



Your CDMO partner
At your side from
DNA to Drug
Substance

0

1 Who
are we ?





3

Therapeutic fields

IMMUNOLOGY
HAEMOSTASIS
INTENSIVE CARE



15

Biomedicines

MARKETED IN
ABOUT
30 COUNTRIES



+ 2500

Employees

LFB GROUP

LFB is a biopharmaceutical group that develops, manufactures and markets plasma-derived medicinal products and recombinant proteins for the treatment of patients with serious and often rare diseases.

Sizeable player with regular capacity add-ons and certifications

1997

- Inception of MAbgène



2003

- First GMP facilities (UP1)



2007

- Acquisition of MAbgène by

2009

- Acquisition of buildings and land
- Implementation of 1,000L disposable bioreactor technology
- Compliance global part II of GMP

2011

- Investments in production capacity
- €5m Capex

1997 - 2007
Inception of Mabgène

2007 - 2012
Integration into the group and creation of LFB Biomanufacturing

2001

- ISO 9001 certification



2006

- ANSM audit (API status)



2008

- Implementation of single-use technology
- On-site support team integration

2010

- Site capacity expansion
Setting up a quality control laboratory and a cell culture and solution preparation area

2012

- MAbgène becomes LFB Biomanufacturing

Sizeable player with regular capacity add-ons and certifications

2014 - 2016

- New GMP facilities (UP2):
- GMP manufacturing area increase from sqm 150 to 750 sqm
- Integrated upstream and downstream capacities
- Single-use equipment
- c.€14m Capex over the period

2020

- Production of first commercial batches
- FDA approval



2012 - 2017

Site expansion and production development

2017 - 2022

Internationalisation of LFB Biomanufacturing

2022 - 2030

Escape30 New development Strategy

2017

FDA pre-licensing
approval inspection

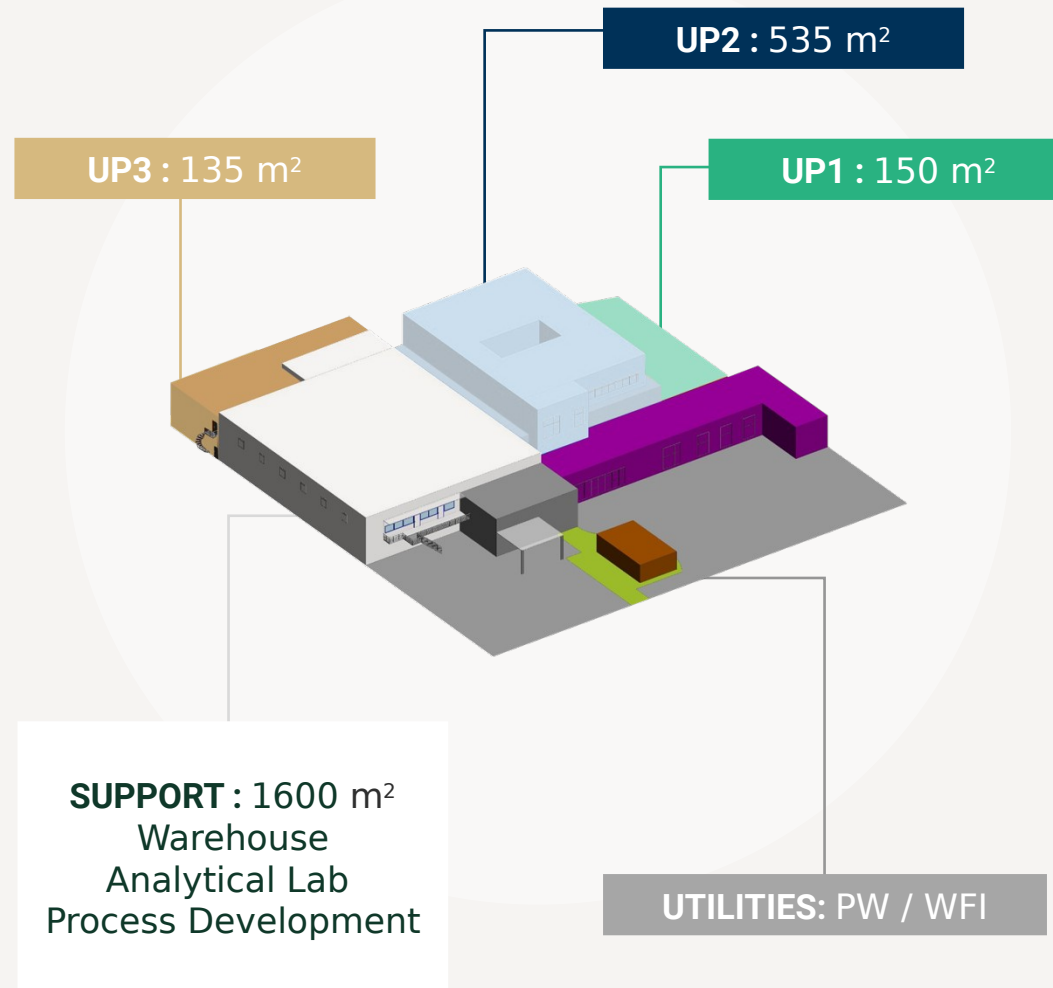


2022

FAD and ANSM
reinscription



Industrial site In Alès



LFB Biomanufacturing :

your CDMO partner

Your partner from Cell Line Development
to GMP manufacturing of drug substance

Using flexible technologies with almost
exclusively disposable systems.

With distinctive customer practice
Focusing on flexibility and cost efficiency

Covering both upstream and downstream
processes



LFB Biomanufacturing :

your CDMO partner



More than 25 years of experience in the development and the manufacture of monoclonal antibodies and therapeutic proteins

Pharmaceutical expertise and support of the LFB Group

Inspected and approved



Commercial capacity

LFB Biomanufacturing :

your CDMO partner



One-stop shop : From DNA to Drug Substance

CHO and Proprietary EMABling®
CLD Platforms

« Platform-type » and customized
process development options

Significant experience and high-level success
rate with single use technology



LFB Biomanufacturing :

your CDMO partner

More than 185 projects

More than 100 batches produced in GMP area
at 1000L and 250L scale in SUB bioreactors

Extensive Downstream process experience
on diverse and complex proteins

Facility Flexibility with additional space
for 2000L bioreactors



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2 What do we do?

A strong track record of prestigious intragroup and third-party projects



LFB Biomanufacturing :

covering a large range of services



DISCOVERY > PRE-CLINICAL DEVELOPMENT > CLINICAL DEVELOPMENT > REGISTRATION > COMMERCIALIZATION



CELL LINE DEVELOPMENT



PROCESS DEVELOPMENT AND SCALE-UP



MANUFACTURING OF CLINICAL AND COMMERCIAL BATCHES

- | | | |
|--|--|---|
| <ul style="list-style-type: none">— CHO and EMABling® platforms | <ul style="list-style-type: none">— Cell culture process development | <ul style="list-style-type: none">— GMP Master / Working cell bank manufacture and secured storage |
| <ul style="list-style-type: none">— Expression vector construction | <ul style="list-style-type: none">— Adaptation to serum-free media | <ul style="list-style-type: none">— GMP media and buffer preparation |
| <ul style="list-style-type: none">— MAb chimerization/ humanization | <ul style="list-style-type: none">— Media optimization, yield improvement | <ul style="list-style-type: none">— Manufacturing of up to 2,000L GMP batches |
| <ul style="list-style-type: none">— Vector transfection and transient expression | <ul style="list-style-type: none">— Downstream process development | <ul style="list-style-type: none">— Analytical methods transfer and validation |
| <ul style="list-style-type: none">— Cell line characterization and comparability | <ul style="list-style-type: none">— Analytical methods development | <ul style="list-style-type: none">— Quality control of drug substance, drug product, IPC, raw materials testing |
| <ul style="list-style-type: none">— Stable cell line generation and cloning | <ul style="list-style-type: none">— Quality by Design (QbD) approach and identification of product Critical Quality Attributes (CQA) and CPP | <ul style="list-style-type: none">— Stability studies for API / Drug substance |
| <ul style="list-style-type: none">— cell banking | <ul style="list-style-type: none">— Manufacturing of non-GMP batches up to 200L | <ul style="list-style-type: none">— Process characterization and Process validation, Regulatory support |

Innovation and Process Development (IPD)

Upstream Process (USP) & Downstream Process (DSP) Main activities



- Process development
- Process optimisation (DoE approach)
- Media screening (USP) & chromatography gel screening (DSP)
- GMP Scale up and tech transfer (in and out)
- Manufacturing support
- Small scale qualification process
- Validation process support / robustness activities
- Investigation / trouble shooting

Process Development technologies



Innovation Section



Innovation and Process Development (IPD)

Upstream Process (USP)
& Downstream Process (DSP) Main activities



Process Development technologies



- Ambr™ System 15ml
- Ambr™ System 250ml
- 4 Single use 3L bioreactors
- Biosat STR® Generation3 50L scale
- Bioprofile FLEX 2®
- Automated Cell counting : Vi-CELL BLU® Beckman Coulter
- USP Machine Remote control
- Chromatography systems :
 - Akta® Avant Laboratory scale with DoE functionality
 - Akta® Pilot for pilot scale batches
- Cogent™ UF/DF and nanofiltration systems

Innovation Section



Innovation and Process Development (IPD)

Upstream Process (USP)
& Downstream Process (DSP) Main activities



Process Development technologies



Innovation Section



- Continuous processing
- Alternative platforms for new therapeutic proteins
- Alternative production systems
- In line analytical solutions



GMP Technical Capabilities



UPMT : Media and buffer preparation unit



- Dedicated buffer and media preparation suites ;
- Weighting station and electronic batch record (Formweigh® Metler toledo) compliant with CRF part 11 ;
- Supply, production and Raw material traçability managed by ERP (Qualiac®)

USP : Upstream process & DSP : Downstream process



GMP global activities



GMP Technical Capabilities



UPMT : Media and buffer preparation unit



USP : Upstream process & DSP :
Downstream process



- Lines of bioproduction with bioreactor capacities (Biostat STR®) up to: 200L & 930/2,000L
- Electronic cell counting and viability analyse (Vi-CELL BLU® Beckman coulter)
- Cell Banking
- Cell bank storage
- Industrial chromatography systems : Akta® Ready/ Sartorius® CHR-1000
- Ultrafiltration/diafiltration : TFF Sartorius® system
- DS freezing/storing
- Column chromatography packing expertise

GMP global activities



GMP Technical Capabilities



UPMT : Media and buffer preparation unit



USP : Upstream process & DSP :
Downstream process



GMP global activities



- Classified areas (C & D) with internal cleaning and environmental monitoring
- Facility Monitoring System (FMS)/Building Management System (BMS)
- Exclusive Single-Use approach for USP & UPMT
- Extensive use of disposable systems for DSP
- Aseptic connections
- In process control follow up by LIMS system
- Quality by design
- Process validation
- Deviation follow up system (Trackwise®)
- Electronic documentation management system (GED : Ennov®)
- Operator training by Virtual reality (step-based deployment)

GMP Technical Capabilities

covering both upstream and downstream processes

UPSTREAM PROCESS

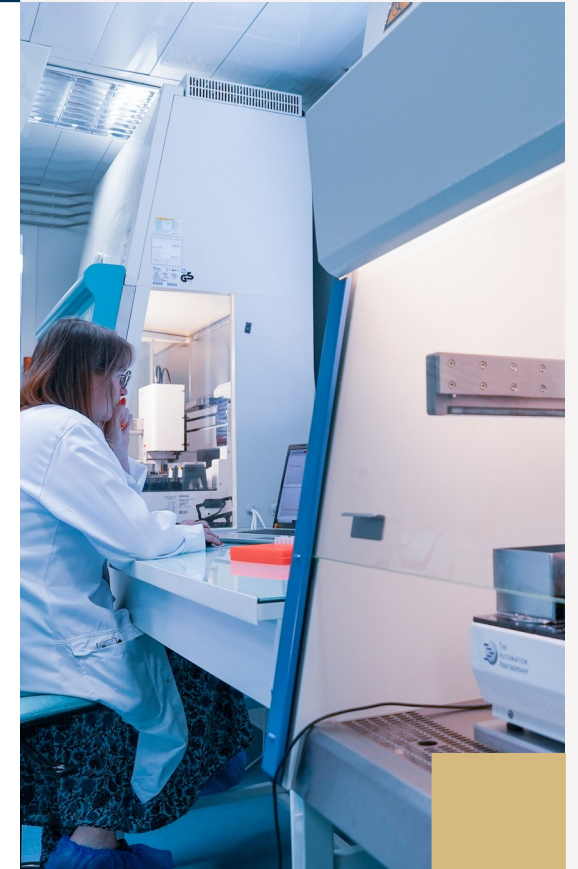
DOWNSTREAM PROCESS

Additional space capable of hosting up to 6 x 2,000L bioreactors (*to be acquired depending on incoming projects requirements*) for manufacturing phase III clinical batches or commercial application batches

2 upstream and 2 downstream workshops generating capacity for phase I, II and up to 1,000L USP clinical batches

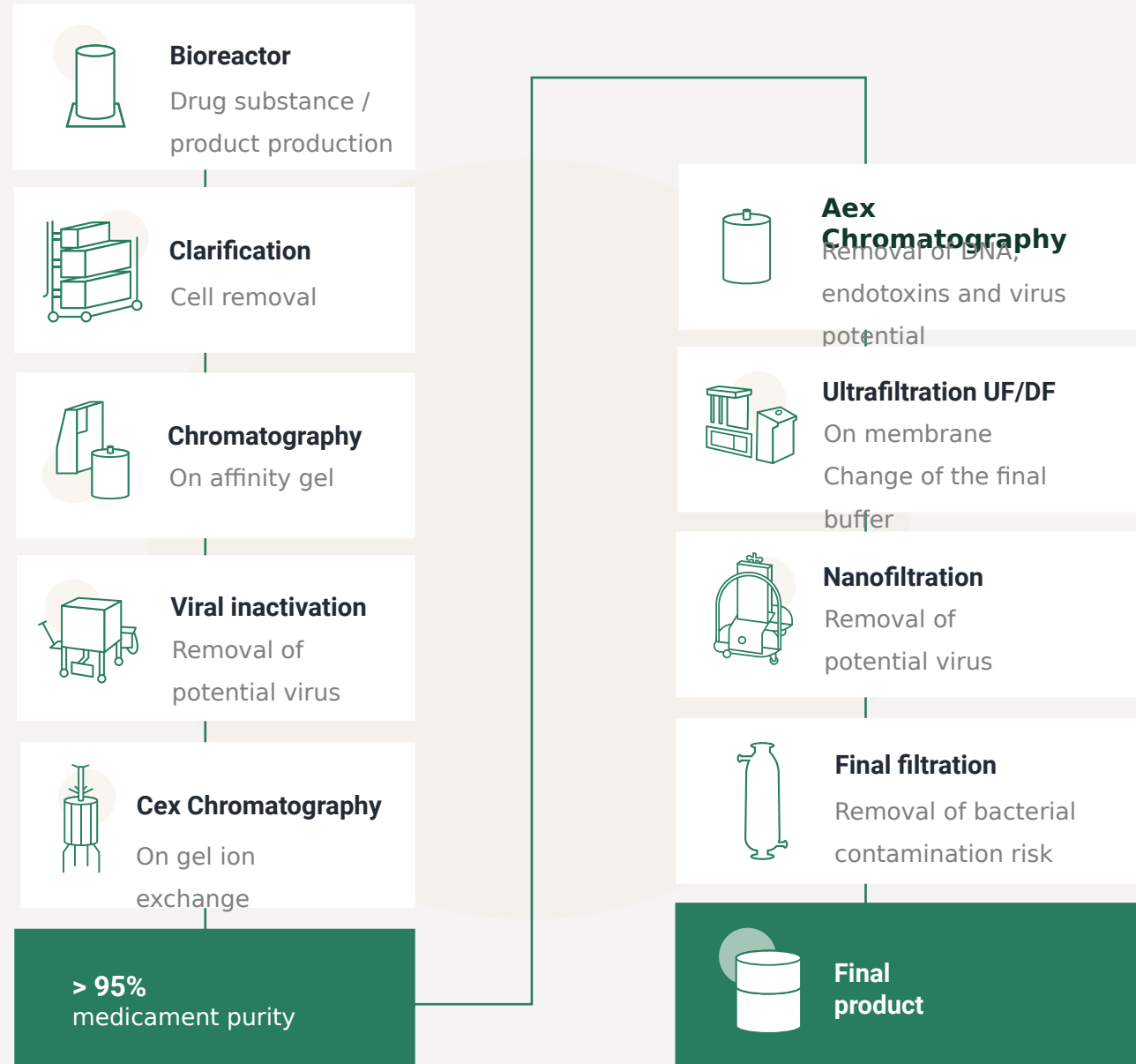


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DSP process overview



Fully integrated player – One-stop-shop services

– Open-platform site including proprietary EMABling® platform for seamless glycan modification

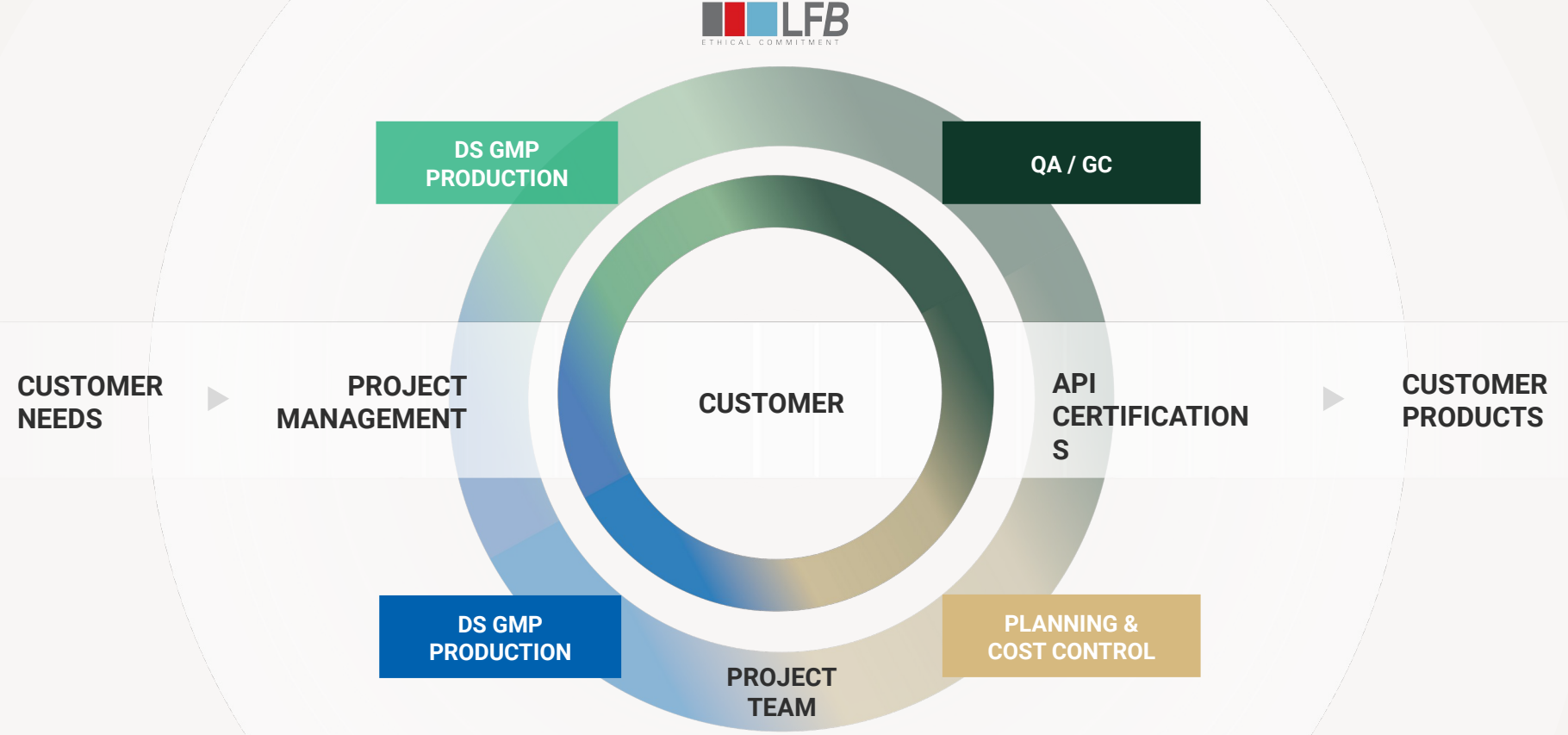


Key attributes

- 1 Fully integrated development program for the production of low fucose, biological activity improved monoclonal antibodies
- 2 Suitable for poorly expressed antigen targets on the cell surface
- 3 Dedicated quality control tests and development of potency assays
- 4 High productivity level up to 10 g/L
- 5 Proven track record of scalability for industrial development
- 6 Demonstrated clinical efficacy of EMABling® antibodies
- 7 Generation of stable clones adapted to Fed batch conditions in an ADCF (Animal Derived Component Free) optimized medium

High value-added project management capabilities

comprehensive and customer oriented services delivered by a fully dedicated team



When a project is initiated, a dedicated team is set up, a single interlocutor in charge of supporting all the services from USP to DSP

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3 Who
is it for ?

Case study (1/4)



project

INTERNAL PROJECT



FDA and EMA Approved
64 batches delivered



PROJECT DETAILS

- Protein type: Recombinant protein-coagulation factor
- Clinical phase: PhII to registration
- Services provided:
 - Process development & scale-up
 - Manufacturing
- Certifications: GMP / FDA
- Complexity: Medium / High

MISSIONS

- Process transfer + scale Up (X5)
- Process validation
- Analytical transfer + validation
- DS manufacturing
- DS/DP analytical testing stability
- Quality upgrade to FDA standard

TIMELINE

- **10/2012** : kick-off meeting
- **Q3-Q4 2013** : scale up and transfer (3 batches)
- **2014** : 1st step of process validation
- **2017** : FDA Pre Licence inspection
- **04/2020** : FDA and EMA approval
- **09/2022** : FDA routine inspection (1 remark)
- **2023** : Transfer of the Intermediate Drug Substance from USA to Ales

ACHIEVEMENT

- Transfer and scale up
- 64 batches including validation batches
- Analytical testing effective on site for DS and DP
- FDA and EMA approval of the DS manufacturing

A process transfer and scale up, a validation of process
and FDA agreement for commercial batches

Case study (2/4)

BMG-167 project

BMG-166 project

EXTERNAL PROJECT

MAB project



10 GMP batches for Phase I/II

PROJECT DETAILS

- Protein type : Monoclonal antibody
- Clinical phase : Phase I/II
- Services provided : Cell line development
- Process development & scale-up
- Manufacturing
- Certification : GMP
- Complexity : Medium

MISSIONS

- Cell line development using platform technology
- USP/DSP process development with partial platform technology
- Product formulation
- Reference standard preparation
- viral safety validation
- Scale up to 250L/1000L
- Manufacturing of Master cell bank (MCB)
- Manufacturing of DS engineering batch for toxicological study + stability studies
- Manufacturing of DS GMP batch for clinical batch + stability studies

TIMELINE BMG167

- **03/2019** : kick-off meeting
- **04/2020** : end of Cell line development- availability of Pre seed stock
- **02/2020** : 1st pilot 50L batch delivery
- **07/2020** : MCB delivery 300 vials
- **08/2020** : 2nd pilot 50L batch delivery expected
- **12/2020** : GMP batch 250L produced
- **06/2024** : 4th GMP batch 250L produced

TIMELINE BMG167

- **2019** : Process transfer from previous CDMO
- **12/2019**: First GMP Batch successful
- **01/2025** : 7th GMP expected

ACHIEVEMENT

- Cell line developed with LFB platform
- Process optimised with high level yield and good Purity/quality of purified product
- Master cell bank available and conform
- Scale up already engaged for engineering batch

Case study (3/4)

BMG-181 project

Development on going

EXTERNAL PROJECT

MAB projects



PROJECT DETAILS

- Protein type : Monoclonal antibody
- Clinical phase : Phase I/II
- Services provided : Process development & scale-up
- Manufacturing
- Certification : GMP
- Complexity : High : Removal of 30% of aggregates in the in-coming USP process

MISSIONS

- Transfer form another CDMO
- USP/DSP process development with partial platform technology with a focus to remove aggregates (HMW)
- Product formulation
- Reference standard preparation
- viral safety validation
- Scale up to 1000L
- Manufacturing of Master cell bank (MCB)
- Manufacturing of Pilot batch for toxicological study + stability studies
- Manufacturing of DS GMP batch for clinical batch + stability studies

TIMELINE BMG181

- **10/2023** : kick-off meeting
- **11/2023** : Transfer, USP and DSP Development
- **03/2024** : consolidation Process Development USP and DSP
- **06/2024** : 1st pilot 50L batch delivery
- **10/2024** : MCB delivery 300 vials
- **11/2024** : 2nd pilot 50L batch delivery
- **11/2024** : Non GMP Stability Studies
- **2025** : GMP batch 250L produced

ACHIEVEMENT

- Process optimised with high level yield and good Purity/quality of purified product
- USP Productivity increase and formulation optimization
- Scale up already engaged for engineering batch

A complete services procurement from cell line to GMP manufacturing

Case study (4/4)

BMG-170 project

17 batches produced

EXTERNAL PROJECT

Therapeutic extracted protein



PROJECT DETAILS

- Protein type: Polyclonal Immunoglobulins- anti-COVID19
- Clinical phase: Phase I/II
- Services provided:
 - Process development & scale-up
 - Manufacturing
- Certification: GMP
- Complexity: Medium / High
- New building construction to fit with manufacturing needs (2 DSP suites)

MISSIONS

- Fast Track Process transfer – COVID-19 context
- GMP batch 1L for clinical use in July 2020
- Analytical transfer and testing
- GMP batch scale up to 5L for clinical supply

TIMELINE

- **04/2020** : kick-off meeting
- **05/2020** : 1st GMP batch delivery
- **06/2020** : 1st GMP release
- **07/2020** : 2nd GMP batch after scale up
- **09/2020** : GMP campaign
- **12/2020 up to 09/2021** : 2 new DSP suites build from scratch
- **2020 📧 2022** : 17 GMP Batches produced
- **2024** : 3 new projects and scale-up for BMG170

ACHIEVEMENT

- Process transfer without small scale evaluation
- Direct GMP batch preparation (no engineering run)

An accelerated process completed in record time (10 weeks)
demonstrating LFB Biomanufacturing's high flexibility and reactivity

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And tomorrow,
with you ?



LFB Biomanufacturing – Future facilities

ESCAPE³⁰ PROJECT

Buffer and media preparation area extension

Analytical laboratory extension to support analytical method development and method validation

Process Development laboratory extension to increase new biological entities development throughput capacity

Warehouse and maintenance area extension



Project duration
48 months



Generated turnover
38 m€



Estimated budget
20,6 m€



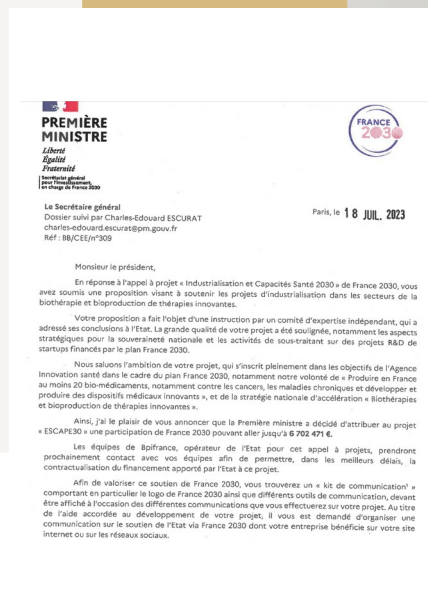
49 direct jobs
by 2026

Our plan ESCAPE³⁰ Winner of « AAP Capacite Sante France 2030 »

“ In response to the “Industrialisation et Capacités Santé 2030” (“2030 Industrialisation and Health Capacity”) call for projects, the French Prime Minister decided to fund LFB’s project for up to €6.7 million. The project, with a total cost of more than €20 million, is fully in line with the objectives of the French Health Innovation Agency and the “France 2030” Health component of the 2030 Health Innovation plan. ”

— Herbert Guedegbe

DIRECTEUR DE SITE



attente visuel
hd

A strategic partnership with Sartorius



Through this collaboration, customers will have access to high-performing Sartorius cell lines and media that support successful transfer and scale-up, along with an integrated drug development process from LFB BIOMANUFACTURING.

By partnering, the companies are enabling a one-stop solution that reduces the logistic and administrative efforts involved when engaging with multiple stakeholders, streamlining development and manufacturing processes.

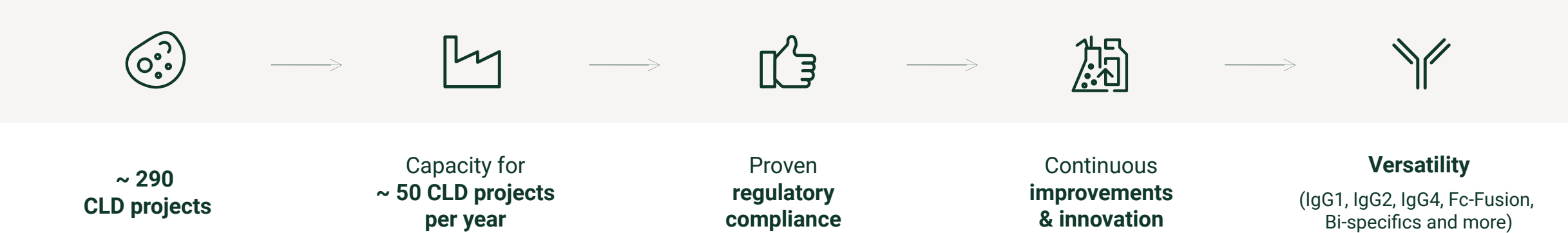
In time, the collaboration can accelerate time-to-clinic and time-to-market for therapeutic molecules.

4Cell® CHO Platform CLD Services

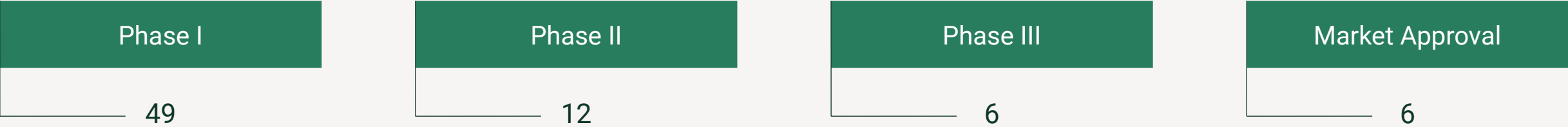
CMTS | Protein-Based Therapies



CLD Experience & Track Record

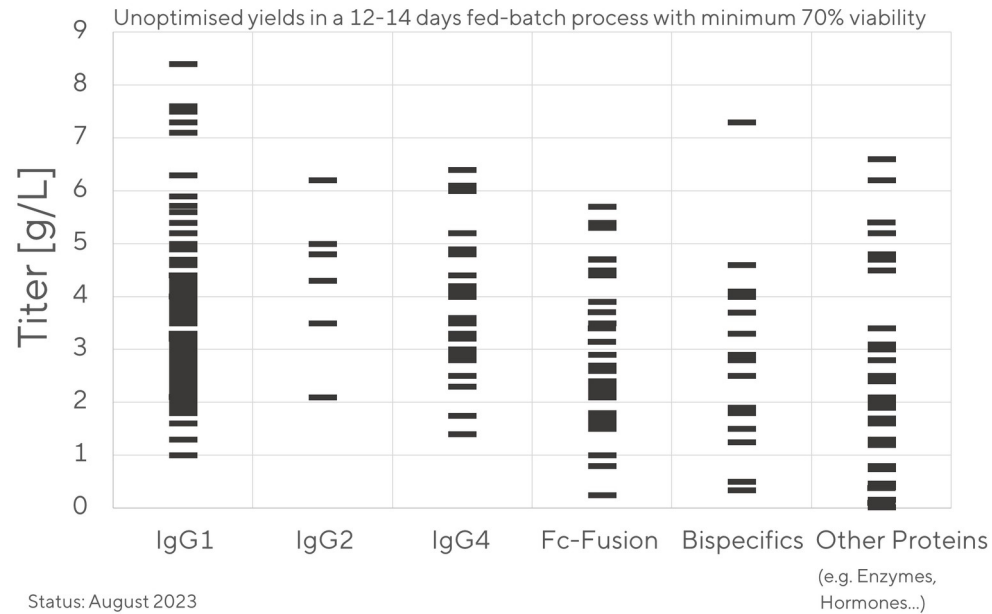


Clinical Track Record



CLD Track Record Across Multiple Molecules

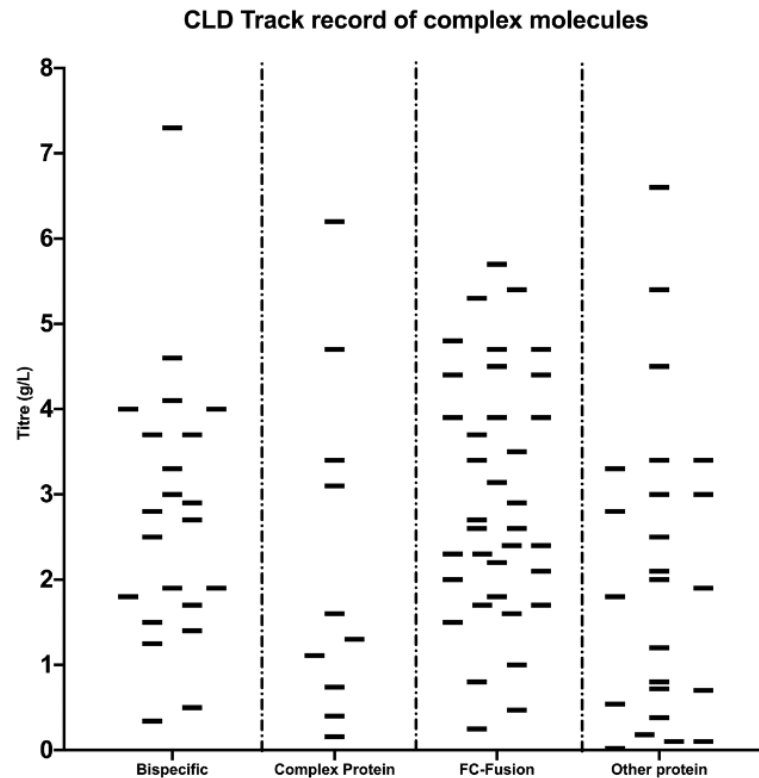
4Cell® CHO Platform Cell Line Development



Proven results across a broad range of molecules

Our CLD platform works with non-mAbs and “difficult to express” molecules.

CLD Track Record – non-mAbs



Other Proteins:

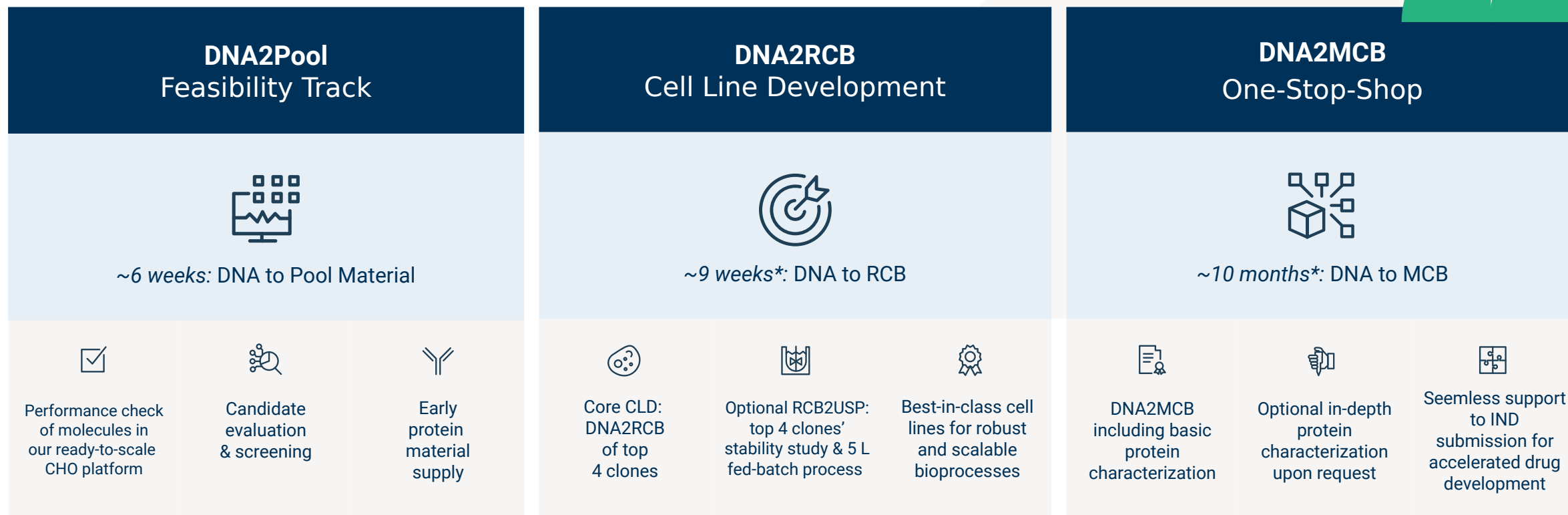
Hormones, small molecules, truncated proteins, cytokines, enzymes

Complex molecules:

Trispecifics, growth factors, Transmembrane glycoproteins, viral glycoprotein, scFV Ab, hs Albumin

Free-for-Service Products (NBEs)

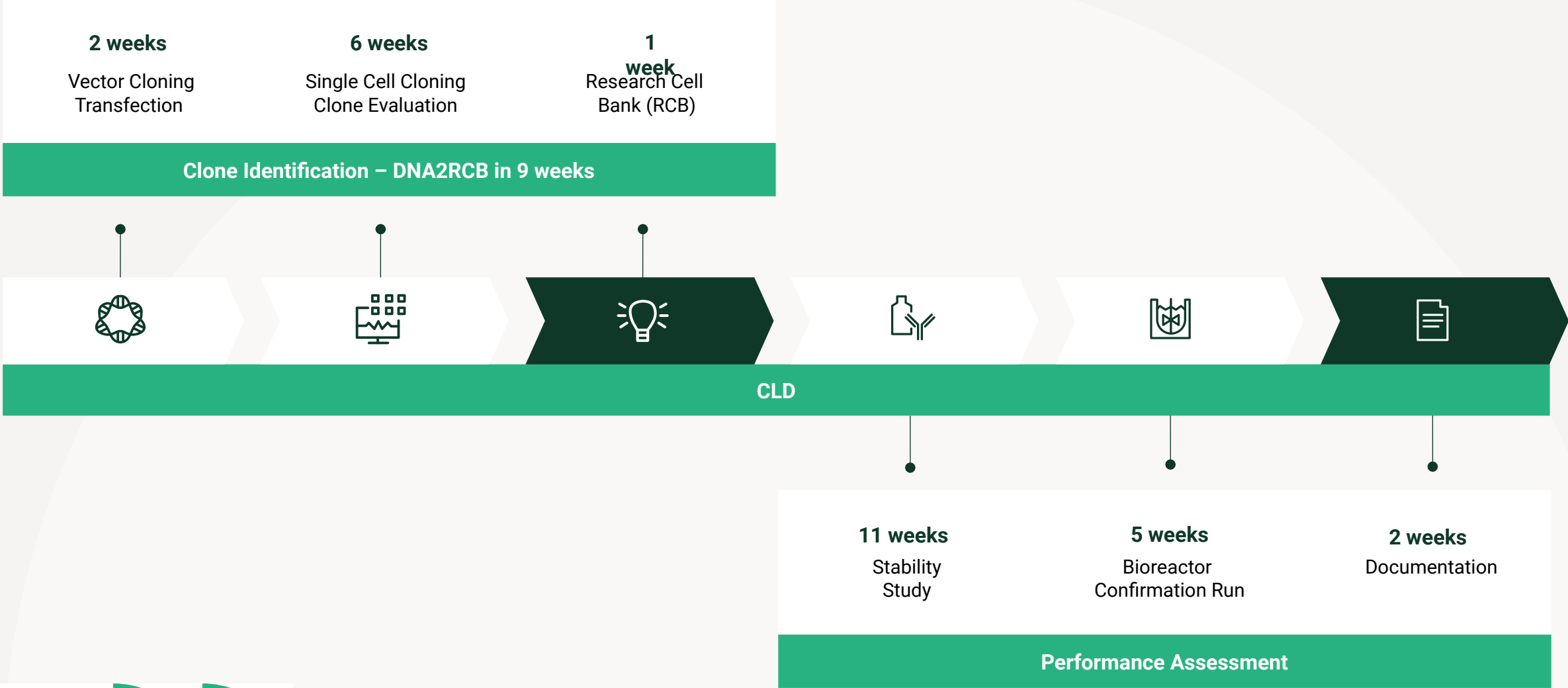
– Standardized Tracks



**Timeline is for a standard IgG1 NBE – scope & timeline can be adapted depending on molecule & client's needs*

For any other molecule than NBE IgG and for any additional CLD work and testing services, customized CLD track is available

Cell Line Development Workflow



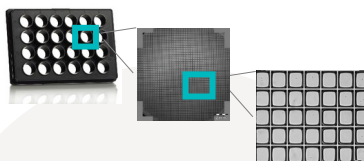
Sartorius CellCelector™ for Single Cell Cloning (SCC)



CellCelector™ device with robotic arm for cell isolation and fluorescent microscope



Software for image analysis and high producer identification



Nanowell plates
(24 well)



Single-use glass capillary
for clone picking

Technical Superiority...

- Single Cell Cloning (SCC) device with automated analysis and picking of single-cell-derived clones; High level of automation reducing human error to a minimum
- Better outgrowth after SCC due to cell cross talk between nanowells
- Early single cell cloning & prediction of high producers

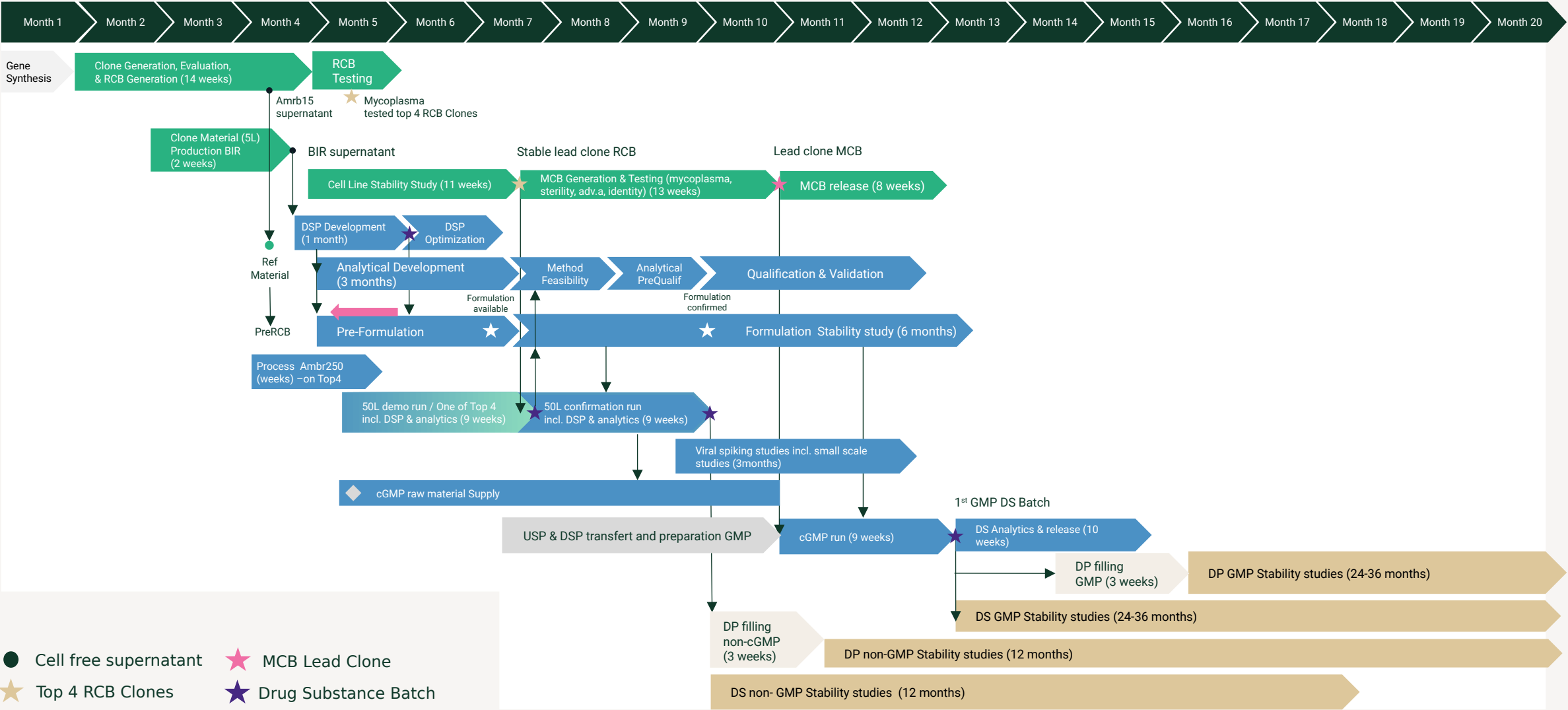
...and Regulatory Compliance

- Internally validated by statistical evaluation
- In accordance with regulatory recommendations*

*Sarah, K. (2014). Establishing clonal cell lines - A regulatory perspective. Food and Drug Administration (FDA) WHO Expert Committee on Biological Standardization (2013). Sixty-first report. WHO Technical Report Series, World Health Organization (WHO).

Integrated Sartorius Cellca & LFB Biomanufacturing Program Timeline

Finalized version – July 2024



The partner you need to
grow, the way you need it,
rapidly and efficiently.

— Flexibility, Reactivity, Process &
Scale-up

