Inspired by research. Driven by compassion. Inspiré par la recherche. Guidé par la compassion.

MANUFACTURING CAR-T

THE CANADIAN EXPERIENCE

FOCR: UNLOCKING NEXT-GENERATION THERAPIES

MAY 9, 2025

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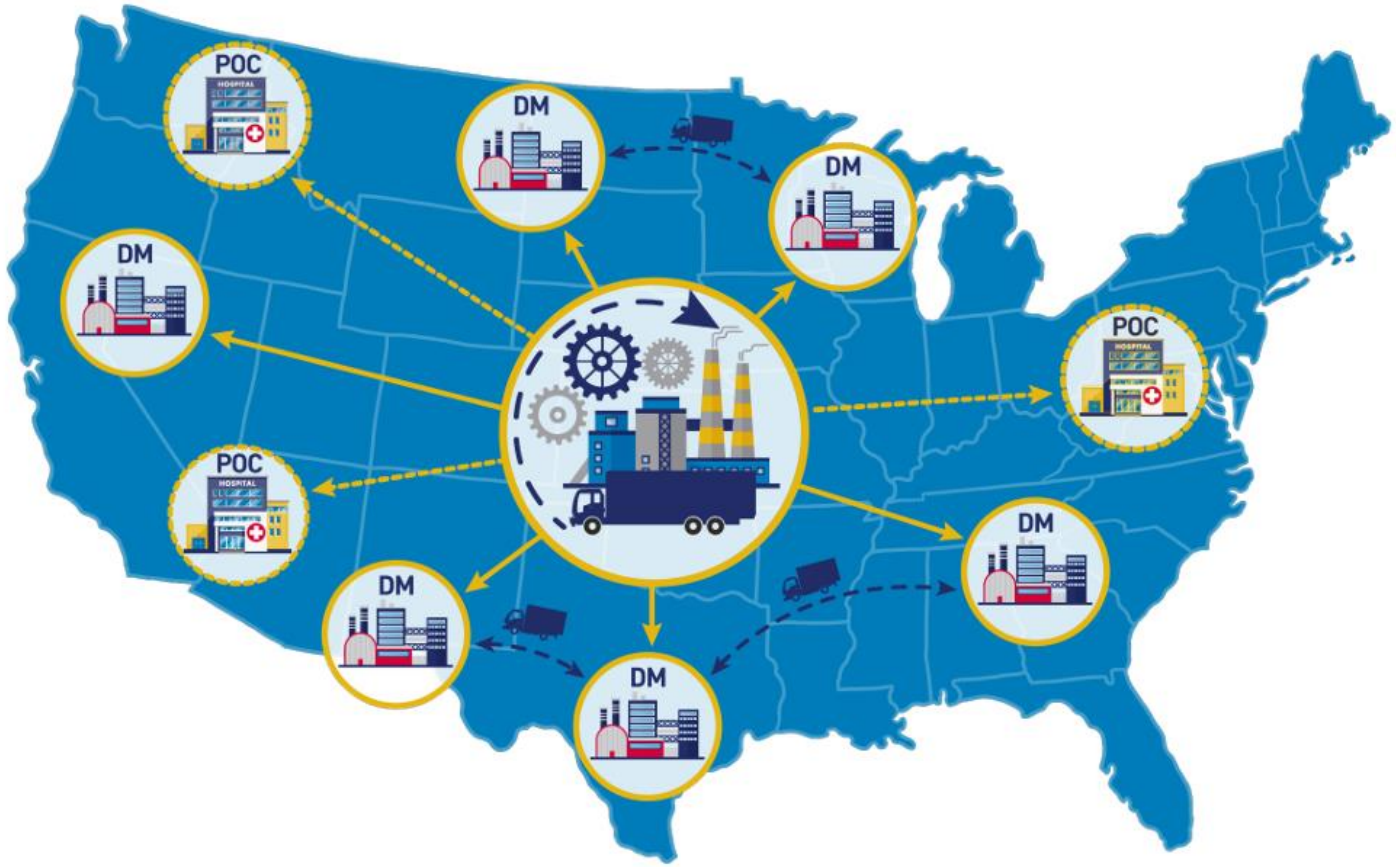
Hematologist, TCT Program, The Ottawa Hospital

DECLARATION/COI

Honoraria/ad board: Novartis, Kite/Gilead, BMS

POINT-OF-CARE (POC) MANUFACTURING MODELS

- Decentralized: Manufacturing at multiple regional facilities, not directly at the patient site
- Distributed: Manufacturing across large-scale centers, with centralized quality oversight and coordination
- Point of Care: Manufacturing done directly at the hospital or clinic where the patient is treated, on-site and on-demand



CENTER FOR DRUG EVALUATION AND RESEARCH Distributed Manufacturing and Point-of-Care Manufacturing of Drugs. 2022.

CLIC NETWORK FORMED IN 2017

Vision:

- Develop a Canadian academic model for cell therapy research and delivery to build expertise and infrastructure, create jobs and foster innovation

Strategy:

- Centralize production of plasmids and lentivirus at research hospitals
- Point-of-care compatible T-cell manufacturing to generate CAR-T cells
- Start with CD19 CAR-T as a proof-of-concept (known efficacy/toxicity; clinical need)

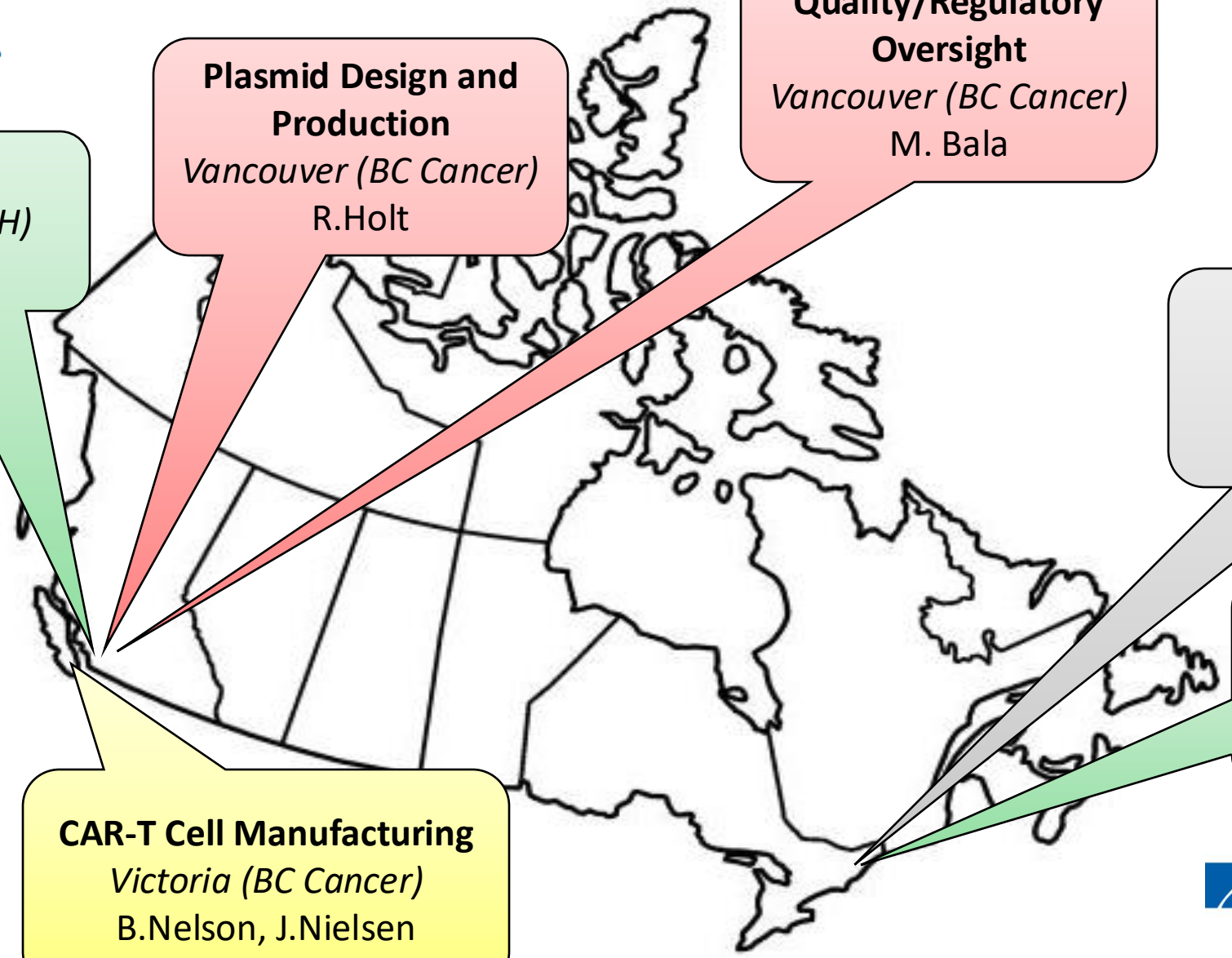
Vancouver CoastalHealth

CLIC-01
Canadian-Led Immunotherapies in Cancer

Clinical Site
Vancouver (VGH)
K.Hay

Plasmid Design and Production
Vancouver (BC Cancer)
R.Holt

Quality/Regulatory Oversight
Vancouver (BC Cancer)
M. Bala



Lentivirus Manufacturing
Ottawa (OHRI)
J.Bell, J.Quizi

Clinical Site
Ottawa (OHRI)
N.Kekre, H.Atkins

CAR-T Cell Manufacturing
Victoria (BC Cancer)
B.Nelson, J.Nielsen

BC CANCER

Ottawa Hospital Research Institute
Institut de recherche de l'Hôpital d'Ottawa

CLIC MANUFACTURING STRATEGY

- Point-of-care, automated T-cell manufacturing
  - Simpler implementation
  - Multiple machines operated by same technologist
  - Automated means less human error
  - Small, closed benchtop system

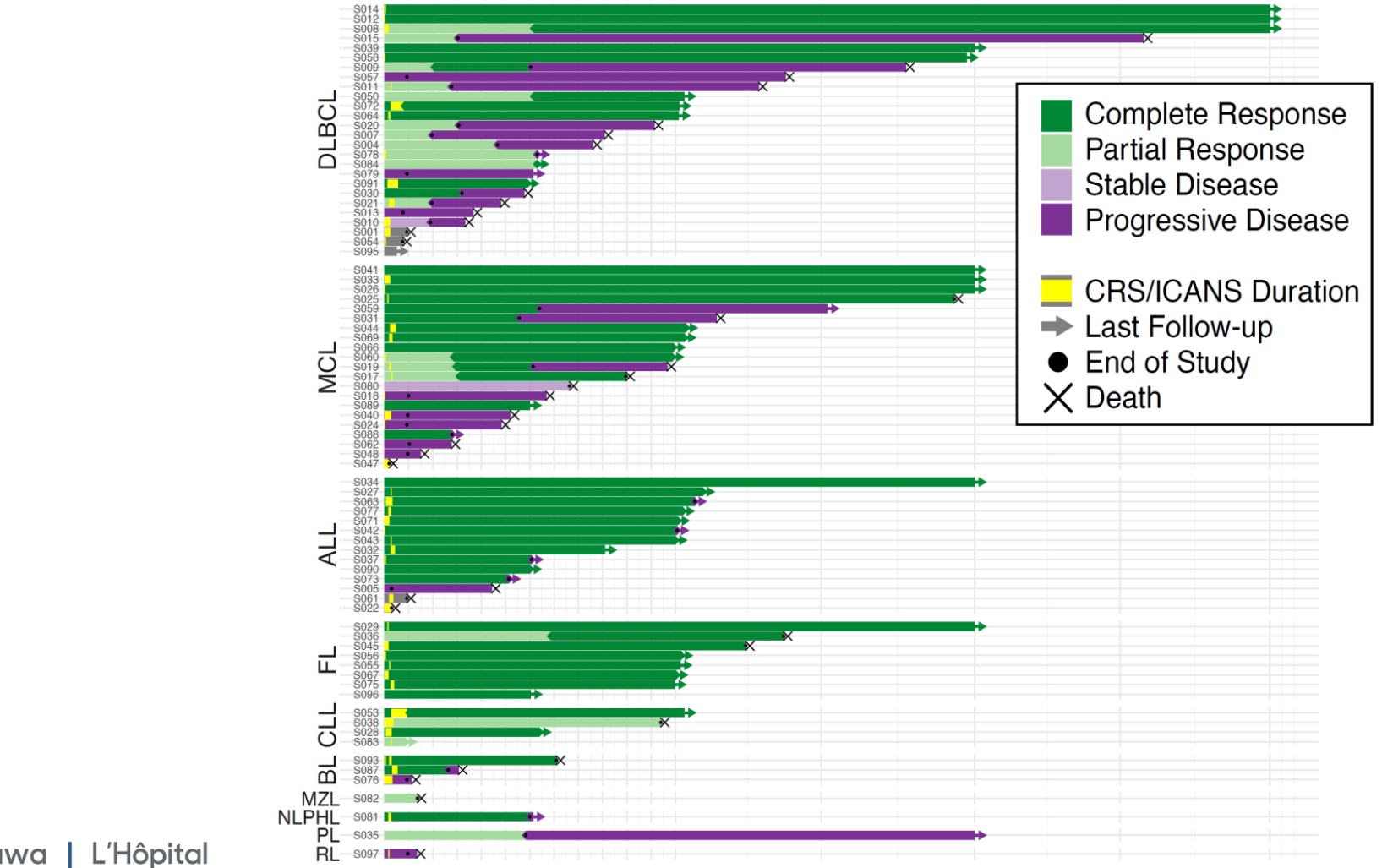
- Established 12-day manufacturing protocol

The Ottawa Hospital Research Institute | L'Hôpital d'Ottawa Institut de recherche

BioCanRx Canada's Immunotherapy Network Le réseau canadien d'immunothérapie

BC CANCER

CLIC-01 UNPUBLISHED RESULTS



DECENTRALIZING CLIC – OUR APPROACH

ONBOARDING NEW SITES:

(1)Gap Assessment: performed by first manufacturing centre to assess level of equivalence/appropriateness of site-specific technology and potential regulatory gaps.

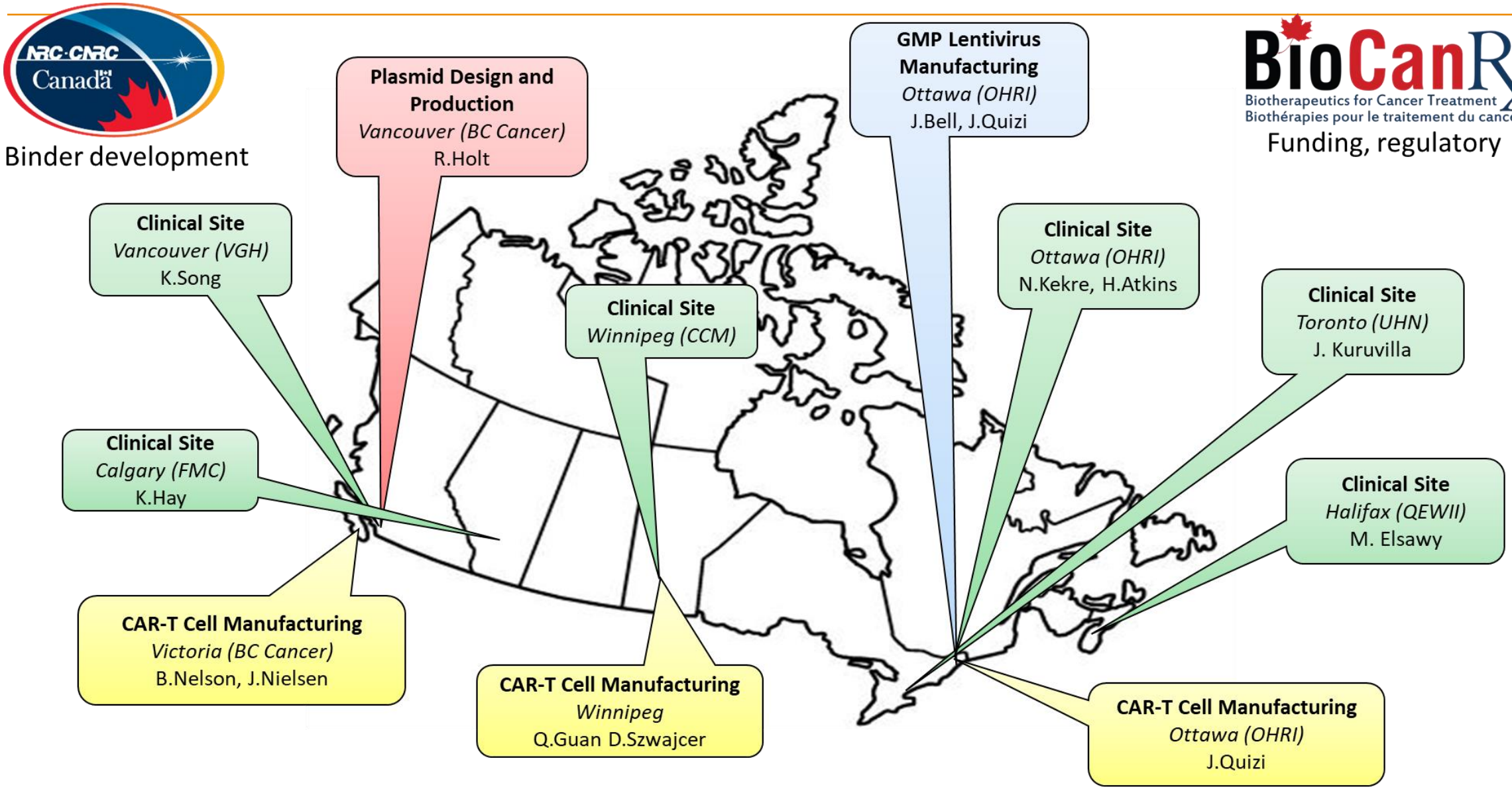
(2)Technology Transfer Package: provide the blueprint for how to implement the technology developed already to the recipient POC site.

(3)Audit: Quality and Manufacturing personnel from chosen site perform an onsite audit of the recipient POC site.

DECENTRALIZING CLIC - CHALLENGES

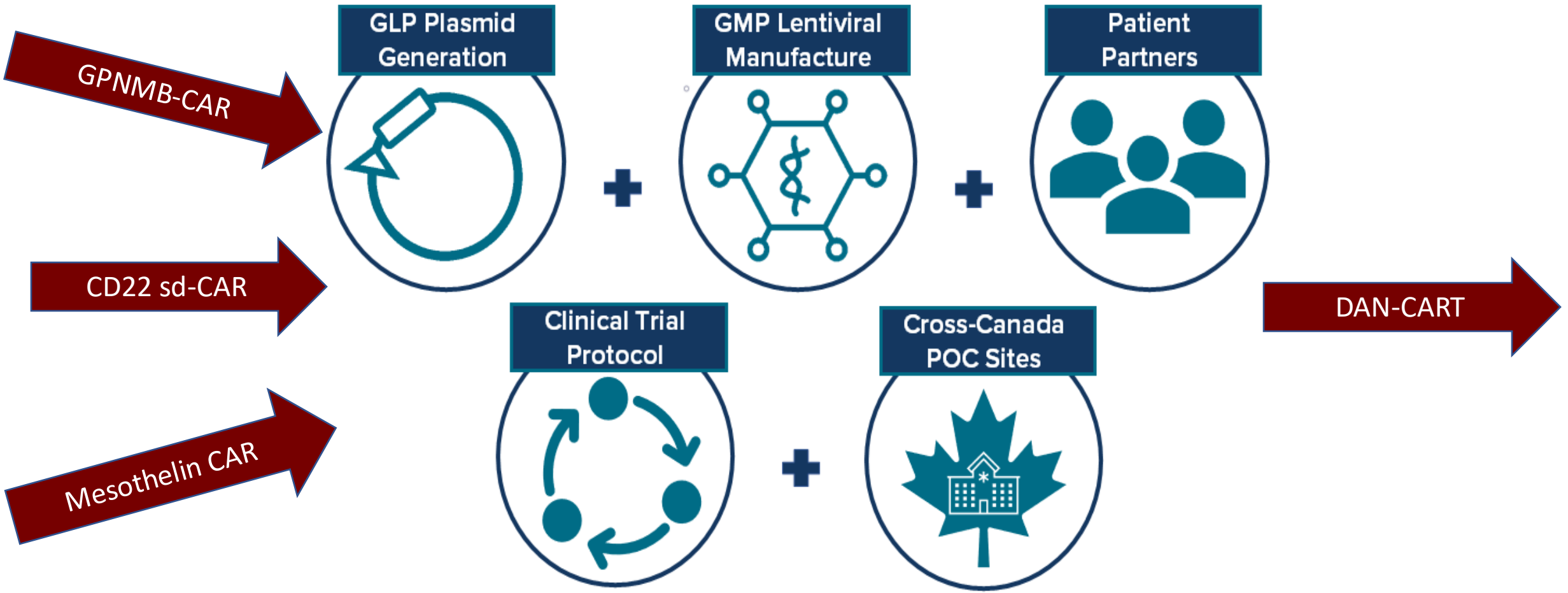
- Ability for different centres to meet regulatory requirements under one IND while having different operating and quality systems
- Multiple trials with different sponsorship and varying priorities and commitments at each manufacturing site make cohesion difficult
- Funding is short-term and trial specific, making investments into long-term infrastructure more difficult

CLIC NETWORK 2.0



CLIC NETWORK 2.0

BioCanRx
Canada's Immunotherapy Network
Le réseau canadien d'immunothérapie



Rapid Deployment of Made-in-Canada Clinical Trials

MARKET AUTHORIZATION – NEW CHALLENGES

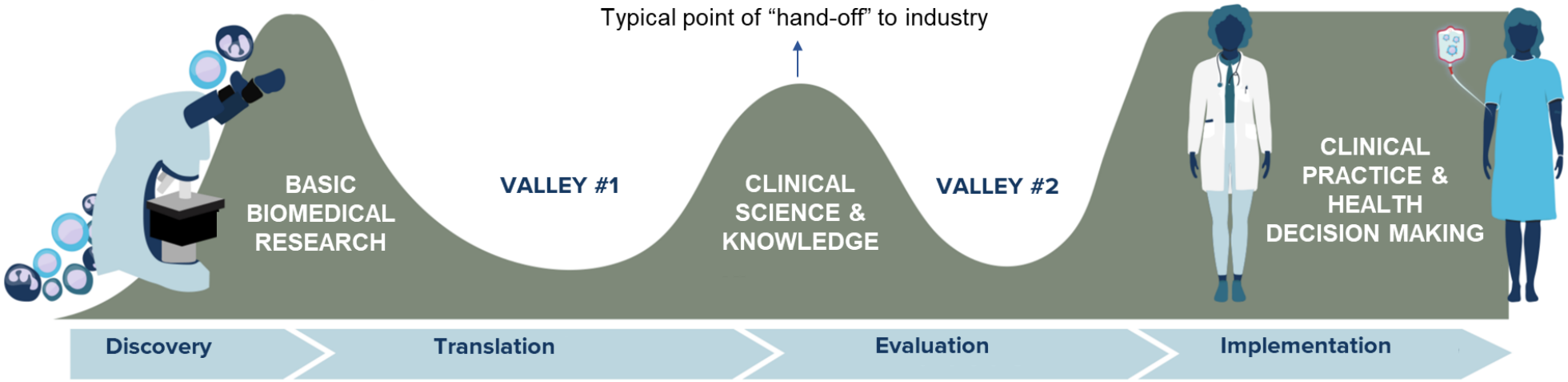
- Developing products for smaller patient populations still requires significant risk and investment, without high return on investment
- Existing models focus on fast-tracking based on clinical safety and efficacy, but these avenues not readily available for advances in biomanufacturing
- Left with conventional commercialization platforms for unconventional organizations just motivated to treat and possibly save more people
- Structured framework for when/how regulatory flexibilities apply to decentralized manufacturing is needed. Case-by-case flexibilities granted in the past, but not readily available.

MARKET AUTHORIZATION – CLIC

- Demonstrate safety and efficacy in robust clinical package
- Phase-specific versus licensed manufacturing: gap assessments, drug establishment licenses, strict GMP standards
- Health Canada meetings
- Sponsorship, funding, liability to organize → under NFP? B-corp? PPP? other?
- Discussions with funders to ensure funding available if product approved

CONCLUSIONS

Innovative decentralized manufacturing can facilitate the valleys from discovery to implementation



1) Decentralized biomanufacturing

2) Creating innovative health system adoption pathways

Requires regulatory & policy strategies

PROJECT TEAM AND ACKNOWLEDGEMENTS

Thank you to our patients!

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