Advancing Lentiviral Vector Manufacturing:

A Platform for Commercial Cell Therapy Success

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PROCESS DEVELOPMENT
ELEVATEBIO BASECAMP

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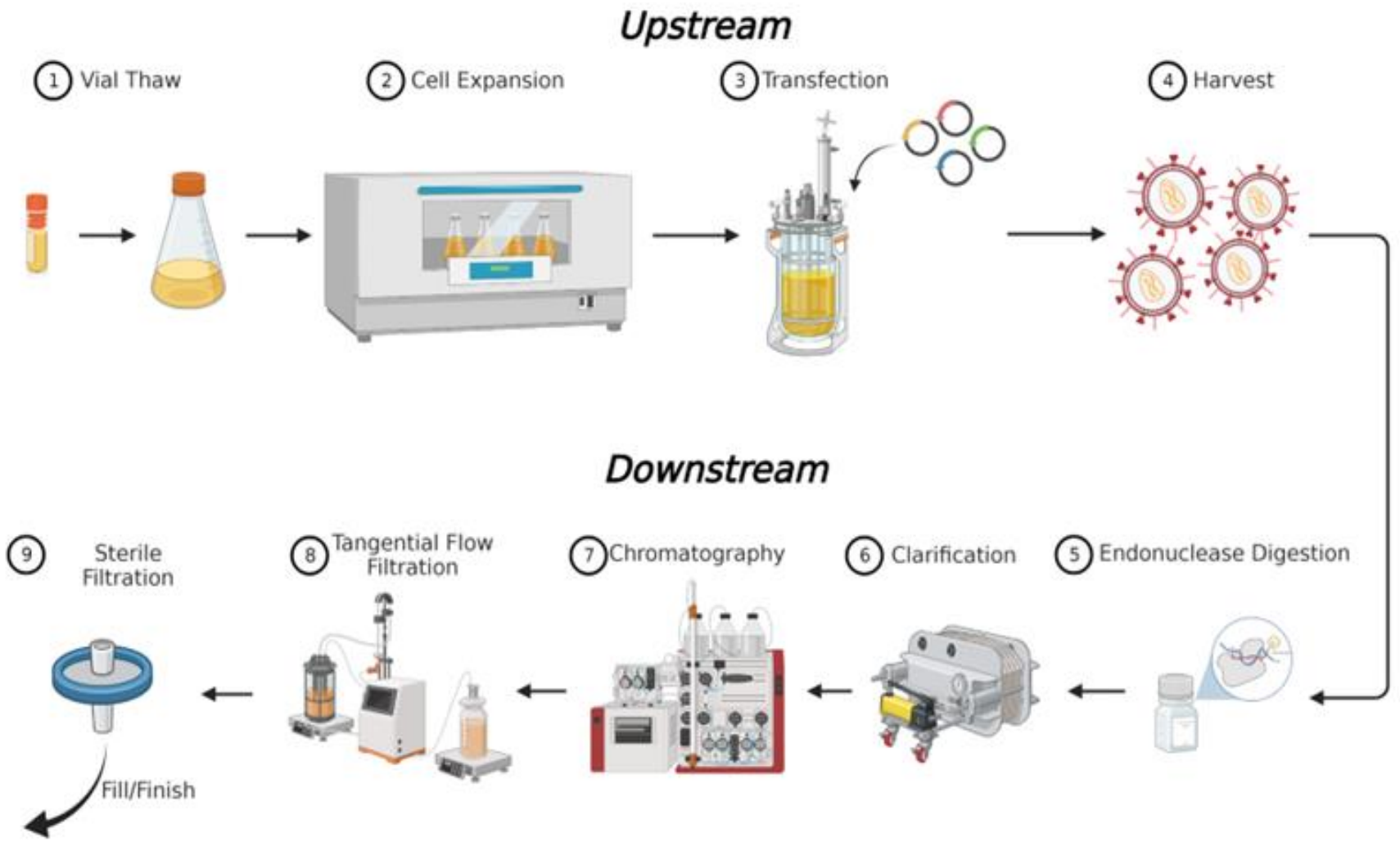
MAY 17TH 2025

Platform Process for Lentiviral Vector Manufacturing



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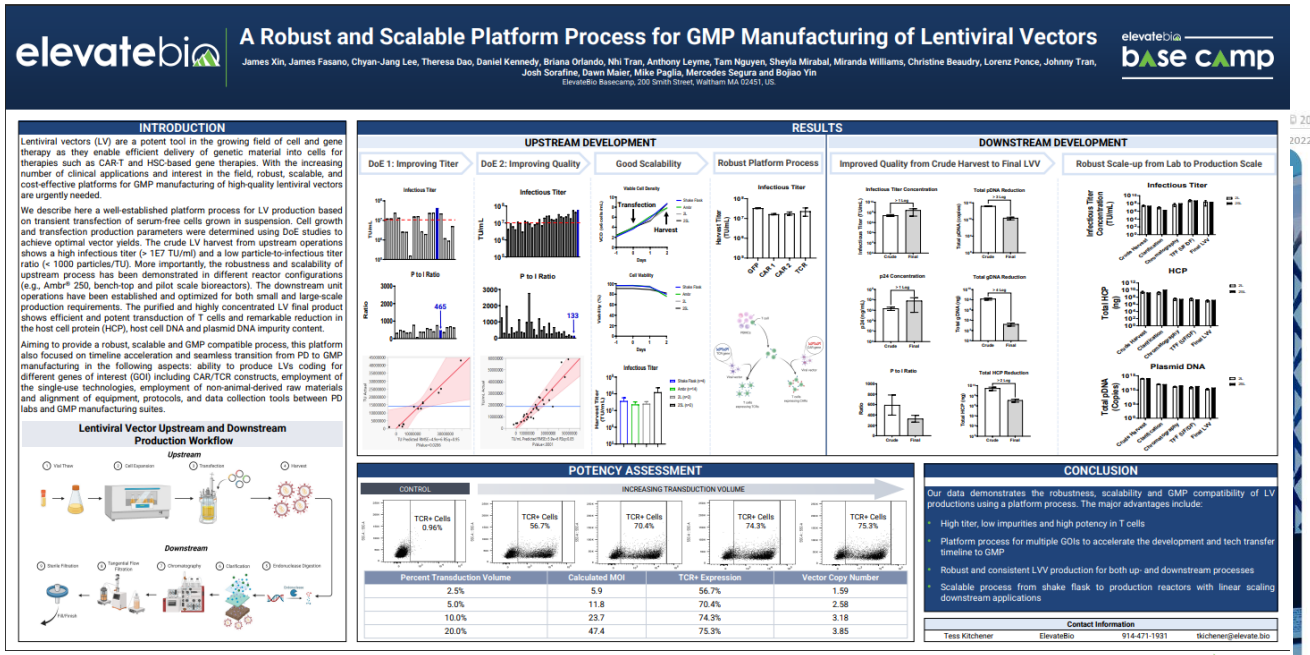
Platform Development History and Current Applications



- Platform development history has been shared in multiple CGT events, including ASGCT 2022.
- Platform used for 3 Phase I clinical programs:
  - Autoimmune disease trial, T-Reg cell program
  - Autoimmune disease trial, T-Reg cell program
  - Oncology trial, TCR-T cell program
- DMF available in US and Canada
- Currently, in preparation for late-stage clinical phases to help accelerate the timeline when needed.

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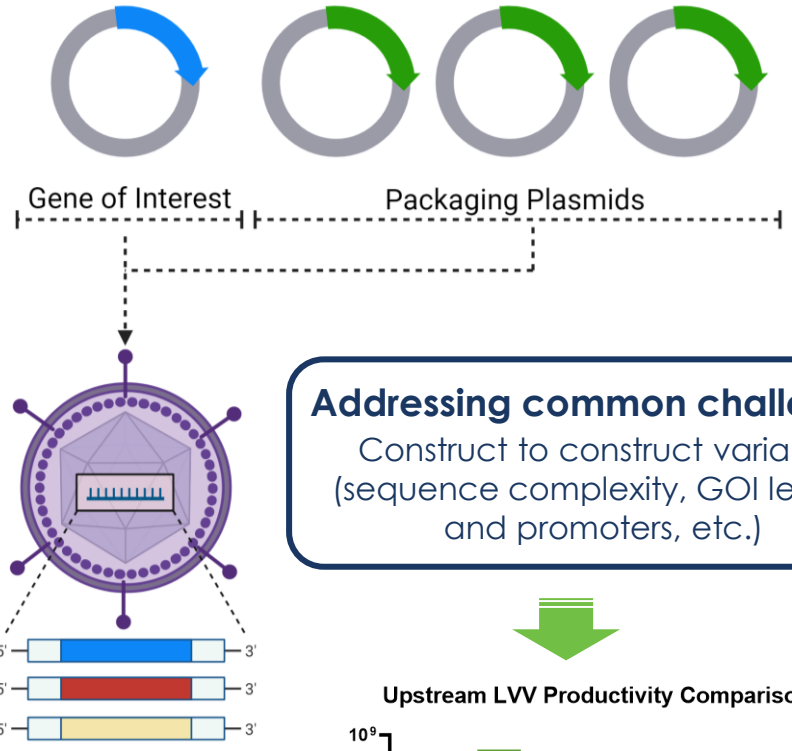
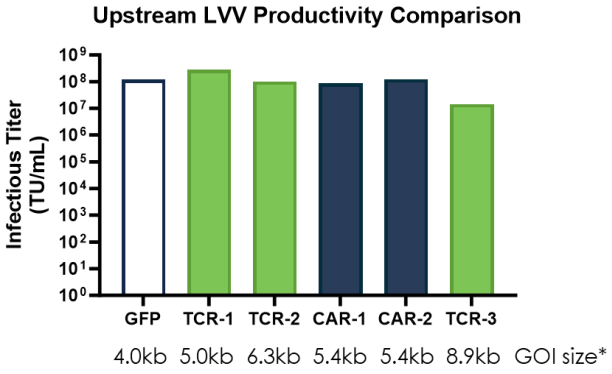
Lentiviral Vector Upstream Process Robustness and Scalability

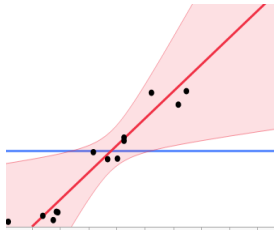


Addressing common challenges

Construct to construct variability (sequence complexity, GOI length, and promoters, etc.)



*LTR to LTR size in base pairs (bp)



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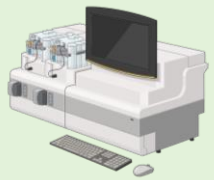
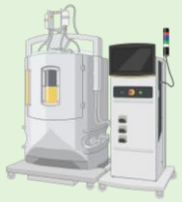
Shake Flask

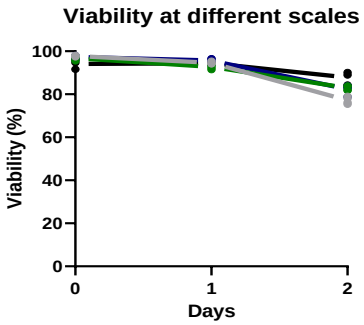


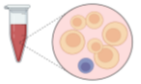
AMBR™ 250

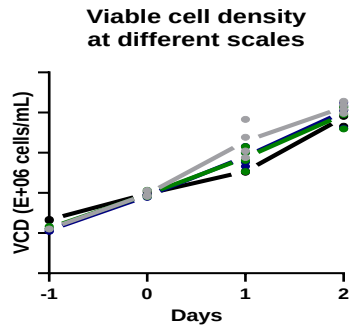
Bench-top Bioreactor



Production Scale



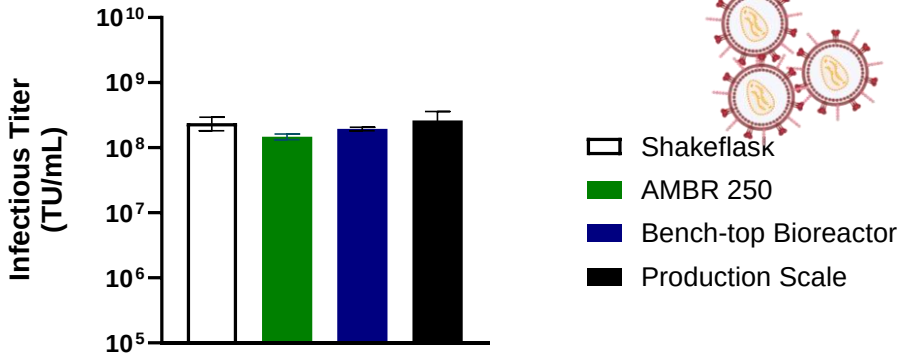




Addressing common challenges

Upstream scalability in different bioreactor systems.

LVV Productivity Across Scales



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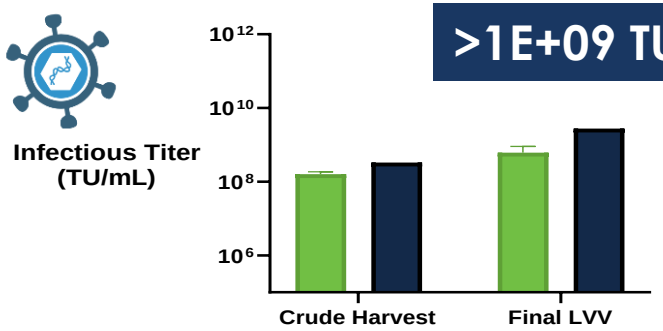
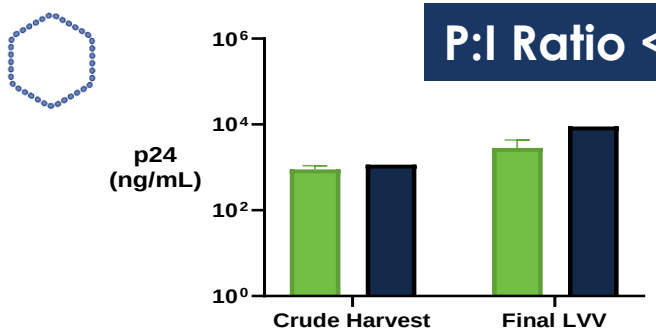
Ensuring Lentiviral Vector Quality via Effective Downstream Process

Lentiviral Product Comparison

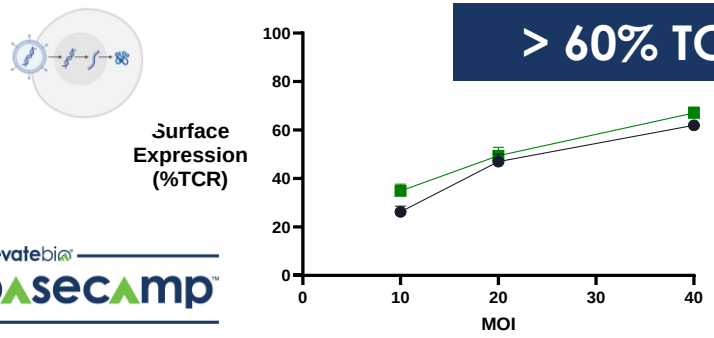
>1E+09 TU/mL



P:I Ratio < 100



> 60% TCR



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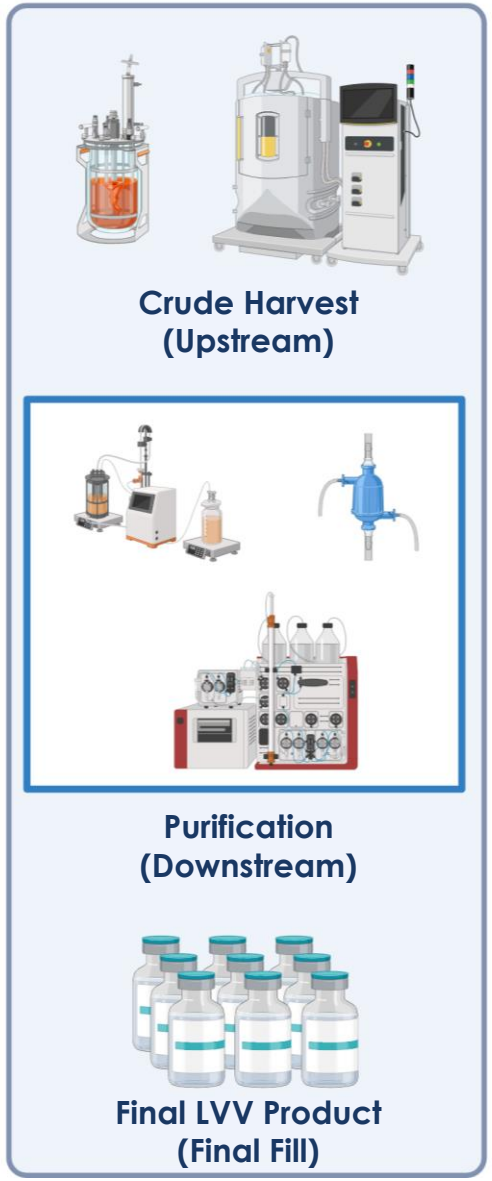

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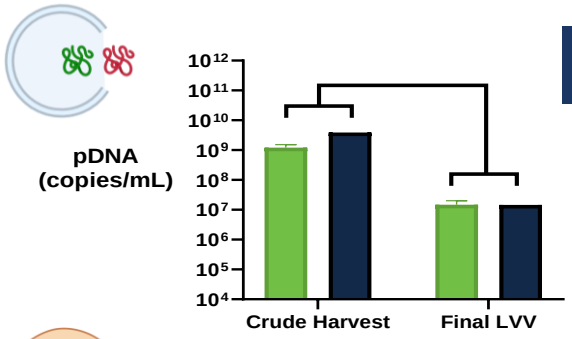
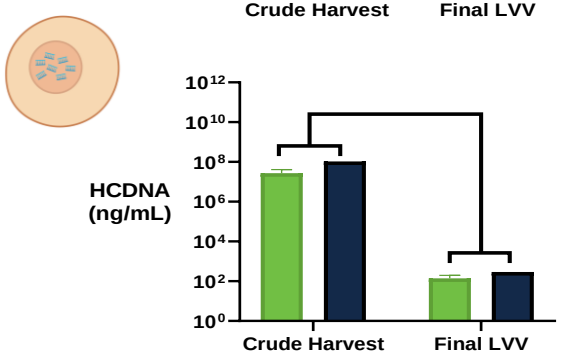
Lentiviral Impurity Comparison

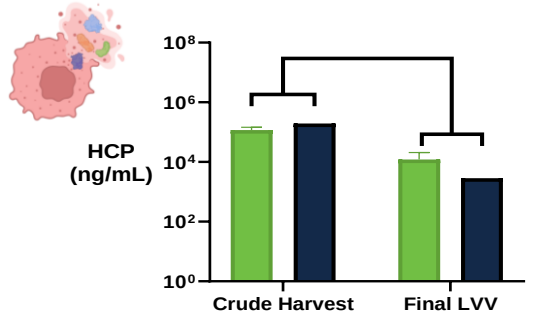
>3 Log



>5 Log

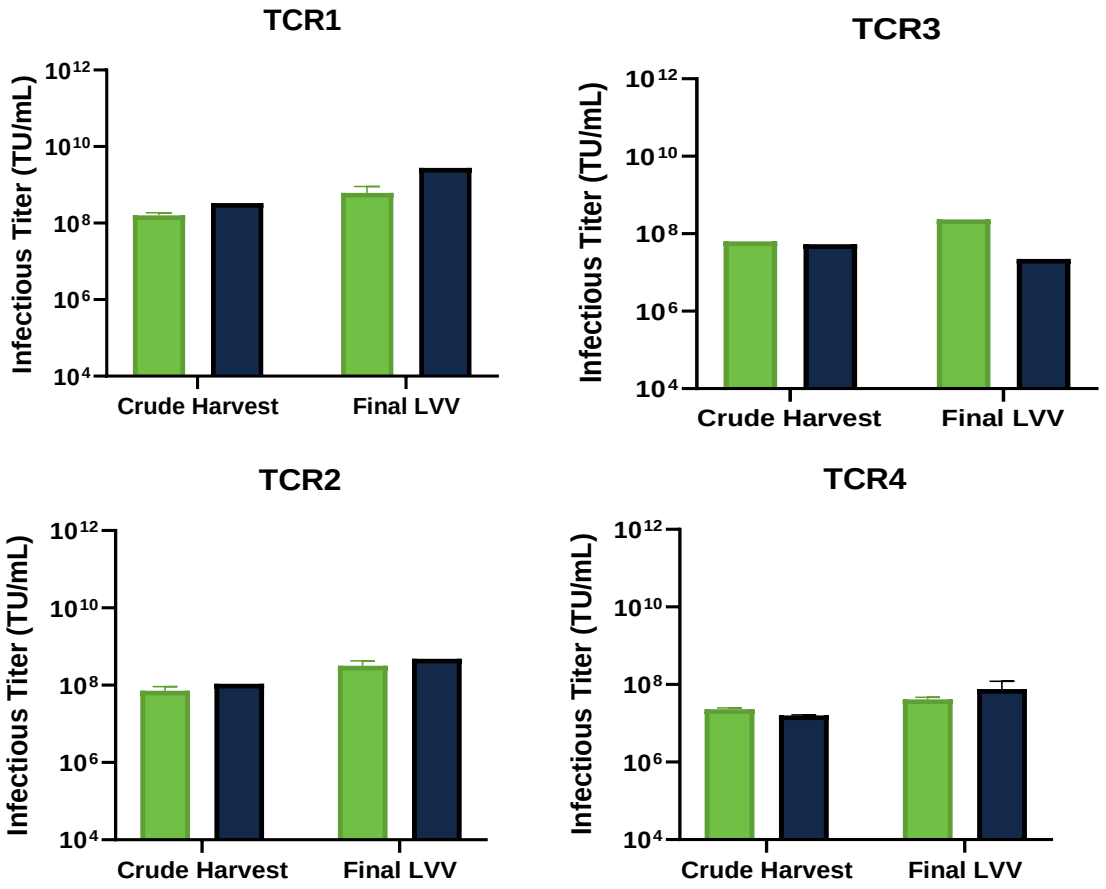


>2 Log

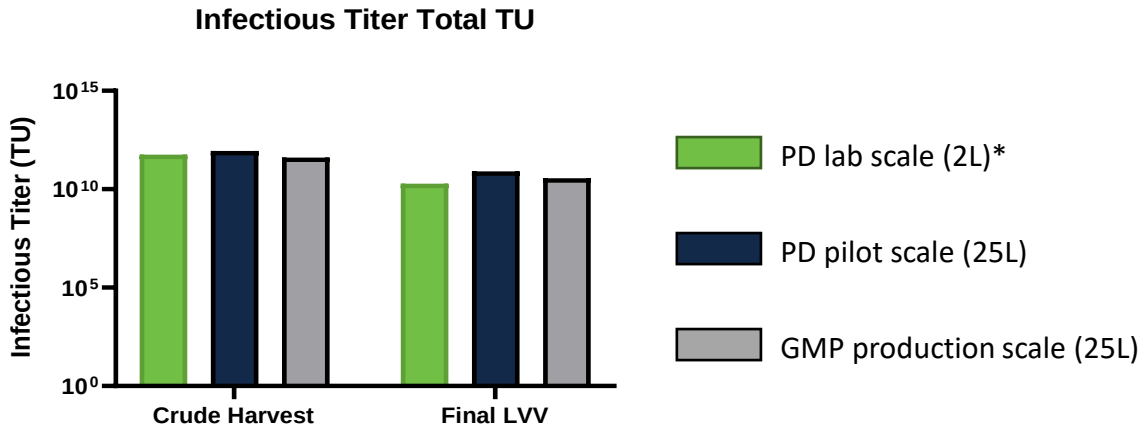


Consistent Performance Across Constructs and Scales

Production in PD using Multiple GOIs



PD and GMP Production



- Same process, multiple GOIs >> Process Consistency USP and DSP
- Consistent LVV production for 2L and 25L scales
- Comparable LVV yields from PD to GMP labs at scale.

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PD lab scale (2L)

PD pilot scale (25L)

* Data from 2L scale was normalized to 25L.

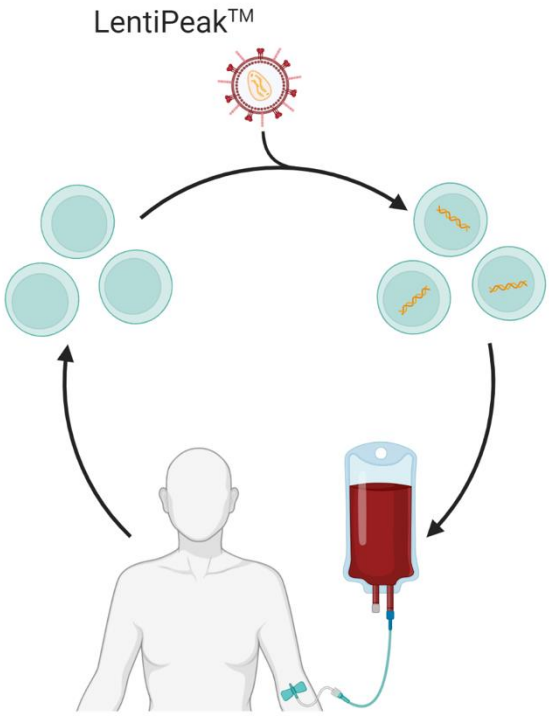
Release Panel for Lentiviral Vector Platform

	Quality Attribute	Assay
Strength/ Identity	Titer (TU/mL)	Cell-based assay + ddPCR
	Proviral Sequencing	Sequencing (outsourced)
	p24 GAG	ELISA
Potency	Biological activity	Product-specific assay (TBD)
Impurities	Particle to Infectivity ratio	Calculation
	Residual Plasmid DNA	ddPCR
	Residual Human DNA	ddPCR
	Host Cell Protein (HCP)	ELISA
Safety	RCL EOP Cells/Final Product	Cell-based assay (outsourced)
	Adventitious virus	Cell-based assay (outsourced)
	Sterility	Compendial (outsourced)
	Endotoxin	Compendial
	Mycoplasma	Compendial (outsourced)
Other	Appearance	Visual
	pH	pH
	Osmolality	Osmolality

- All release assays are developed and qualified.
- Need to be validated for pre-PPQ .
- Additional product-specific and characterization assays will be development as needed in support of late-stage activities.

Clinical-Scale Capacity Based on Real-World Cases

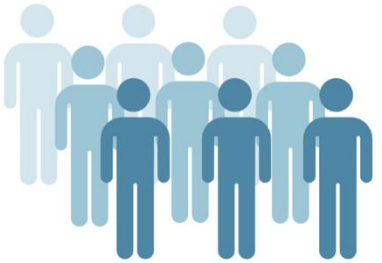
Platform process is used to supply batches for multiple clinical programs



One batch of production

Transduced Cells (millions)	Patient number (MOI = 40)
50	182
100	92
200	46

300-500M TCR Cells within 7-10 days



Treatment up to 180 patients*

Calculations:
Number of cells x MOI= TU needed per patient
TU from batch divided by TU/patient = Number of patients
Total TU from demo batch was 3.72e11 TU (not considering QC test needs)
180 patients* (a single 25L batch, depending on clinical trial design, level of surface expression and vector construct)

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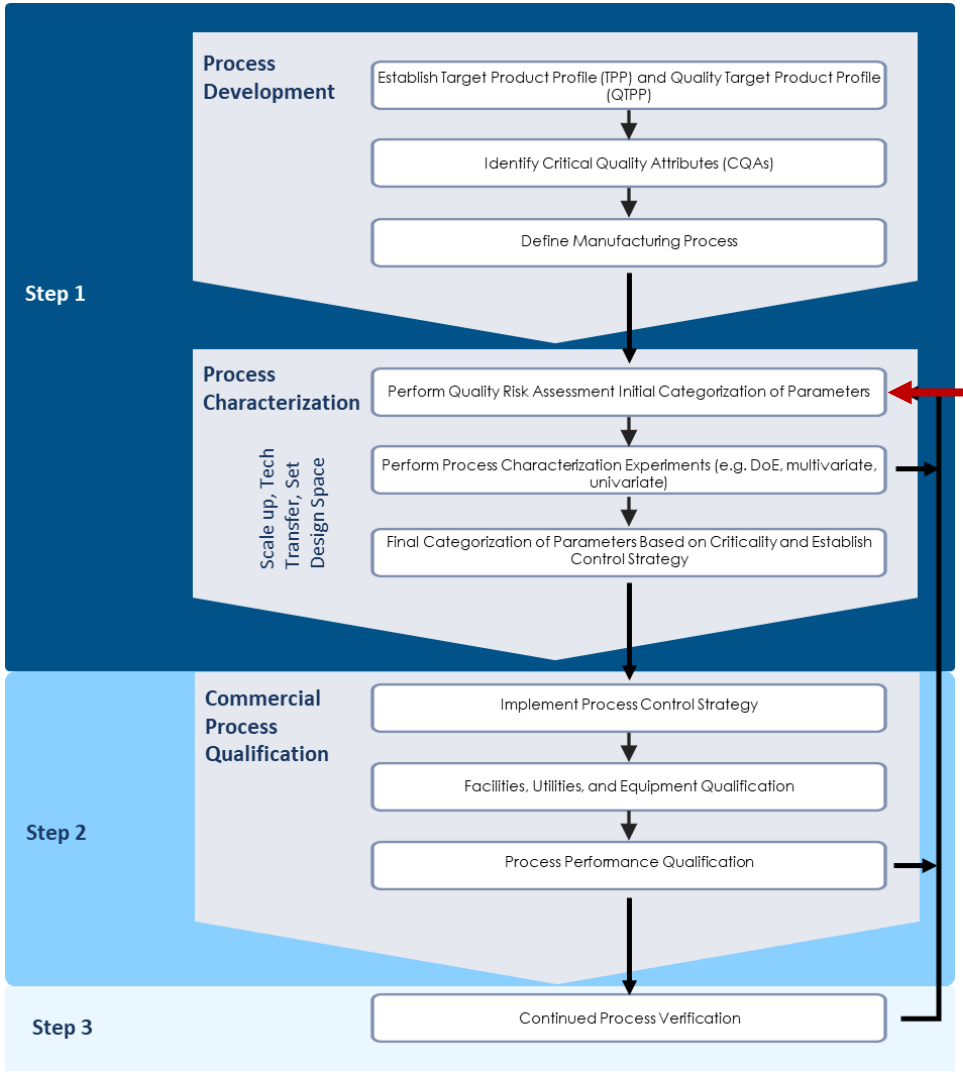
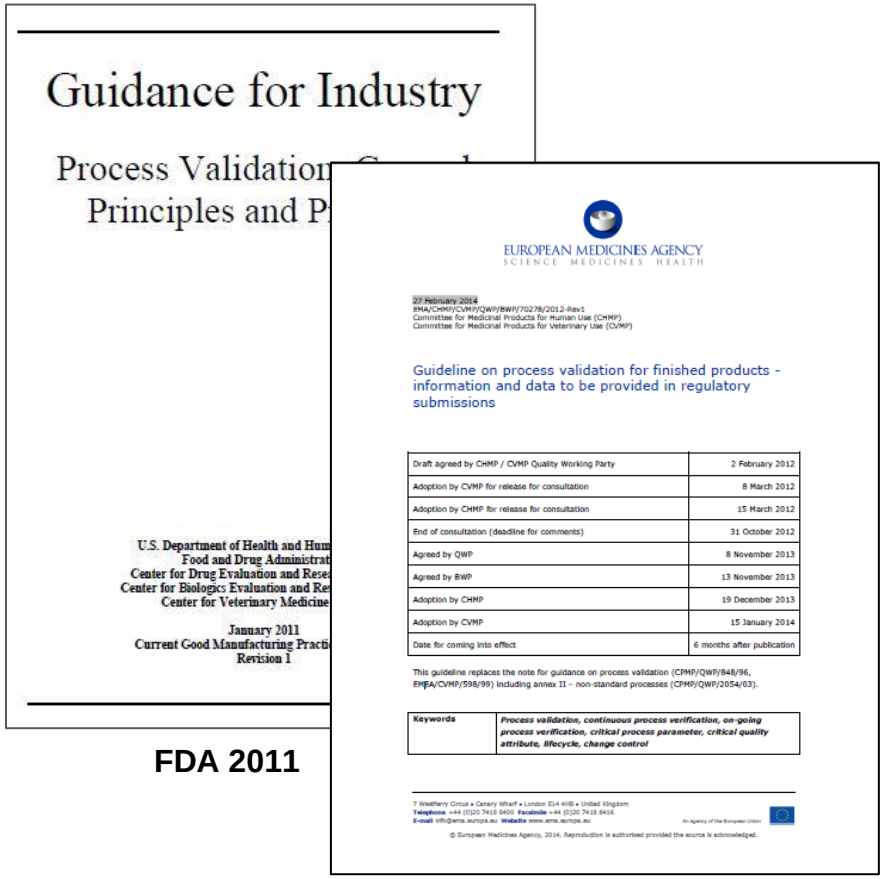
Process Validation: A Lifecycle Approach



Here now



FDA 2011

EMA 2014

Source: PDA Technical Report No. 60 (2013) Process Validation: A Lifecycle Approach

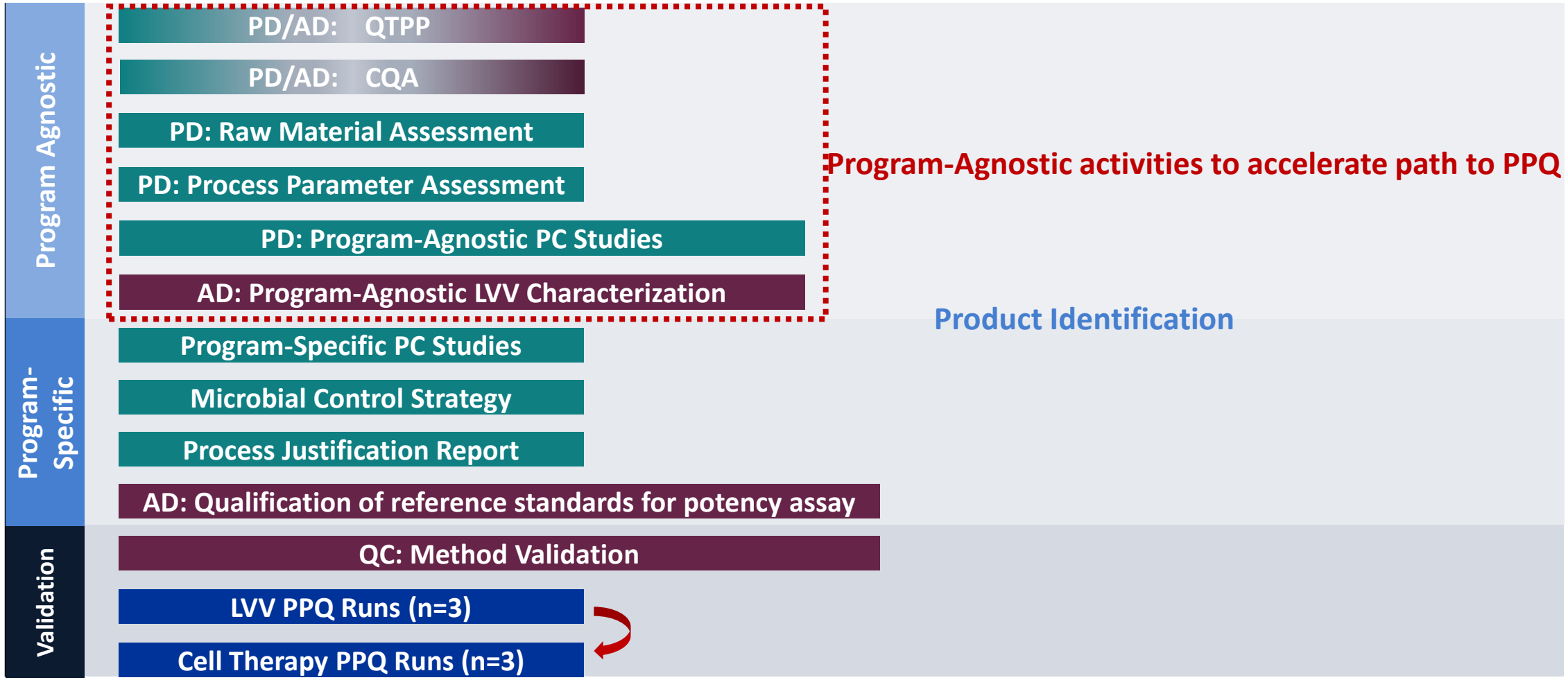
Documenting Program-Agnostic Quality Target Product Profile (QTPP)

QTPP Category		QTPP Element Attribute	QTPP Element Target	Guidance Document
Purified LVV Product Attributes	**Therapeutic Indication**	Product Specific	N/A	
	Description	The LentiPeak™ platform utilizes HEK 293 host cells and a four-plasmid transient transfection- based process to generate a LVV product for *ex-vivo* cell therapy applications.		
	Dose Volume	Product Specific		
	Dose Regimen	Product Specific		
	Volume per Vial	Comply with the test for extractable volume		
	Container Closure System	Sterile AT-Closed Vial designed for cryogenic storage		
	Container Closure Adapter	Sterile AT-Caps fitted to the vial		
	Formulation	Product Specific		
	Stability and Storage Conditions	Store frozen for 36 months		
Purified LVV Product Quality Attributes	**Safety**	Bacteria Endotoxin for Release Testing	< 6.25 EU/mL[2]	• FDA (2020)
		Mycoplasma	Negative for the Presence of Mycoplasma	• FDA (2020)
		Sterility*	No Growth	• Ph. Eur. 5.14 • 21 CFR 610.12
		Replication Competent Lentivirus on End of Production Cells and Crude Harvest Supernatant	No Replication Competent Lentivirus Detected	• FDA (2020)
		Viral Adventitious Agents	Negative for the Presence of Viral Contaminants	• ICH Q5A • ICH Q5D
		Container-Closure Integrity	N/A	N/A
	Identity	Identification	Uniquely identify the LVV product and distinguish it	• FDA (2023) • Ph. Eur. 5.14

QTPP Category		QTPP Element Attribute	QTPP Element Target	Guidance Document
			from other products in the facility	
	Content	pH	Compatible with LVV and cell therapy product stability data	• Ph. Eur. 5.14 • EMA (2018)
		Osmolality		• Ph. Eur. 5.14 • EMA (2018)
		Appearance		
	Purity	Residual Host-Cell DNA	< 10 ng/dose for DNA amount and below Approximately 200 bp for DNA size	• Ph. Eur. 5.14 • FDA (2020) • FDA (2010) • ICH Q6B • WHO (2013)
		Residual HEK293 Host-Cell Proteins	TBD	• Ph. Eur. 5.14 • FDA (2020) • EMA (2010) • EMA (2018)
		Residual Plasmid DNA	TBD	• Ph. Eur. 5.14 • FDA (2020) • EMA (2010) EMA (2018)
		Residual Endonuclease	TBD	• Ph. Eur. 5.14 • FDA (2020) • EMA (2010) • EMA (2018) • ICH Q6B
		Residual E1A	TBD	• Ph. Eur. 5.14 • FDA (2020) • EMA (2018)
		Residual Heparin Chromatography Ligand	TBD	• FDA (2024) • FDA (2013) • FDA (2016)
		Co-packaged Unwanted Genetic Sequences	TBD	• EMA (2018)
		Residual Reagents during Manufacture	TBD	• FDA (2020) • Ph. Eur. 5.14
		Ratio of Vector-Particle Concentration to Infectious Vector Titer	TBD	• Ph. Eur. 5.14 • EMA (2018) • FDA (2020)
	Strength	Transduction (Infectious) Titer	Product Specific	• EMA (2018) • Ph. Eur. 5.14
		Physical p24 Titer	Product Specific	• Ph. Eur. 5.14

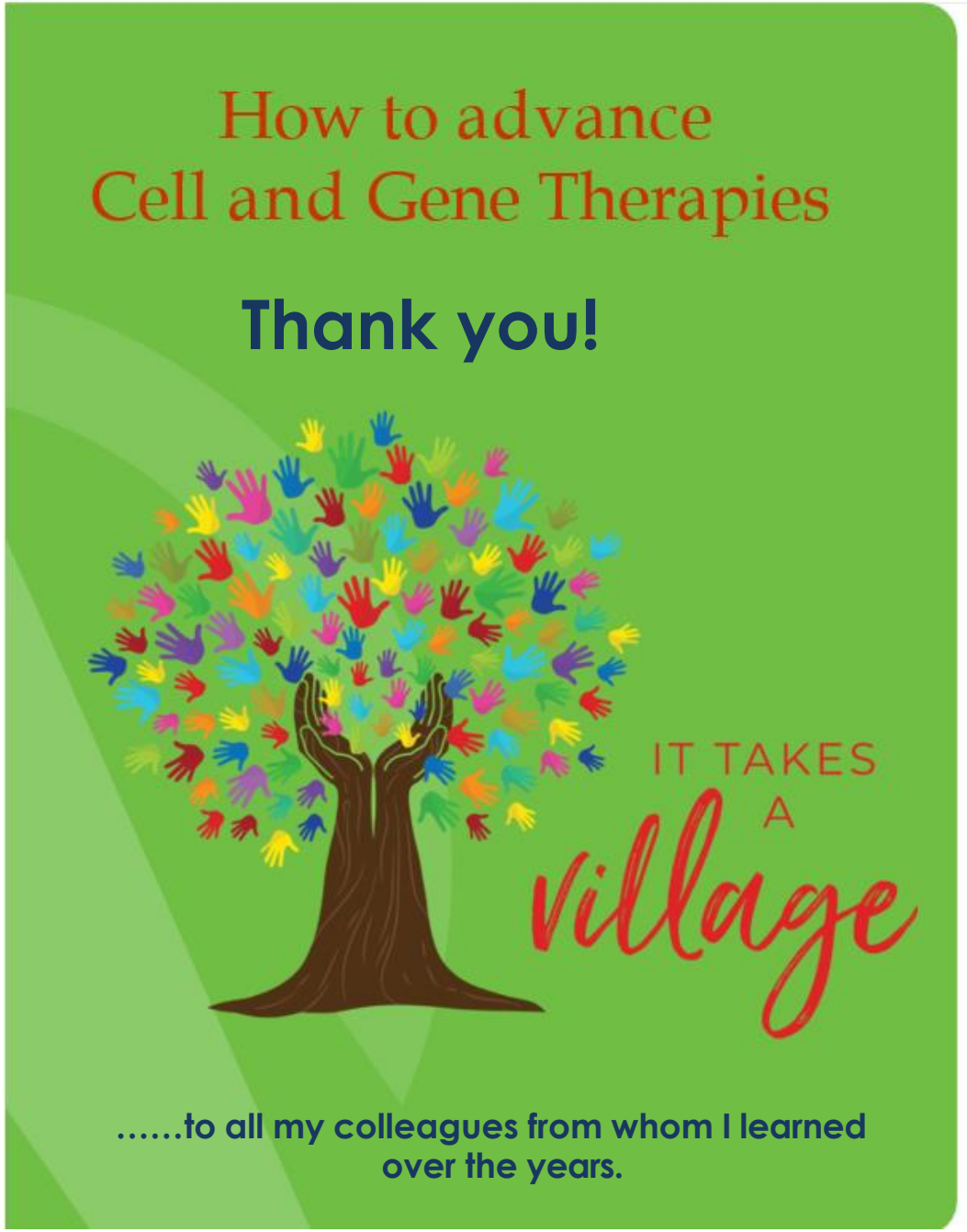
- Most of the QTPP attributes can be assessed as program-agnostic ones, including Safety, Identity, Content and Purity.
- Once specific product is identified, a product specific QTPP will be drafted using this one as a baseline

QbD Strategy to Accelerate PPQ Readiness



Recap and Thank You

- A LVV platform was developed and its being used in 3 phase I clinical programs.
- The platform has shown the robustness and scalability and delivers high quality LVV for multiple indications
- A phase appropriate DMF is available in US and Canada to facilitate regulatory IND filings.
- A product agnostic quality by design (QbD) strategy is currently being used to accelerate PPQ readiness



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