



UCL eXmoor Workshop: Manufacturing Strategies for Successful ATMP Development

6th March 2024





Introduction to eXmoor

Trusted Cell & Gene Therapy Partner

Full service CDMO accelerating therapies from research to patients

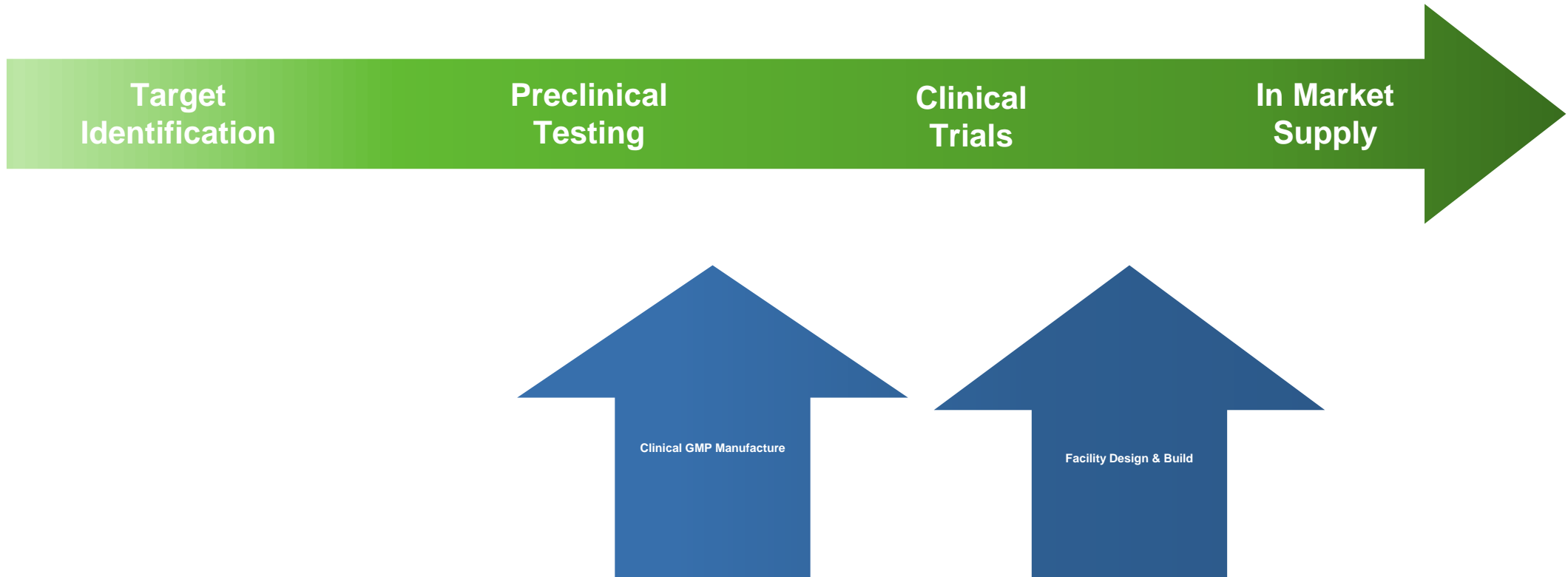
- ” >20 Years of Experience
- ” 85+ Employees
- ” 65,000 ft² GMP Facility
- ” Global Customer Base
- ” Dedicated

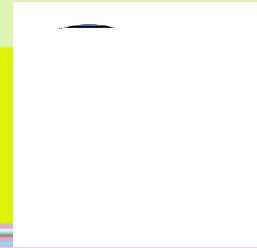
Our Services:

- ” CMC Consulting
- ” Process & Analytical Development
- ” GMP Clinical Manufacturing
- ” Facility Design & Build Consulting



Accelerating your Commercialisation Journey

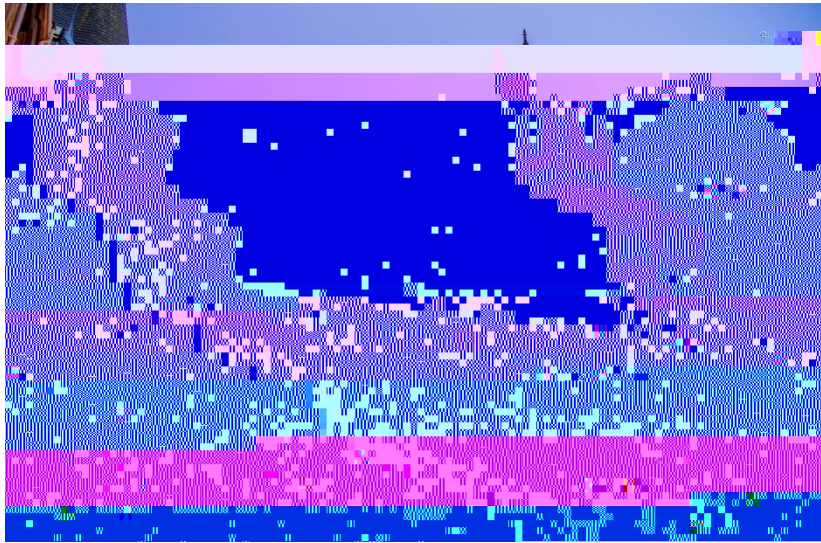




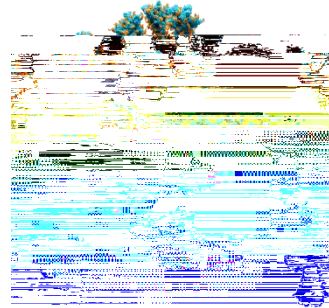
How CMC Expertise Early in Development Can Maximise Chances of Product Success

Clare Blue, Senior CMC Consultant



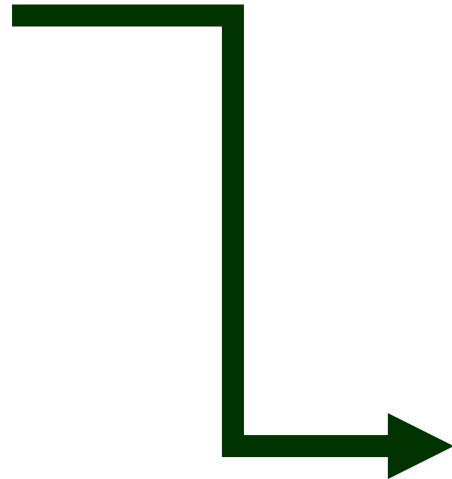


 BioReliance®

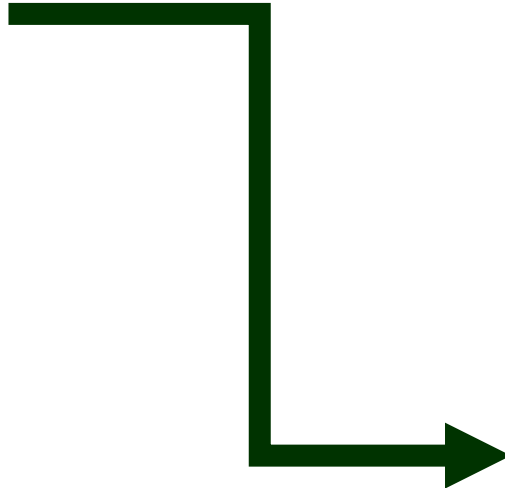


What is CMC?

**POC
Therapeutic**



**Chemistry
Manufacturing &
Controls**



**Safe &
efficacious
product**

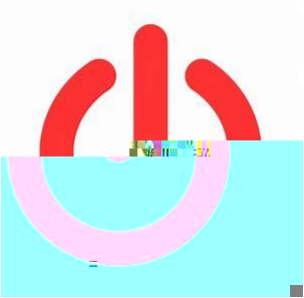


Why is Early CMC Expertise Important?

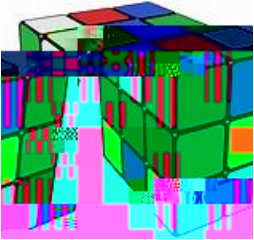
- “ Complex products
- “ $\rho[\hat{A}] \wedge \hat{A} \tilde{a} \wedge \hat{A} \tilde{a} \hat{A} \tilde{a} | q$
- “ Variation in AAV serotype, novel capsids, route of administration, formulation, delivery device
- “ Manufacturing process, scale, analytical testing, stability
- “ Separate considerations & development for different products
- “ Product understanding essential



From Concept to Clinic: Importance of QTPP



R2D



Research / Clinical / Preclinical

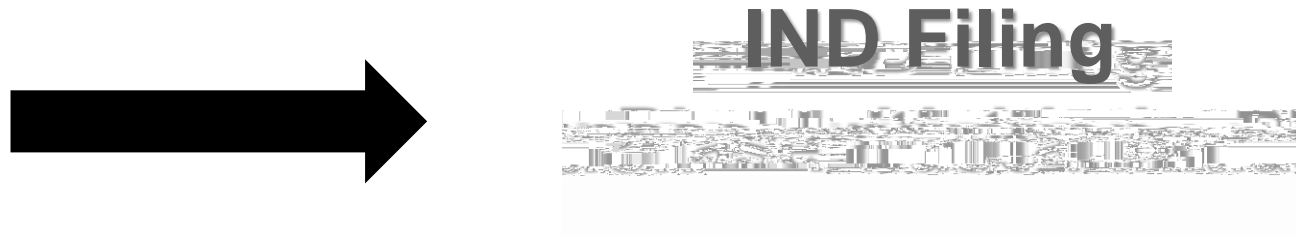
CMC

Supply Chain

Clinical



The Squeeze to IND Filing





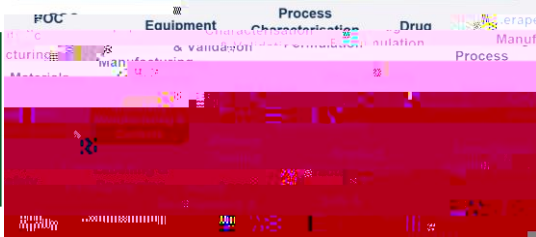
The Squeeze to IND Filing

12-18 mth



**Research / Clinical / Preclinical /
Supply Chain / Regulatory /
Quality / CMC**

**Fix
TPP/QT**



Why early collaboration is essential



“ Vector Design

“ Size of payload . impact on product quality

”

Impact of Pre-clinical Activities on CMC

- “ Tox / In-
“ Product concentration
“ Product quality (tox to be worse case)
“ Formulation
“ **Changes later in development may require repeat of tox**



Impact of Clinical Strategy on CMC

Final product concentration, dosing strategy, delivery device, target tissue, PQA, locations of clinical trial sites



Selection of appropriate manufacturer. 48-014ED)]Tecdbs648

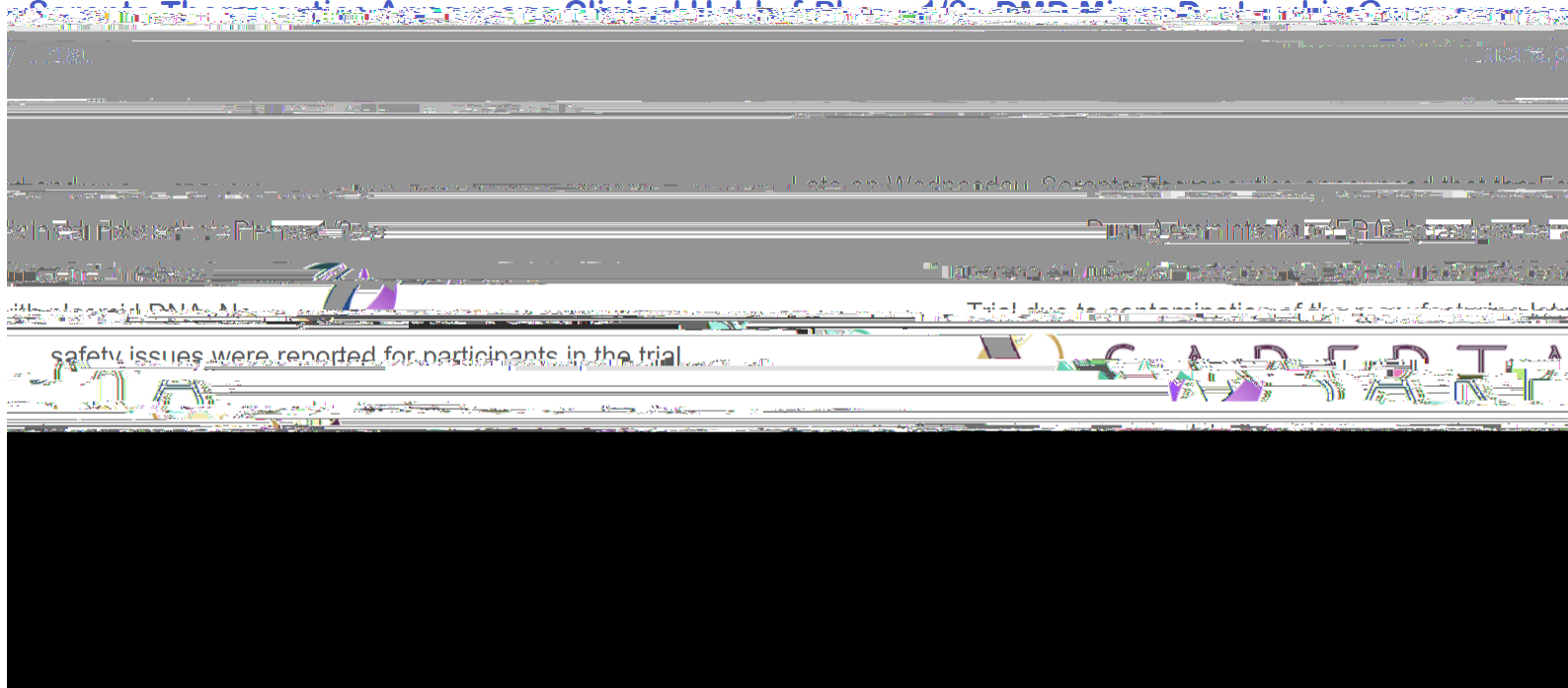
Case Study: Contamination of Plasmid Starting Material

Plasmid Starting Material

- “ Plasmids - a critical starting material for AAV manufacture
- “ Manufactured according to Principles of GMP
- “ Different grades of plasmid manufacture exist
 - “ Research grade
 - “ High Quality
 - “ GMP
- “ CMC / quality input essential to ensure correct quality & patient safety



Contamination of AAV Plasmid Starting Material



There's nothing particular in the sequence that was troubling." The issue was essentially that the fragment was there, and shouldn't have been



**CONTAMINATION
DETECTED**



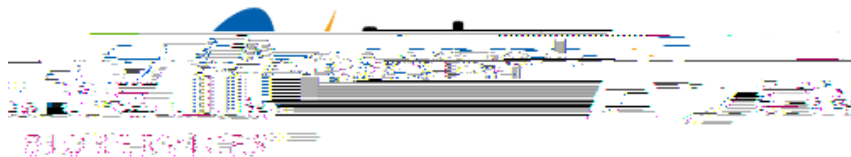
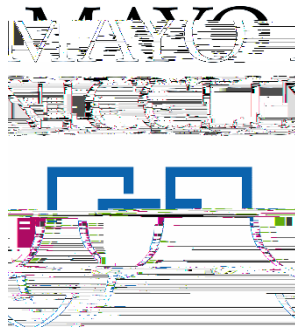
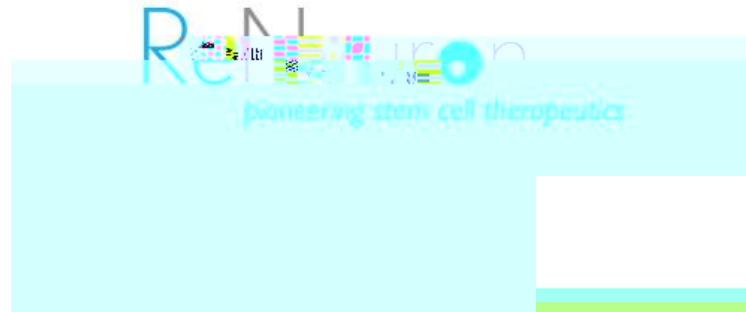


Health Check Questionnaire





Drew Hope, PhD, MRSB, UK QP



Straight road to success

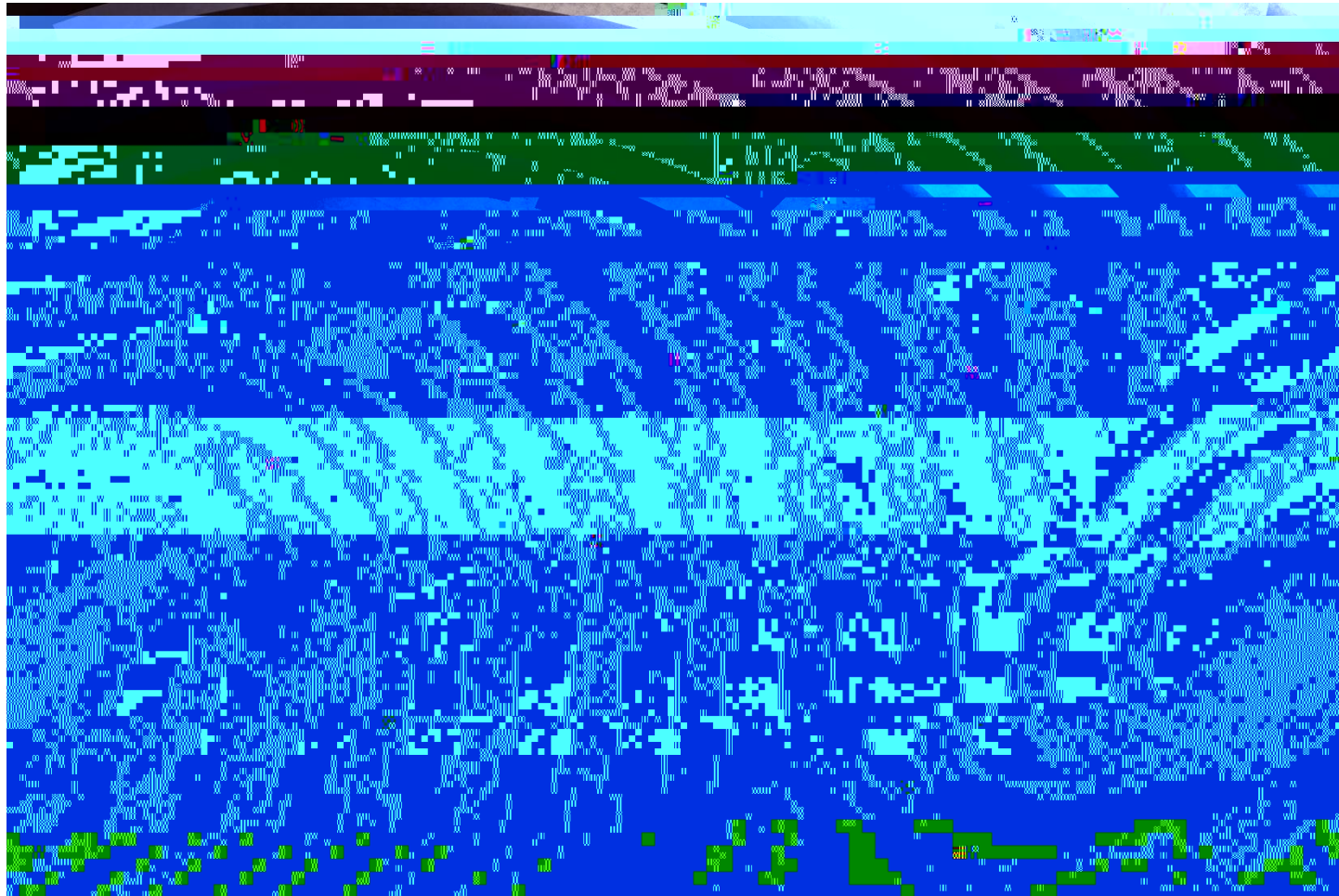
Is that horizon your destination?

Is this the right road?

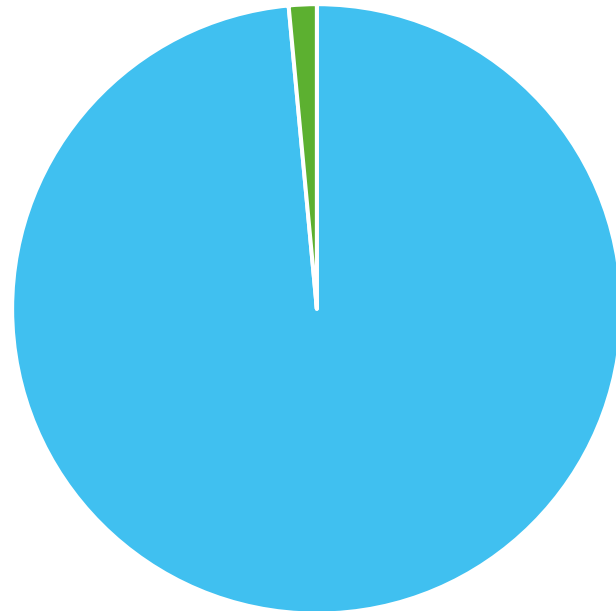
Is this heading in the right direction?



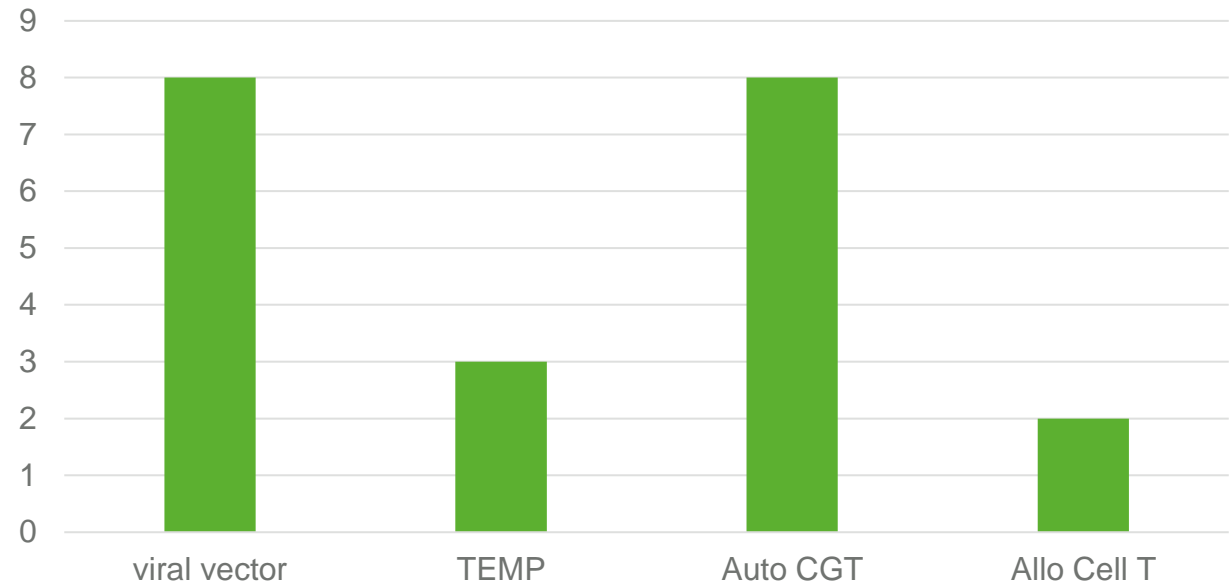
The reality



The evidence – Marketed << Trials



■ Clinical Trials ■ Marketed



The evidence – market failure

Product	Licence Holder	Approval and Withdrawal Date	Reason for MA withdrawal
ChondroCelect	TiGenix	Oct 2009 . Jul 2016	Commercial
Glybera	UniQure	Oct 2012 . Oct 2017	Access restrictions and commercial
MACI	Vericel	Jun 2013 . Sep 2014	Closure of an authorized EU manufacturing facility
Provenge	Dendreon	Sep 2013 . May 2015	Commercial
Zalmoxis	MolMed	Aug 2016 . Oct 2019	Insufficient clinical efficacy
Zynteglo	Bluebird bio	May 2019 . early 2022	Commercial

Q&A ^ Á Á [• c Á - Á ~]] | ^ Á Á } ^ & [} [{ æ

Pharmaceutical development lifecycle

Discovery

Non- and pre-clinical

Phase I

Phase II

Foresight

The image shows a 3x5 grid with a blue header row and a blue vertical bar on the left. A blue arrow points downwards along the left bar, containing the text 'Shortsights' and 'Longsights'. A green pill icon is located in the top-left cell of the grid.

Shortsights					
Longsights					

What causes short-sightedness?

One inflection point at a time,
c̃æ̃ ̃} åā̃ *
(repeat)

Founded by
passionate
scientists
lacking
perspective

VC funding
stage-gated

No early
funding for late-
stage
preparation

Focus on
clinical product,
blurred view of
commercial
product

“ Know your Quality Target Product Profile
”



Foresight: Build your CMC data

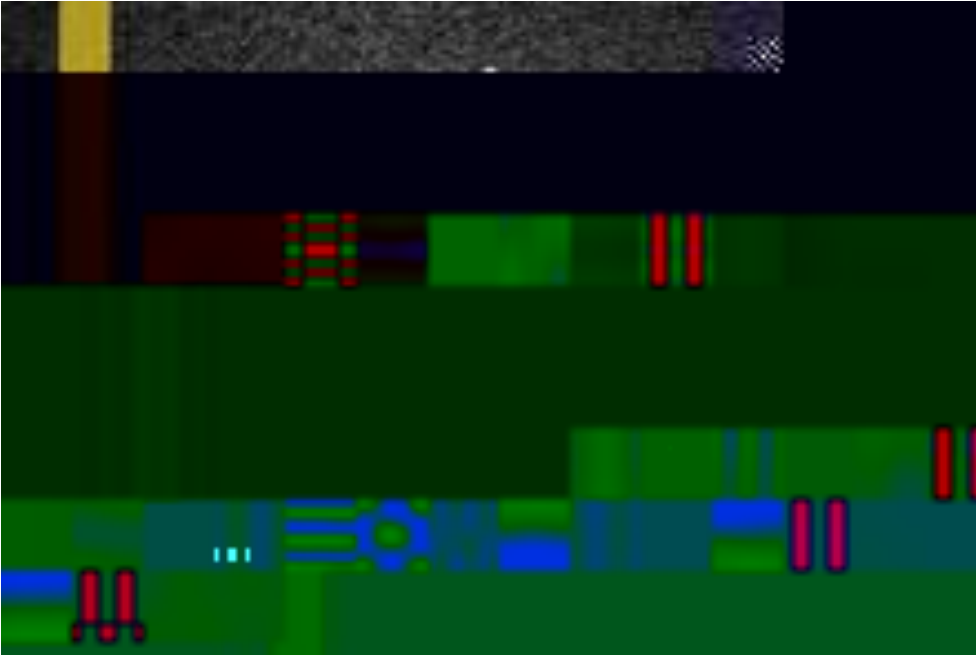
- “ CTA CMC supports MAA
- “ Material assessments of suitability . TSE, toxicity, particles, SAL
- “ Evidence of container integrity & leachables/extractables, particles
- “ Put down GMP lots for stability at Phase I for MAA/BLA



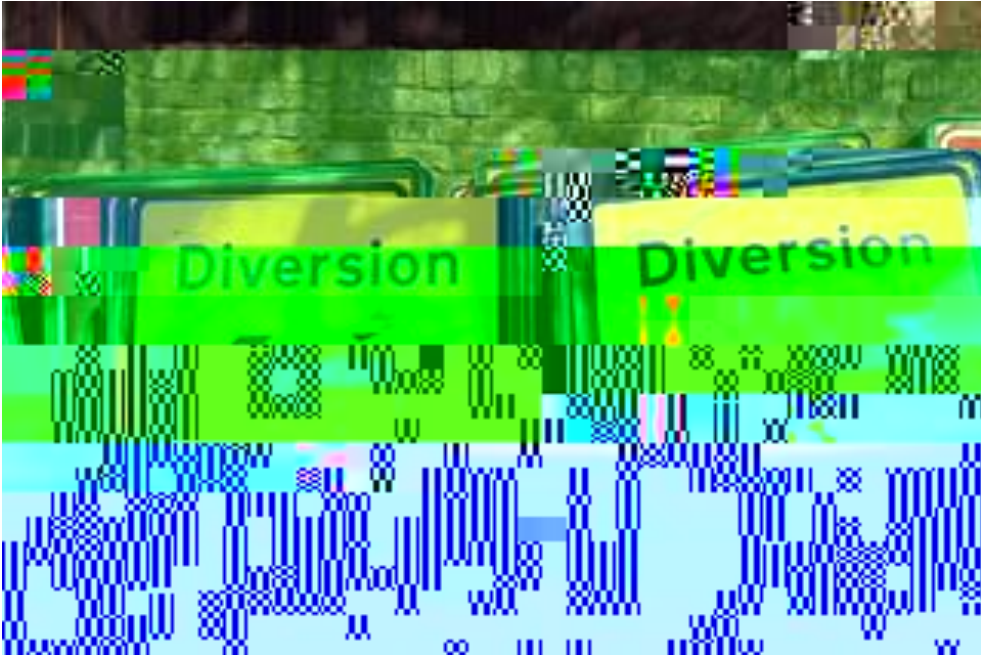


Stay on the direct route

GOOD



BAD



Recognise the horizons and destination



Strategize and fundraise wisely

1

Build a business case on commercial success

2

Build CMC data during the clinical phases

3

Avoid dead-end or return-to-start development

Thank you!
Any questions?

Ori Spotlight

Jim Faulkner
JDB BioConsulting

Jim Faulkner: Why unaffordable?

Structured Portfolio Assessment

Health Check Questionnaire

