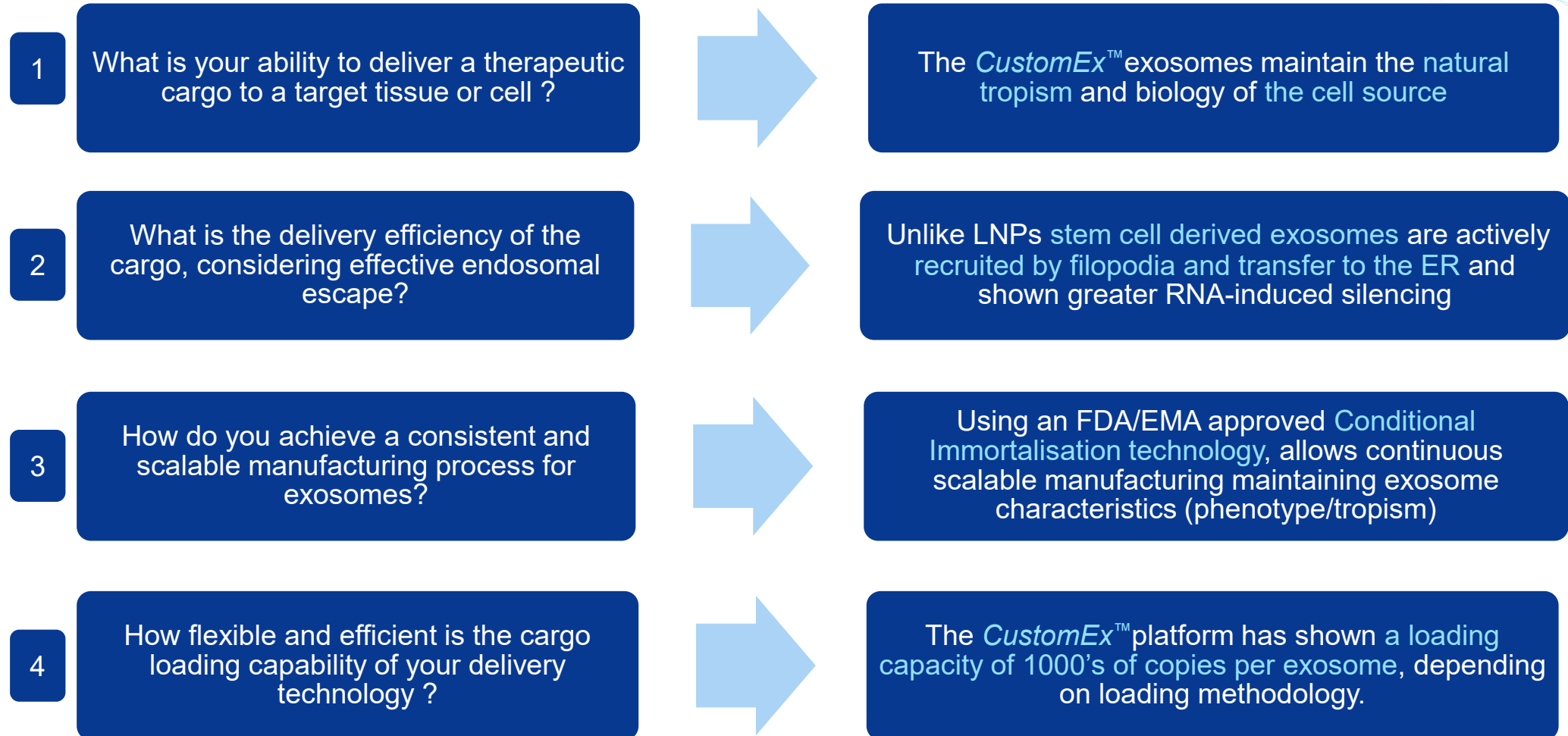


⦿ Stem cell exosomes - targeted delivery platform for complex drug modalities

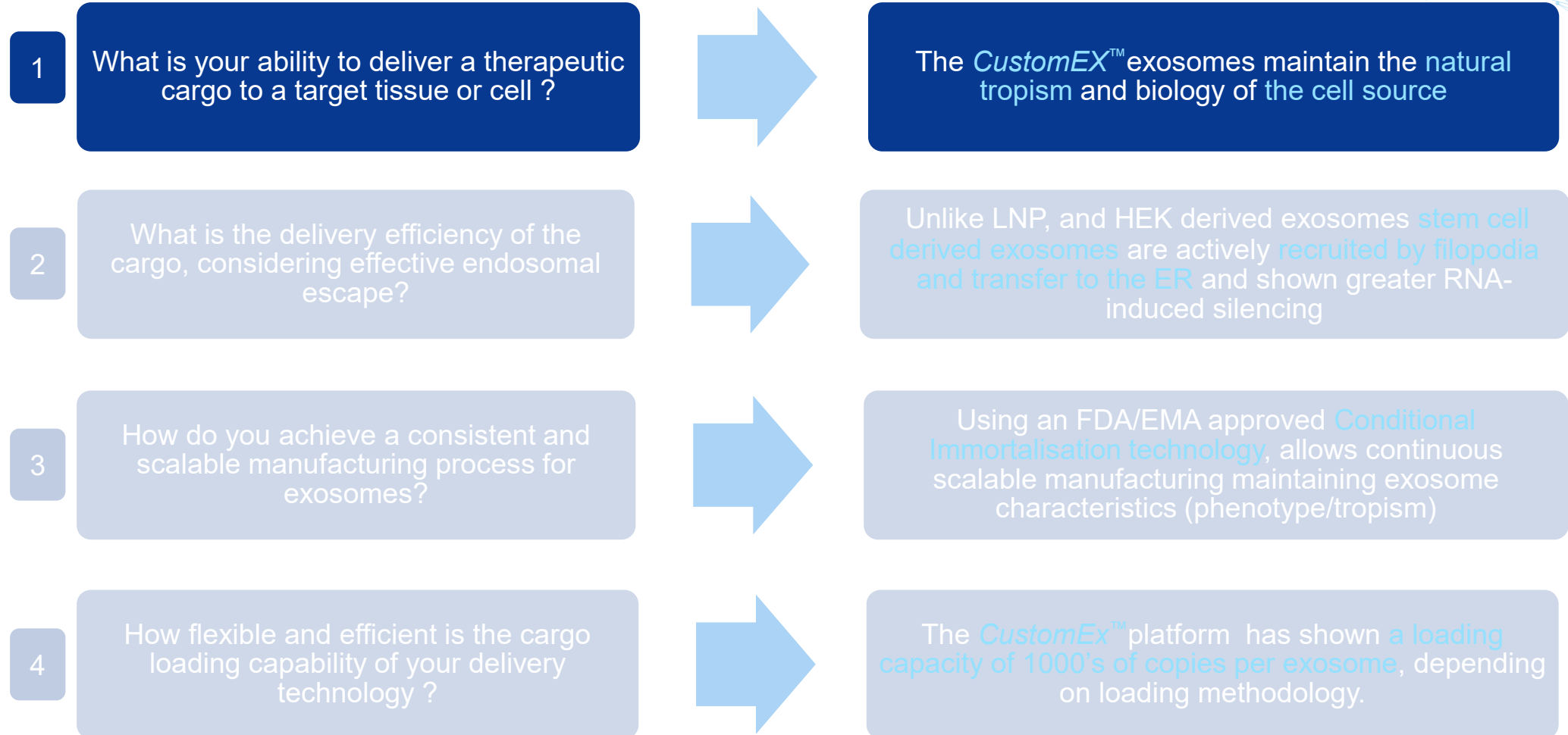
- **Safety** - Naturally occurring nanoparticles released by all cells for the purpose of intercellular communication – non immunogenic
- **Efficiency of loading and delivery** - Proven ability to carry and deliver more than one bio-active cargo simultaneously including proteins and nucleic acids
- **Tissue/cell targeting** - Critically, they target recipient cells via specific surface proteins that are determined by their cell of origin

EXOSOME CELL SOURCE IS AN IMPORTANT CONSIDERATION FOR TARGETED DRUG DELIVERY

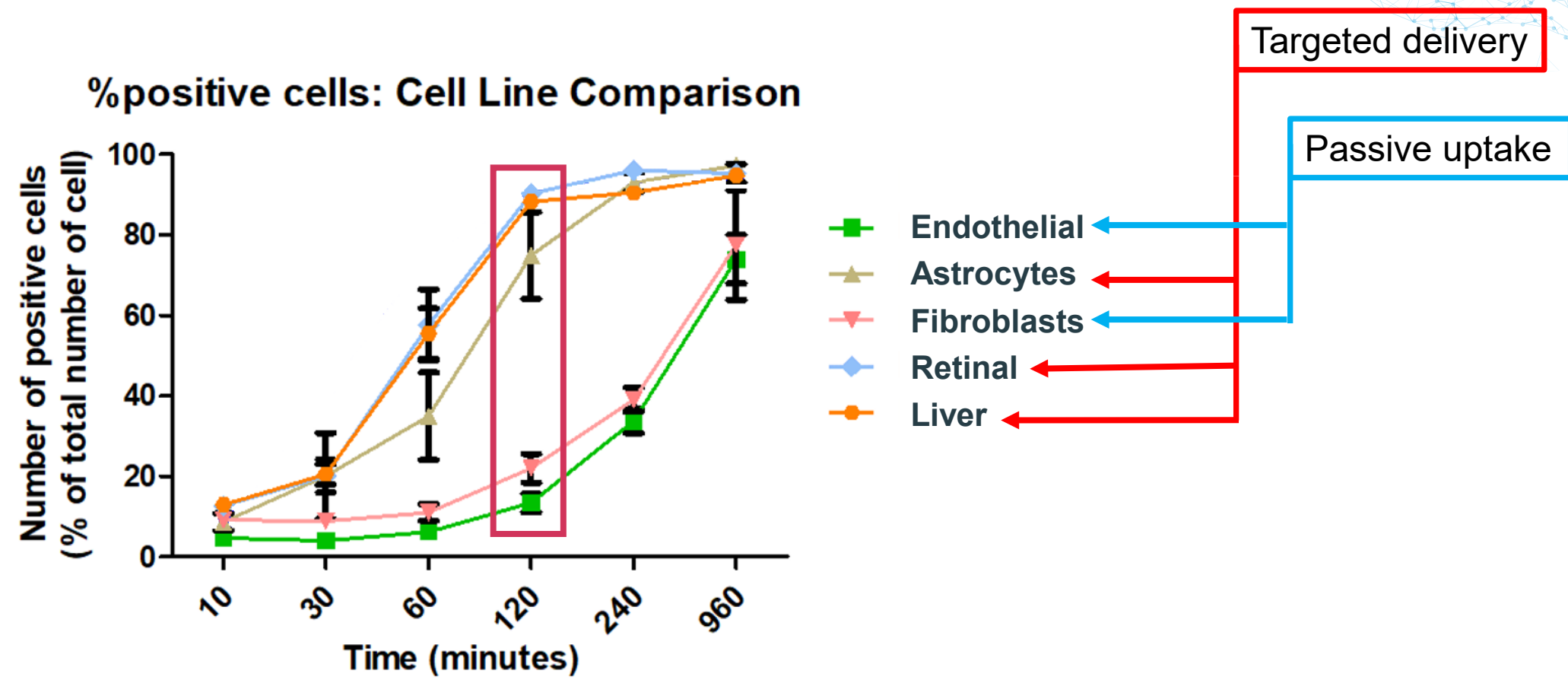
Questions around exosome delivery technology



Questions around exosome delivery technology



ReNeuron's stem cell exosomes are preferentially taken up by specific cell types

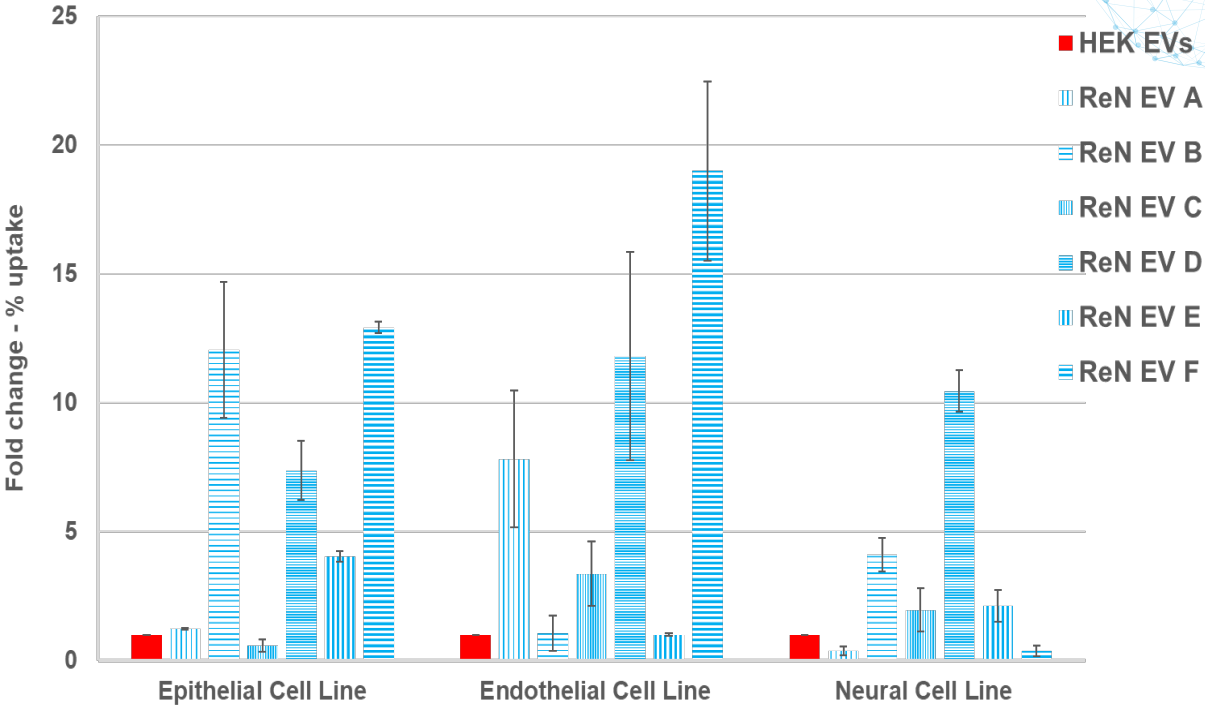
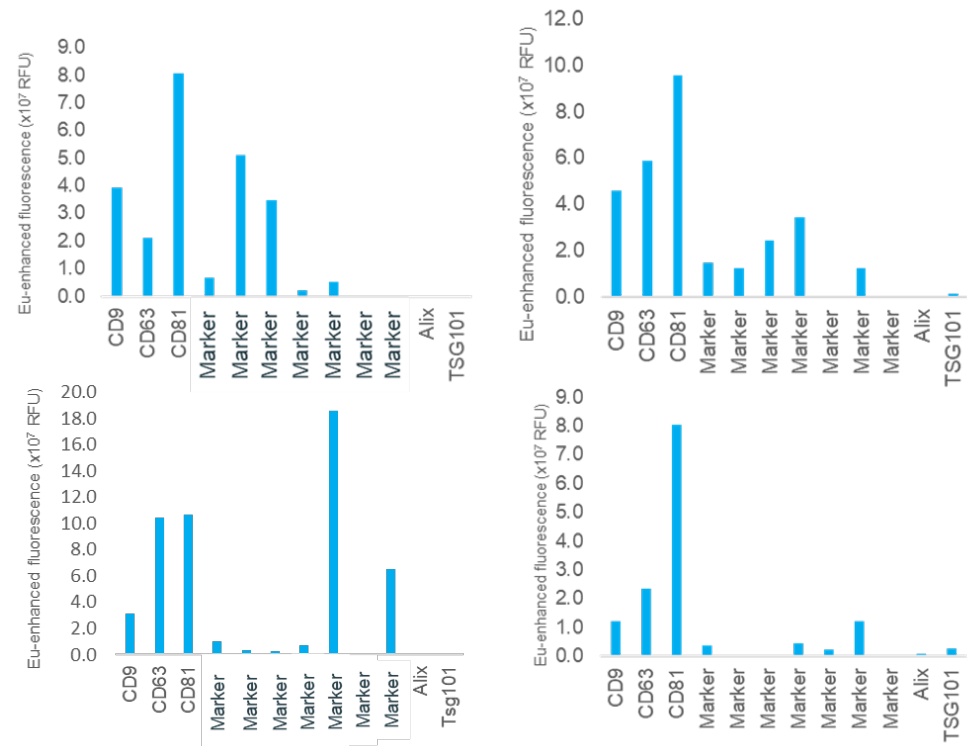


- By assessing the number of positive cells over time, 2 distinct profiles emerge
- Astrocytes, retinal and liver cells rapidly take up the exosomes while fibroblasts and endothelial cells show delayed uptake

Selection of exosome type an important consideration when developing a targeted drug delivery system

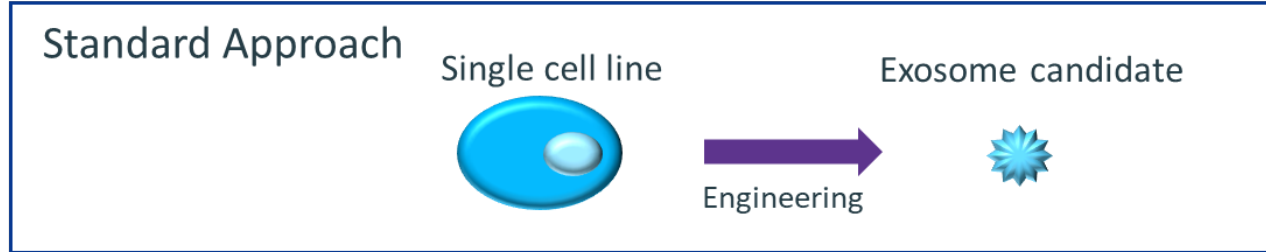


ELISA surface marker profile



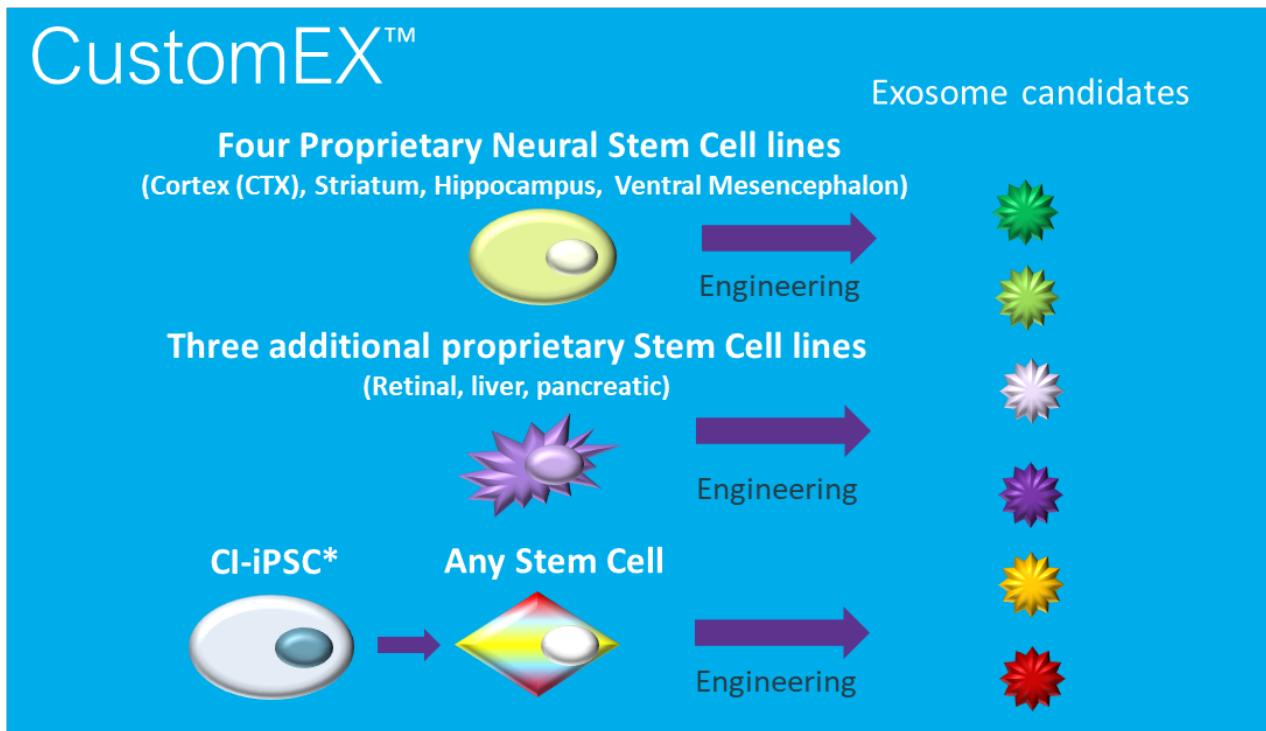
EXOSOME BIOLOGY INFLUENCES CELLULAR TROPISM AND DELIVERY OF CARGO.

CustomEX™ - A customisable, exosome delivery platform optimised for specific drug delivery needs



Competitors – Single cell line approach

- Single cell line, single outcome
- 'One size fits all'



ReNeuron – Portfolio of stem cell derived exosomes

- Exosomes have functional properties based on parent stem cell
- ReNeuron's multiple stem cell lines allow exosomes to be chosen for specific targets and payloads

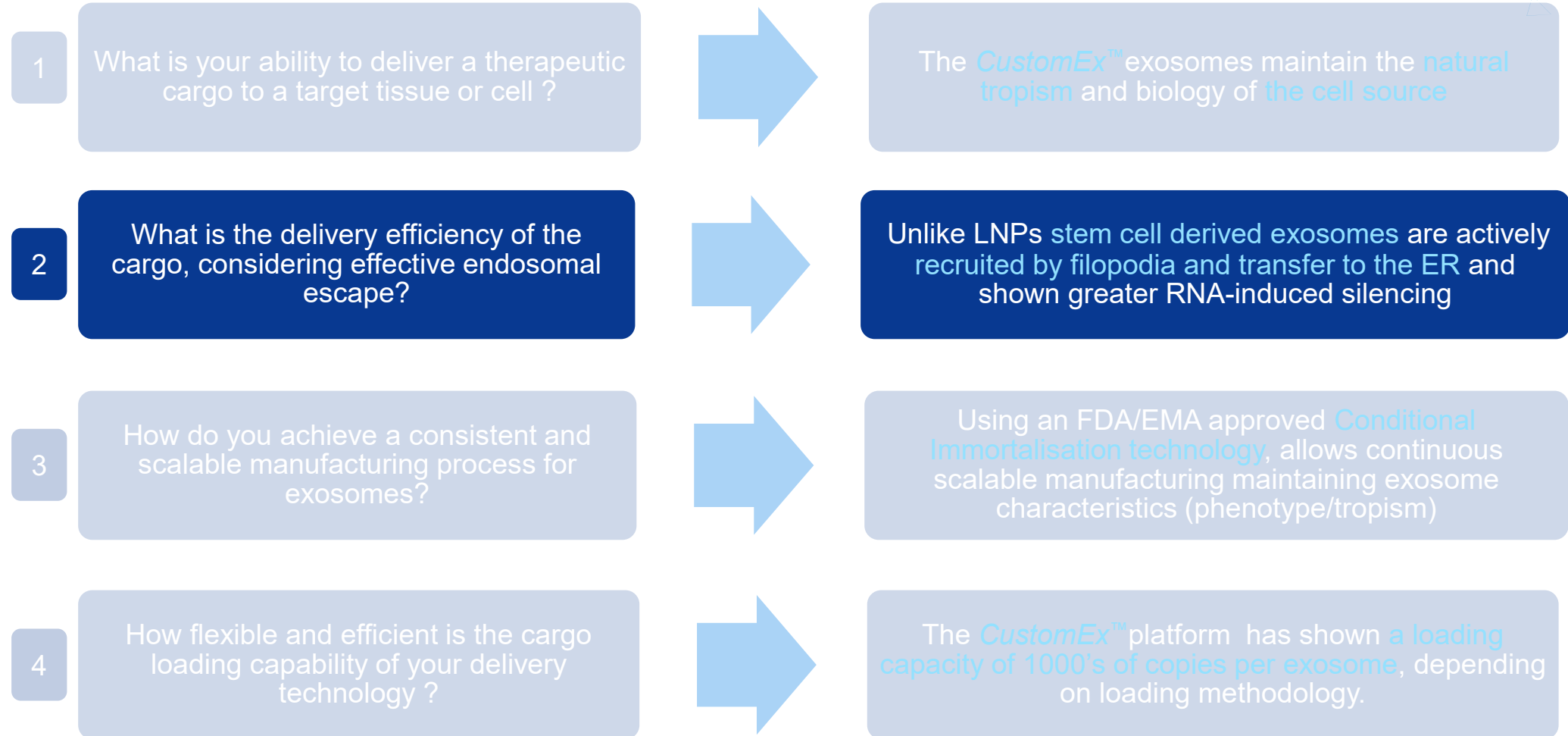
Producer stem cell line optimised for:

- Tissue targeting (on and off-target effects)
- Delivery (cytoplasm / nuclear)
- Engineering efficiency

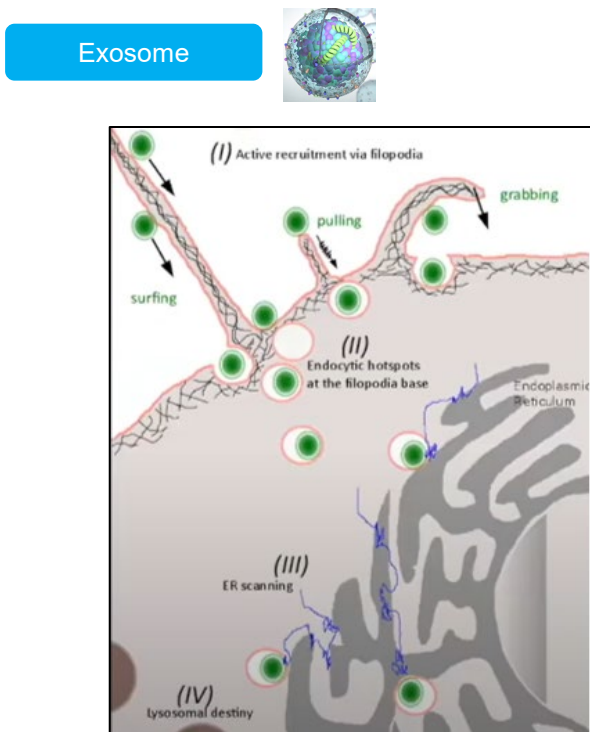
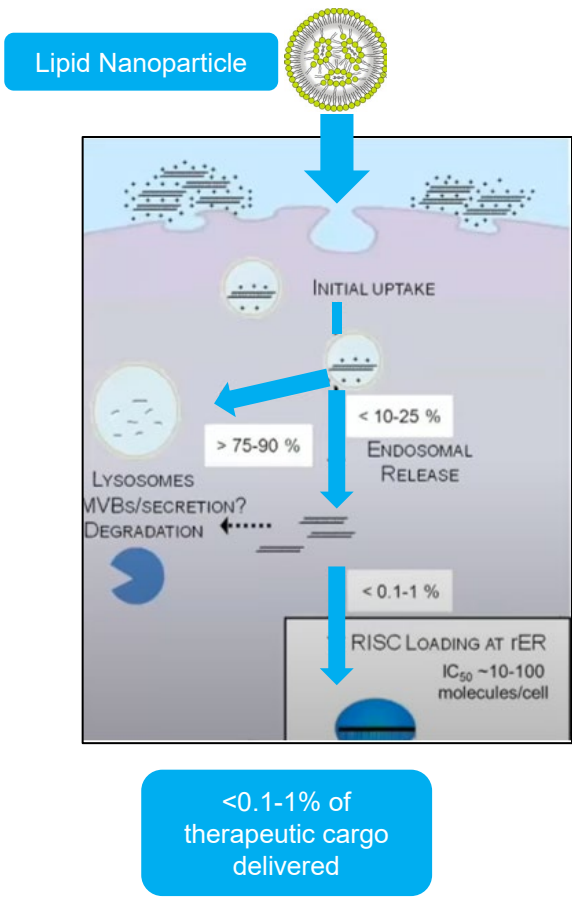
CustomEX™ is a trade mark of ReNeuron Limited

*CI-iPSC: Conditionally immortalised induced pluripotent stem cells

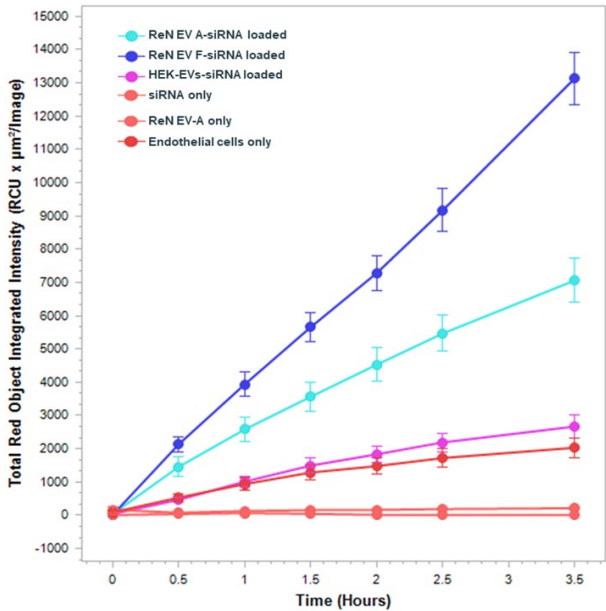
Questions around exosome delivery technology



Endosomal Escape : Why stem cell exosomes?



Delivery of fluorescently labelled siRNA loaded onto different exosome types



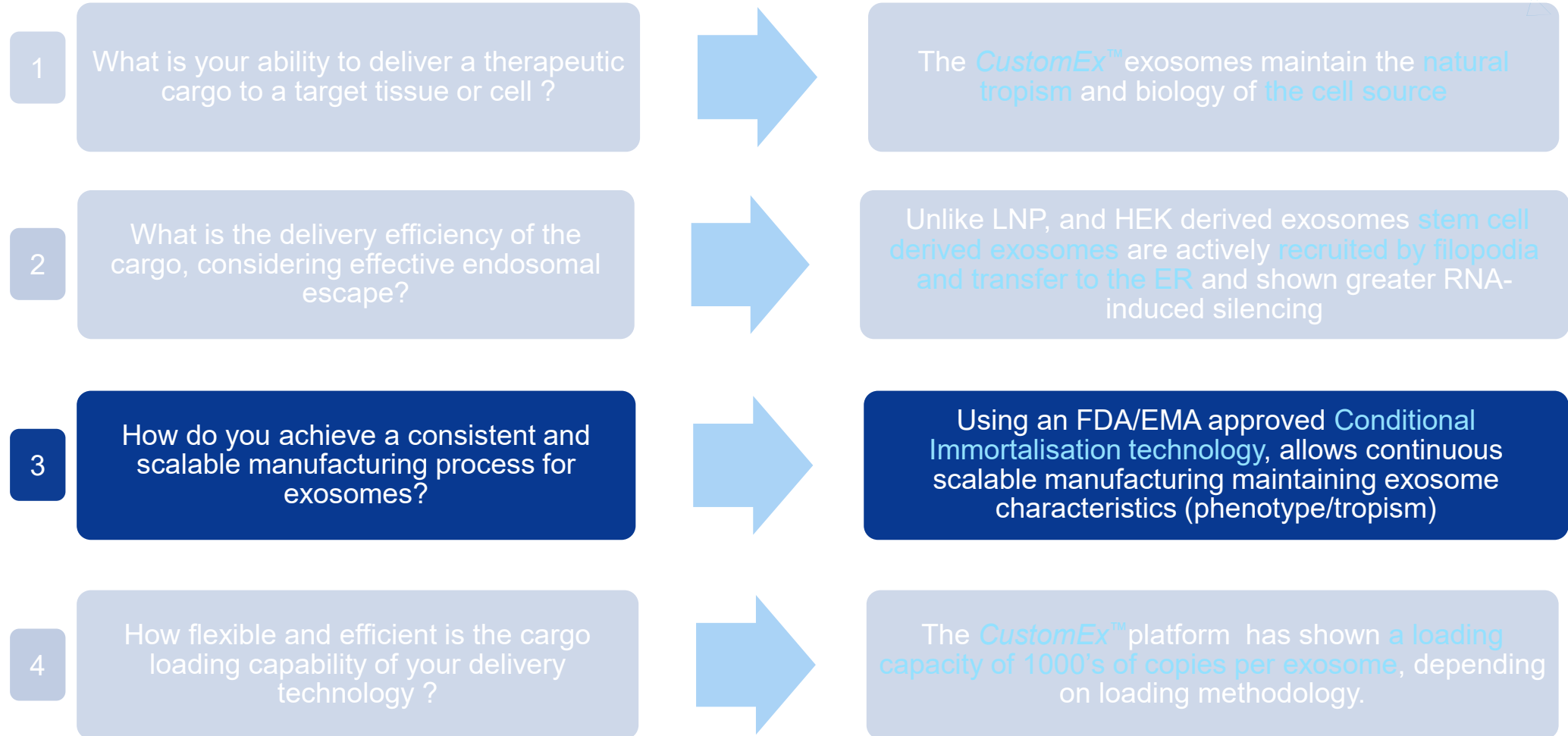
6 fold increase in delivery of siRNA compared to HEK exosome

Stem cell-derived exosomes

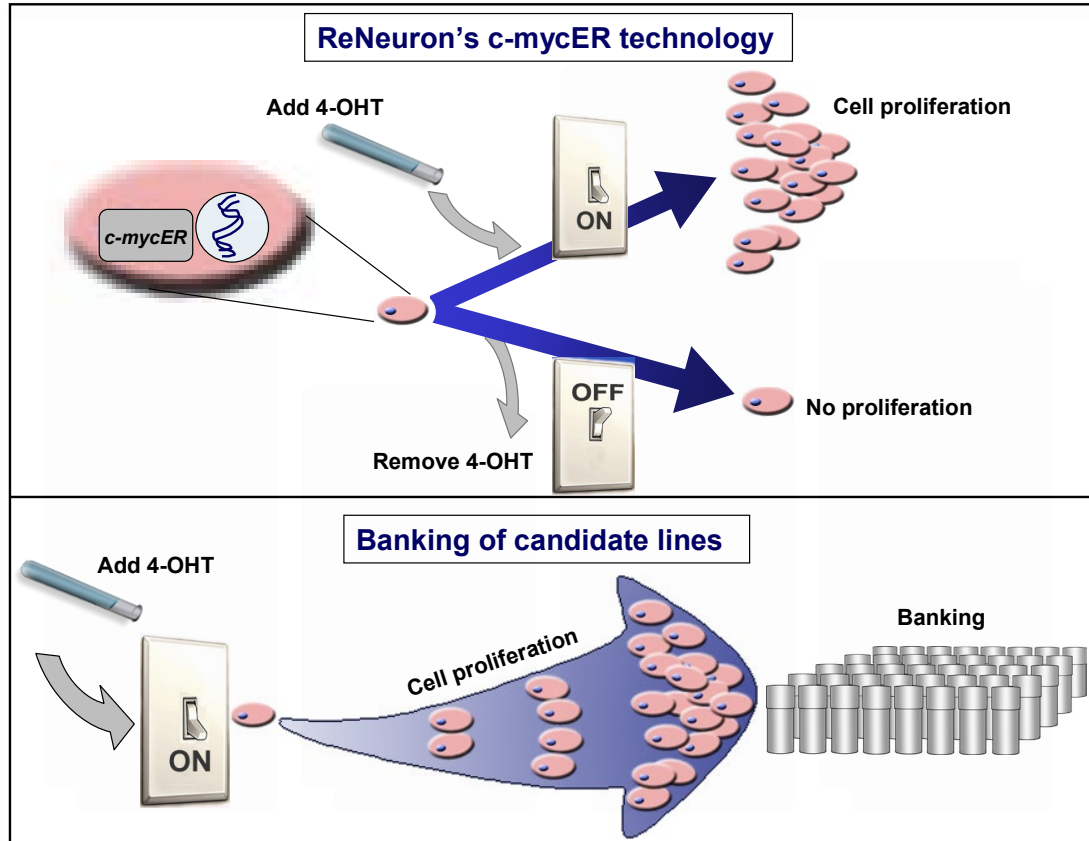
Active recruitment by filopodia and transfer to the ER for greater RNA-induced silencing

EXOSOME CELL SOURCE IS AN IMPORTANT CONSIDERATION FOR EFFICIENT DRUG DELIVERY

Questions around exosome delivery technology



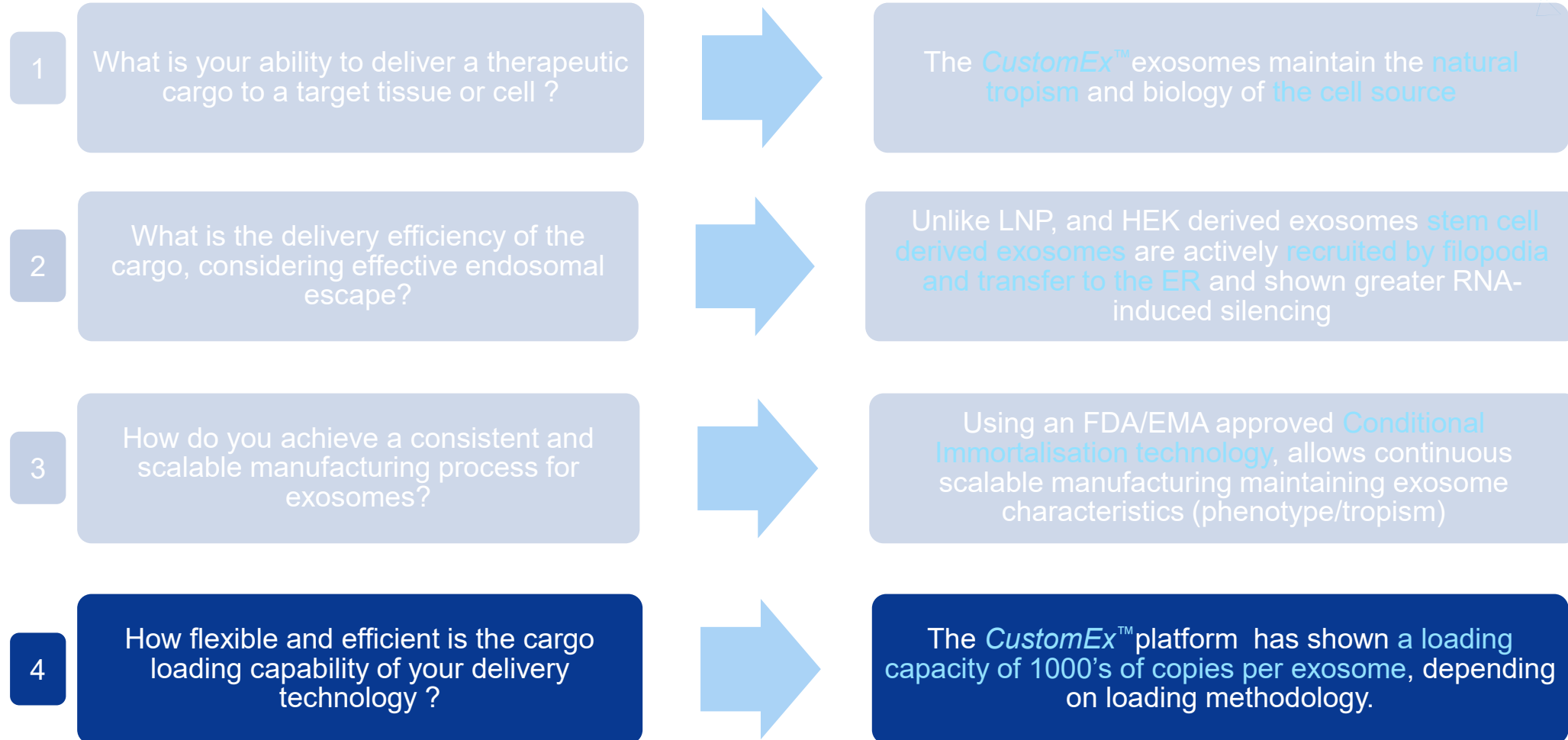
Why ReNeuron's CustomEX™ platform?



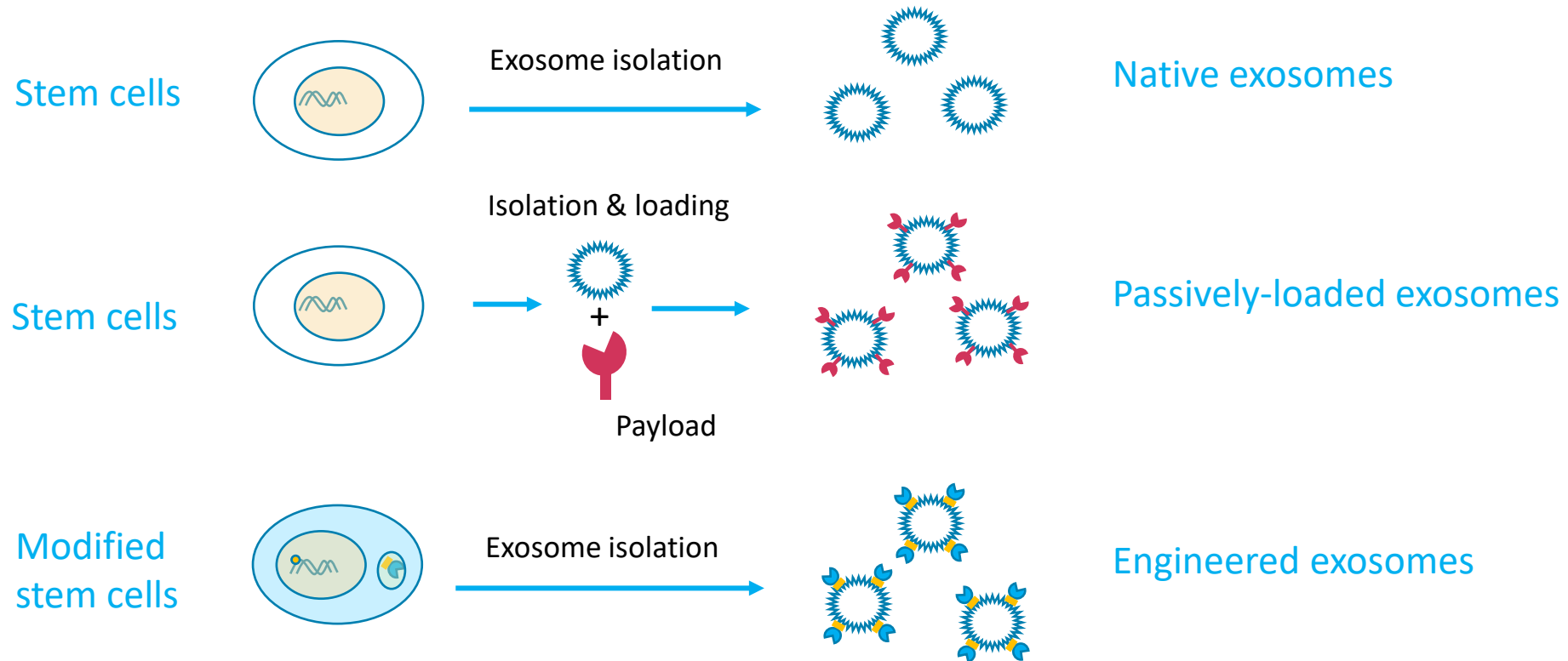
- Standard stem cell exosomes have significant barriers to their clinical translation
 - Heterogeneity
 - scale
- Consistent and Scalable Exosome Production through Conditional Immortalisation of the producer cell line
 - Stable producer cell line - Consistent phenotype maintained over multiple passages
 - Fully qualified xeno-free GMP process – tightly controlled USP with strict release criteria
 - Scalability - produced to a commercially relevant scale in multi-tier tissue culture flasks or bioreactors
 - Stable exosome product at 4°C, -80°C
 - Safe: No c-MycER^{TAM} within exosomes

CONDITIONAL IMMORTALISATION FOR THE PRODUCTION OF CONSISTENT EXOSOMES AT A CLINICALLY RELEVANT SCALE

Questions around exosome delivery technology

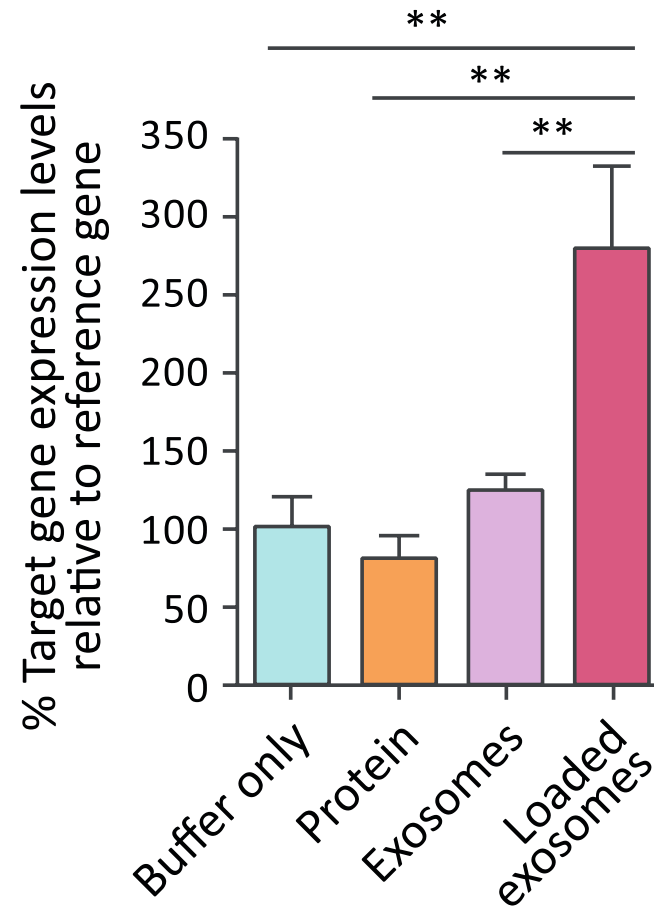


ReNeuron's ability to produce native, passively-loaded and engineered exosomes



PROVIDING AN EXPANDED RANGE OF EXOSOME PRODUCTS

Delivery of therapeutic proteins with ReNeuron's engineered exosomes



WE BELIEVE THIS IS THE FIRST TIME THAT A POTENTIALLY THERAPEUTIC PROTEIN PAYLOAD HAS BEEN DELIVERED TO A SPECIFIC SITE IN THE BRAIN USING EXOSOMES*

- Delivered by Intrathecal injection (lumbar puncture)
- Response observed only with exosomes loaded with therapeutic protein (BDNF)
- This area of the brain (the striatum) is affected in Parkinson's and Huntington's disease
- Further *In vivo* functional studies are planned

*In a preclinical setting

ReNeuron a leader in the exosome field



- ◎ CustomEX™: A customisable targeted delivery platform for complex drug modalities
 - Seven proprietary conditionally immortalised exosome producer stem cell lines producing unique exosome populations
 - ReNeuron's iPSC platform allows further production of unique exosomes that have the functional properties based on parent stem cells
 - Capable of delivering variety of payloads including proteins, nucleic acids and gene editing technologies
 - Data highlights increased uptake and delivery of payload when compared to a conventional delivery platforms and HEK-derived exosome approach
 - Our CustomEX™ portfolio of exosomes that have distinct surface marker profiles (tropisms) enabling a greater tissue targeting capability

ReNeuron

Pencoed Business Park | Pencoed
Bridgend | CF35 5HY | UK
T +44 (0)20 3819 8400 | E info@reneuron.com
www.reneuron.com
Ticker: RENE.L

