AGC Biologics
Your friendly CDMO expert

From Bottleneck to Breakthrough:

Scaling the Viral Vector Without Breaking the Bank

€1,000 per CAR-T patient is already achievable

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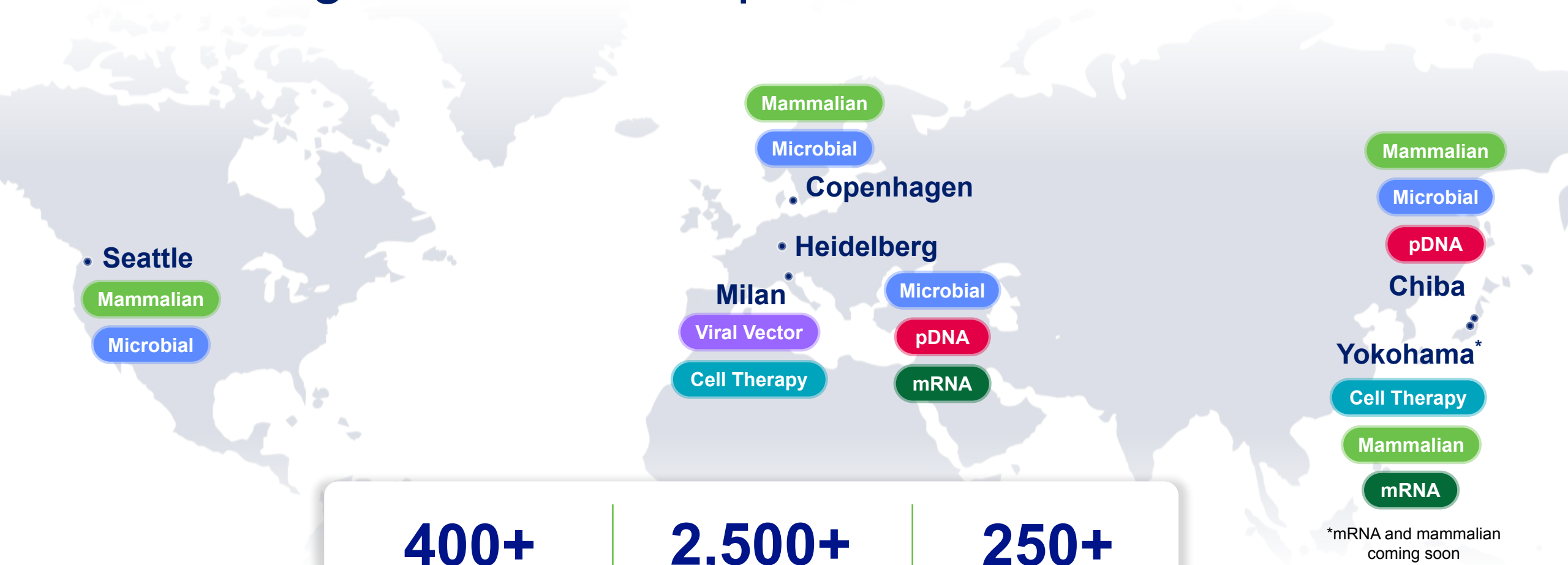
AGC
Life Science Company

Our global network spans three continents



*mRNA and mammalian coming soon

400+	2,500+	250+
PROJECTS SUPPORTED	TEAM MEMBERS	CUSTOMERS SERVED

Milan Site

Italy

Cell Therapy | Viral Vector

- **30 years** of industry-leading expertise and **14 commercial approvals**
- Cell therapy and viral vector clinical and commercial capabilities with multi-room GMP capacity
- **AAV / LVV / RVV** manufacturing and fill / finish
- Suspension: 50 L, 200 L, and 1,000 L bioreactors
- Adherent: 24 L / 48 L cell factories, 200 - 750 L fixed-bed bioreactor (iCELLis™ 500)
- **Cell therapy**: 10+ suites performing open and closed processes for both autologous and allogeneic products
- Processes and capabilities for virtually any cell type, $CD34^{+}$HSC, T-Cells, NK Cells, hMSCs and more.
- **160+ in-house analytical methods** ensure rapid turnaround
- 20+ active clients, the site has supported 50+ projects.
- Multiple viral vectors and cell therapy products approved in EU and US, and 15 process validation campaigns completed to date and 4 planned over the coming years

AGC Life Science Company

Commercially Approved Cell and Gene Therapy Products

Ex vivo

Product Name	Company	Approval	Product Type
Strimvelis®	**Fondazione Telethon**	**EMA**	**CD34+ (RVV)**
Zalmoxis®	**Molmed**	**EMA□**	**Allo-T (RVV)**
Kymriah®	Novartis	FDA/EMA	CAR-T(LVV)
Yescarta®	Kite/Gilead	FDA/EMA	CAR-T (RVV)
Zynteglo®	Bluebird Bio	EMA□/FDA	CD34+ (LVV)
Tecartus™	Kite/Gilead	EMA/FDA	CAR-T (RVV)
Libmeldy/Lenmeldy™	**Orchard**	**EMA/FDA**	**CD34+ (LVV)**
Skysona™	Bluebird Bio	EMA□/FDA	CD34+ (LVV)
Abecma®	Brystol-Myers	EMA/FDA	CAR-T (LVV)
Breyanzi®	Brystol-Myers	EMA/FDA	CAR-T (LVV)
Carvytki™	Janssen	EMA/FDA	CAR-T (LVV)
Lyfgenia™	BlueBird Bio	FDA	CD34+ (LVV)
Casgevy™	CRISPR/Vertex	FDA/EMA	CD34+ (CRISPR)
Kresladi™	**Rocket Pharma**	***FDA****	CD34+ **(LVV)**
Aucatzyl™	**Autolus**	***FDA/EMA***	CAR-T **(LVV)**
Afami-Cel	Adaptimmune	*FDA**	TCR-T (LVV)
Waskyra	**Fondazione Telethon**	**EMA/FDA**	**CD34+ (LVV)**
Zevaskyn™	Abeona	FDA	Keratinocytes (RVV)

In-vivo

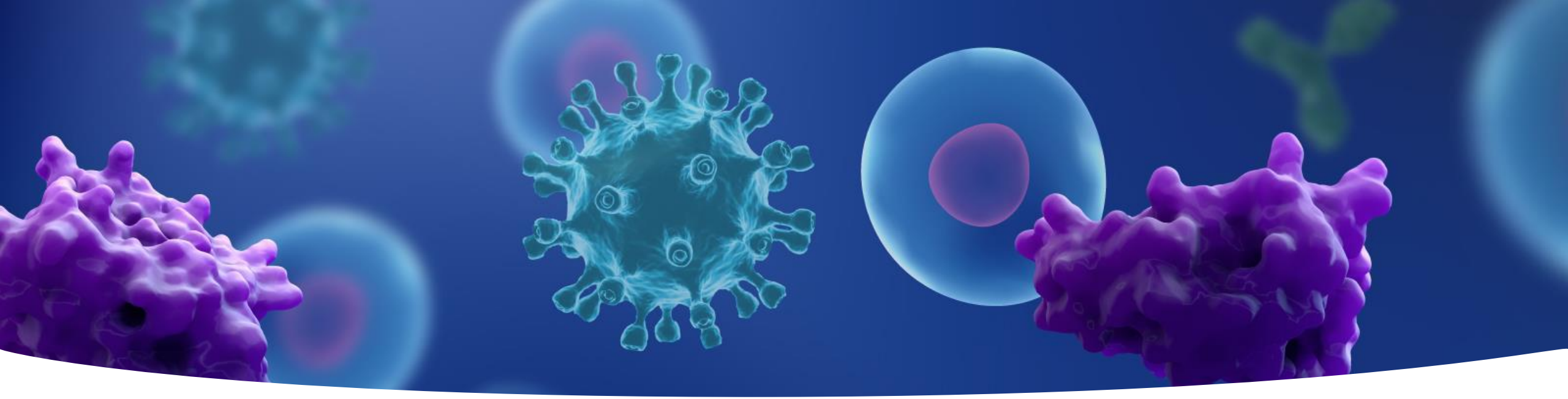
Product Name	Company	Approval	Product Type
Glybera®	uniQure	EMA□	AAV
Imlygic®	Amgen	EMA/FDA	HSV
Luxturna™	Spark/Novartis	FDA/EMA	AAV
Zolgensma®	Novartis	FDA/EMA	AAV
Upstaza™	PTC	EMA/FDA*	AAV
Hemgenix®	CSL Behring	FDA/EMA	AAV
Roctavian™	BioMarin	EMA/FDA	AAV
Adstiladrin®	Ferring	FDA	AdV
Vyjuvek™	Krystal Biotech	FDA/*EMA**	HSV
Elevidys	Sarepta	FDA	AAV

FDA/EMA* = BLA/MAA submitted

Green background designates products ***manufactured by AGC Biologics***

Non-GM cell therapy products not included

□ = *withdrawn from market/MA not renewed*



Achieving the €1,000 cost for LVV per CAR-T Patient

Key Message

Achieving €1,000 cost for Lentiviral Vector (LVV) per patient production is possible

- **Optimize Operations:** Select locations with lower labor costs and high employee retention to maximize expertise and output. Ensure that large-scale facilities are highly utilized to make economies of scale effective.

- **Standardize the Platform:** Adopt a standardized approach using off-the-shelf starting materials to drastically cut initial investment and timelines. Implement close processes completely single–use.

- **Maximize Manufacturing Efficiency:** Increase production yield and scale up batch sizes to match clinical demand. This spreads fixed costs over a larger number of doses, directly lowering the cost per dose.

LVV should not be seen merely as a cost.

It is the "engine" of the therapy, and investing in its quality and consistency is a direct investment in patient safety, regulatory success, and reducing the risk of costly batch failures.

Deconstructing the cost of LVV

Batch Price

Personnel
- Location
- Retention

Facility
- Size / Classification
- Utilization

Materials
- Cell Lines
- Plasmids
- BoM

Number of Patients per Batch

Batch Size
- Process Scale-up
- Capacity

Productivity
- Productivity
- Process Yields

Quality
- Testing capability

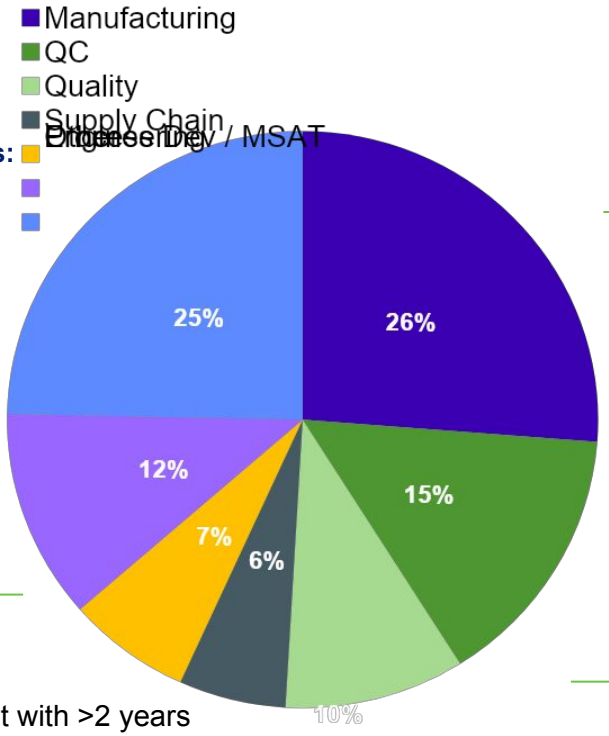
Ideal location has low cost of labor and high retention rate

Region / Country	Labour Cost Level (€/hr)
Luxembourg (EU)	~55
Denmark (EU)	~50
United States	~45–50
Belgium (EU)	~48
France (EU)	~44
Germany (EU)	~43
Japan	~35–40
Italy (EU)	**~31**
South Korea	~30–35
Spain (EU)	~25
Eastern EU (e.g., Romania)	~10–13
China	< ~15

Data for EU: Source Eurostat 2024
Data for US and JPN: Source Organisation for Economic Co-operation and Development (OECD)

Number of Employees:
351

Retention Rate:
94%



Average Tenure of Leadership Team:
>15 Years

Average Overall Tenure*:
>5 Years

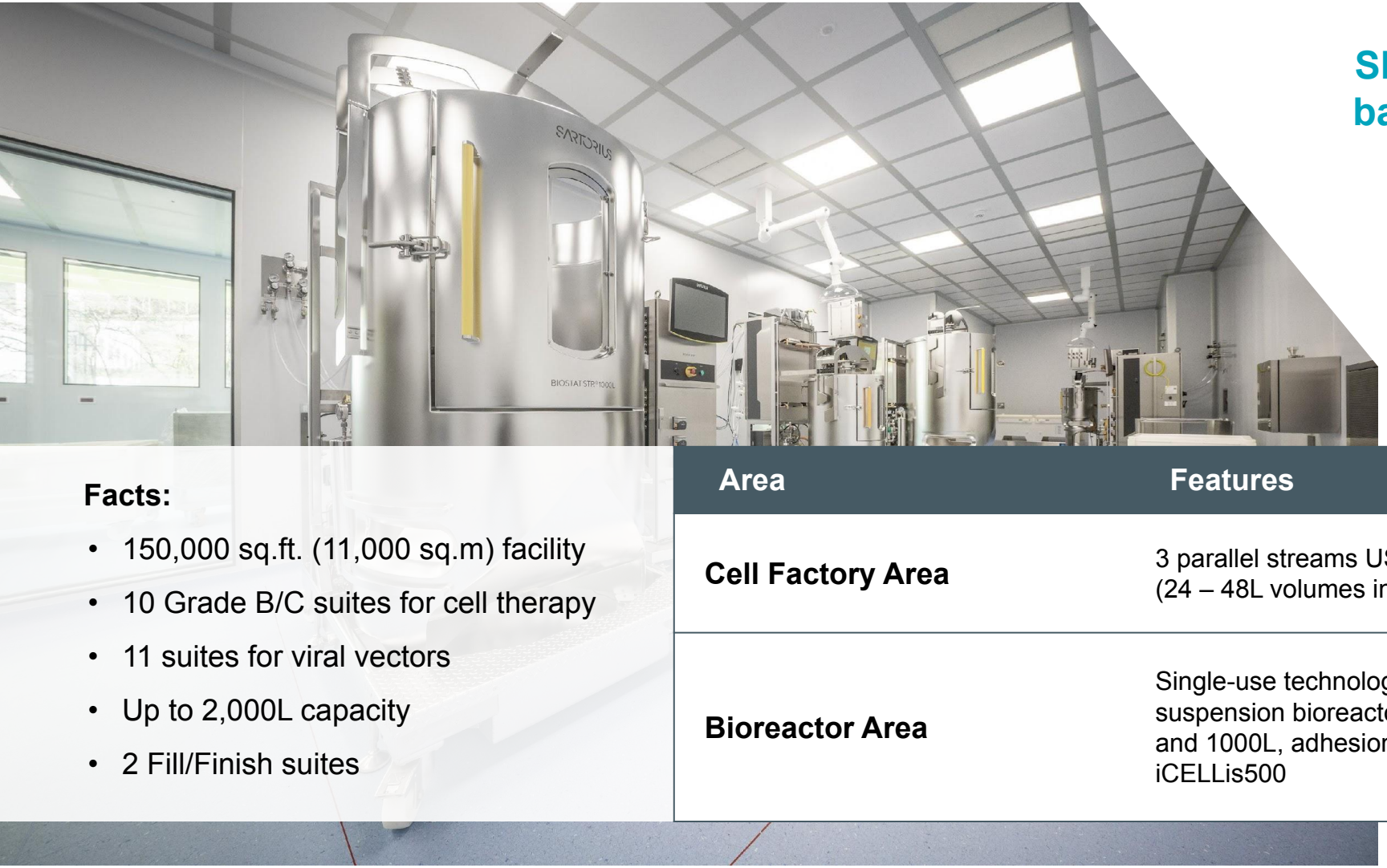
Education:
85% University degree
Of which 25% PhD

***75% Technical talent share**
Employees in technical department with >2 years tenure over the total employee base

Geo-economical and Retention Rate are key factors

High retention in a location with a favorable cost of labor retains critical technical know-how, maximizing efficiency and reducing overall costs.

Ideal balance between facility capacity and utilization



Shared suites enable lower cost per batch while single-use technologies safeguard quality

Adequate utilization of the facility, with upside for large-scale (capacity still available)

Facts:

- 150,000 sq.ft. (11,000 sq.m) facility
- 10 Grade B/C suites for cell therapy
- 11 suites for viral vectors
- Up to 2,000L capacity
- 2 Fill/Finish suites

Area	Features	Throughput
Cell Factory Area	3 parallel streams USP and DSP (24 – 48L volumes in CF)	70 Batches / year
Bioreactor Area	Single-use technology multiple suspension bioreactors 50L, 200L and 1000L, adhesion bioreactor iCELLis500	70 – 80 Batches / year

Off-the-shelf starting materials to reduce costs and timeline

Dedicated production

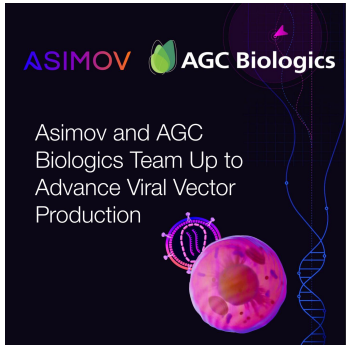
Material	Description	Estimated cost	Estimated Timeline
Packaging pDNA	3x HQ grade batches to be manufactured	3 x € 300,000 – 500,000	6 Months
Cell Banks (MCB, WCB and PPCB)	1x GMP grade batch to be manufactured characterized genetic stability	€ 500,000 - € 1,000,000	6 - 9 Months

Provided off-the-shelf

ProntoLVV™

Material	Description	Estimated cost	Estimated Timeline
Packaging pDNA	Already available – Costs per used mg	About € 6,000 per vial	Already available
Cell Banks (MCB, WCB and PPCB)	Already available – Cost per used vial	About € 5,000 per vial	Already available

Stable, 'plug and play' LVV manufacturing platform that lowers costs, reduces variability, and increases yields with a simplified single-plasmid process



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Number of Patients

Batch Size
- Process Scale-up
- Capacity

Productivity
- Productivity
- Process Yields

Quality
- Testing capability

A templated approach to vectors built on 30 years of experience

ProntoLVV™

Characteristic	Info
Support	3D culture in suspension
Process	Automatic (Bioreactor)
Bulk Scale (Platform)	50 L, 200L, 1000L
Final Purified Volume	625 mL, 2,500 mL, 12,000 mL

Characteristic	Info
Support	Plastic
Process	Manual
Bulk Scale (Platform)	48 L
Final Purified Volume	500 mL

Characteristic	Info
Support	Fixed bed
Process	Automatic (Bioreactor)
Bulk Scale (Platform)	200 L or 750 L
Final Purified Volume	2,500 mL – 9,000 mL

QC testing impacts on final costs per LVV dose

A fixed **QC sample volume disproportionately affects cost** and usable yield at low production scales, but becomes negligible as scale increases.

Internalization of testing allows us to:

- **Optimize the consumption** of final material to be tested.
- **Reduce external suppliers'** costs in terms of shipment and analysis execution costs.
- **Reduce testing and release timeline**.

Proposed IPC testing

Test	Performed At
Infectious Viral Titer	AGC Biologics
Physical Viral Titer	AGC Biologics
Infectivity	AGC Biologics
Residual Host Cell Proteins	AGC Biologics
Residual BSA	AGC Biologics
Total Residual DNA	AGC Biologics
Total Plasmid DNA	AGC Biologics

Proposed testing on final purified vector (for ex-vivo applications)

Test	Performed At
Infectious Viral Titer	AGC Biologics
Physical viral titer	AGC Biologics
Infectivity	AGC Biologics
Residual Host Cell Proteins	AGC Biologics
Residual BSA	AGC Biologics
Total Residual DNA	AGC Biologics
Total Plasmid DNA	AGC Biologics
Residual LTA DNA	AGC Biologics
Residual E1A DNA	AGC Biologics
Residual Benzonase	AGC Biologics
Transgene and Regulatory Elements Sequence	External laboratory
Transgene Presence	AGC Biologics
pH	AGC Biologics
Osmolality	AGC Biologics
Visible Particles	AGC Biologics
Clarity	AGC Biologics
Sterility	AGC Biologics
Endotoxin	AGC Biologics
Mycoplasma	External laboratory
In vitro Adventitious Viruses	AGC Biologics
RCL on LVV	AGC Biologics
RCL on End of Production Cells (EPC)	AGC Biologics

LVV manufacturing economical models: €1000/patient

Description	48L scale (Cell Factories)	50L scale	200L scale	1000L scale
Final Available LVV*	**2,5E+11 – 5,0 E+11 TU**	**8,5E+11 – 1,0E+12 TU**	**3,0E+12 TU – 9,0E+12 TU**	**1,4E+13 TU – 8,1E+13 TU**
Final Volume	0,5L	0,5L	2,5L	12L
Estimated CT Batches with this titer**	**30 - 100**	**100 - 200**	**600 - 1700**	**2,700 - 8,000**
Average cost of one LVV Batch (range)	€ 0,5 - 0,8 M	€ 0,75 - 1,2 M	€ 1,2 - 2,5 M	€ 2,5 – 4,0 M
Estimated cost range of LVV per CT Batch	**€ 8K - 17K**	**€ 5K – 8K**	**€ 2K – 4K**	**€ <1K**

*QC sampling: 20% up to 50L, about 5% at 200L and <1% at 1000L)

** CAR T program : 1 X 10^9 cells transduced at MOI5

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Thank You

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*Our purpose is to **bring hope to life** by enabling life-changing therapies for patients around the globe, creating a healthier and happier tomorrow.*

CGT Center of Excellence

Top CDMO for Cell & Gene Therapy

Milan, Italy

Service overview:

- End-to-end pre-clinical to commercial services
- Viral vector and cell therapy development and manufacturing
- Fill/Finish capabilities

Highlights:

- **30+ years of expertise**
- **15 commercial approvals (the most in the industry)**
- **One of the only CDMOs to achieve approval for a lentiviral with both FDA and EMA**

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