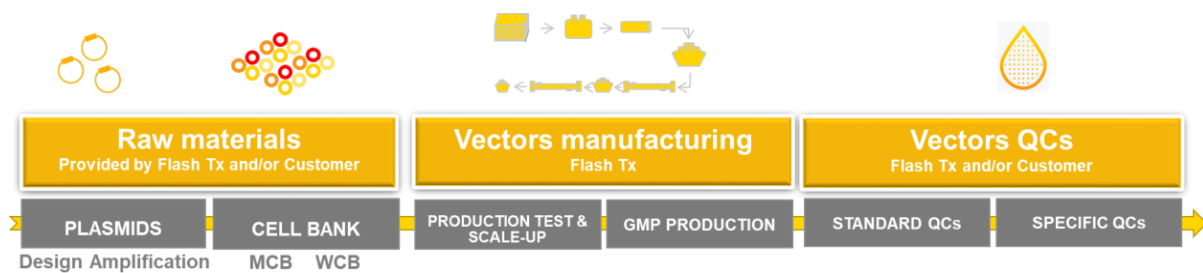


GMP MANUFACTURING OFFER

While supplying high quality vectors for research and preclinical purpose, the Flash Therapeutics' platform is now accelerating its development by providing GMP large-scale Lentiviral vectors production for clinical applications.

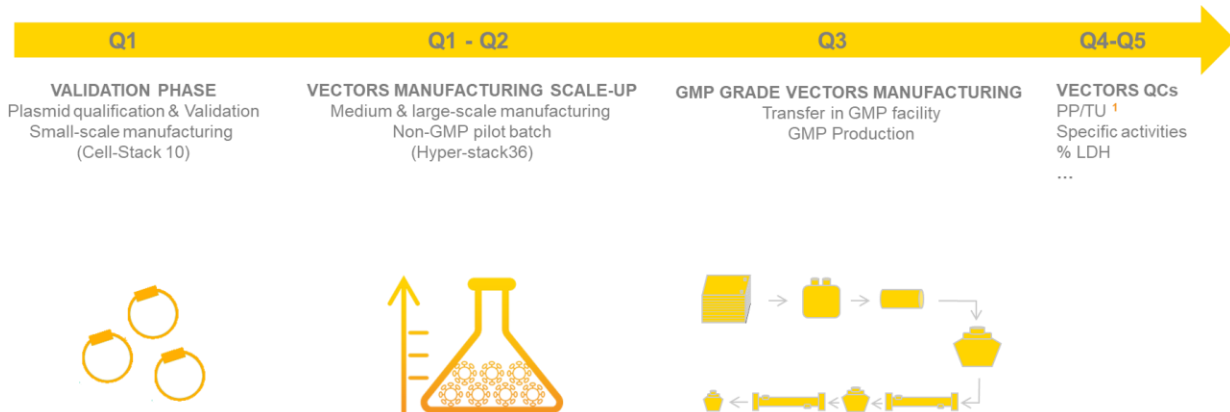
1. An integrated offer: a continuum from R&D to clinic

Flash Therapeutics offers high level expertise to develop, conduct and validate custom studies, optimize and scale-up manufacturing projects. Our CDMO activity is conducted on a customized basis according to your starting material:



2. Qualification plan

The validation stages of a GMP production project are done step by step in close cooperation with our customers.



¹: Potency assay to be defined

2.1 Q1 Validation phases

Stages	Assays
1.a- Plasmid sequence validation	
Sequence of each plasmid	Plasmid Sequencing
Sequence analysis	Bioinformatic analysis
Full plasmid QCs	Sterility, Gel electrophoresis, DO, restriction...
Go/NoGo	
1.b- Crude vector Productions (~ 10⁶ TU/ml & 50 ml)	
Production of crude supernatant (~ 10 ⁶ TU/ml; 50ml)	Quadri-transfection of 293T cells
Particles basic QCs (TU, PP, Protein, DNA, %LDH) to measure crude specifications	Functional titer (TU?), p24 (PP), Bradford, Picogreen, LDH detection
Go/NoGo	
1.c- Small scale vector productions in CellStacks-10 (~10⁹ TU/ml & 1 ml) 3 productions to show the low titer variability	
Production, concentration and purification of 1 ml	Quadri-transfection of 293T UF
Particles basic QCs (TU, PP, Protein, DNA, sterility)	Functional titer (Potency assay to be defined), p24, Bradford, Picogreen, LDH detection
Go/NoGo	

2.2 Q1-Q2 Vector Manufacturing Scale-up

Stages	Assays
2.a- Medium scale vector production in HyperStacks-36 (~ 10⁹ TU/ml & 3-4 ml)- 3 productions to show the low titer variability	
Production, concentration and purification of 4ml	Quadri-transfection of 293T UF
Particles basic QCs (TU, PP, Protein, DNA, sterility)	Functional titer (Potency assay to be defined), p24, Bradford, Picogreen, LDH detection
Go/NoGo	
2.b- Large scale vector production - 1 line of 4 HyperStacks-36 (~ 10⁹ TU/ml & 15 ml)	
Production, concentration and purification of 15ml	Quadri-transfection of 293T UF
Particles basic QCs (TU, PP, Protein, DNA, sterility)	Functional titer (Potency assay to be defined), p24, Bradford, Picogreen, LDH detection
Go/NoGo	
2.c- Non GMP Pilot batch production - 2 lines of 4 HyperStacks-36 (~ 10⁹ TU/ml & 30 ml)	
Production, concentration and purification of 30ml	Quadri-transfection of 293T UF
Particles basic QCs (TU, PP, Protein, DNA, sterility)	Functional titer (Potency assay to be defined), p24, Bradford, Picogreen, LDH detection
Go/NoGo	

2.3 Q3 GMP Grade Vector Manufacturing

Stages	Assays
3.a- Transfer in GMP facility - Large scale vector production 1 line of 4 HyperStacks-36 (~ 10⁹ TU/ml & 15 ml)	
Production, concentration and purification of 4ml	Quadri-transfection of 293T UF
Particles basic QCs (TU, PP, Protein, DNA, sterility)	Functional titer (Potency assay to be defined), p24, Bradford, Picogreen, LDH detection
Go/NoGo	
3.b- Transfer in GMP facility - GMP Pilot batch production 2 lines of 4 HyperStacks-36 (~ 10⁹ TU/ml & 30 ml)	
Production, concentration and purification of 15ml	Quadri-transfection of 293T UF
Particles basic QCs (TU, PP, Protein, DNA, sterility)	Functional titer (Potency assay to be defined), p24, Bradford, Picogreen, LDH detection
Go/NoGo	
2.c- GMP batch production - 2 pooled productions of 2 lines of 4 HyperStacks-36 (~ 10⁹ TU/ml & 60 ml)	
Production, concentration and purification of 60ml	Quadri-transfection of 293T UF
Particles basic QCs (TU, PP, Protein, DNA, sterility)	Functional titer (Potency assay to be defined), p24, Bradford, Picogreen, LDH detection
Go/NoGo	

2.4 Q4 GMP Vector QCs

Filled product	-
Eur Ph 5.14	Osmolality
	pH
	Extractable volume
	BSA assay
	Vector particle concentration
	Infectious titer
	Vectors particles/infectious particles ratio
	Expression of the genetic insert
	Sterility
	Endotoxins
	Biological activity

For specific applications or for testing, feel free to contact us at tech@flashtherapeutics.com.