GenScript
PROBIO

Biologics Development Service

Inspire, Accelerate & Co-create Biomedical Innovation

Why ProBio:
Proactive

Proactive in anticipating customers' needs

Why ProBio:
Professional

Professional solutions with high integrity

Why ProBio:
Process

Efficient processes rooted in good science and phase appropriate quality

GenScript ProBio

GenScript ProBio is the bio-pharmaceutical CDMO segment of the world's leading biotech company GenScript Biotech Corporation (Stock Code: 1548.HK). Founded in 2002 in New Jersey, GenScript started business from gene synthesis. Now, GenScipt 's businesses encompass four major categories based on its leading gene synthesis technology, including operation as a Life Science CRO, enzyme and synthetic biology products, biologics development and manufacturing, as well as cell therapy.

In Jan 2019, GenScript established the Biologics Development Business Unit (BDBU) which is the predecessor of GenScript ProBio. In 2020, GenScript ProBio brand was officially launched.

The name of "ProBio" indicates 3 core philosophies - being PROACTIVE, PROFESSIONAL and PROCESS-oriented. GenScript ProBio shows our dedication to proactively provide end to end service (discovery to commercialization) with professional solutions, and efficient process to accelerate drug development for customers.

GenScript ProBio provides an integrated biologics discovery & development solution from target to IND. With our cutting-edge technology platforms in therapeutic antibody discovery & development, GenScript ProBio is able to deliver functional antibody lead with good developability and safety in discovery phase, as well as reliable, productive and regulatory-compliant process & drug product for IND filing in development phase, which significantly save client's time and cost.

Lead Generation

- Hybridoma generation
- Single B cell screening
- Human and llama naïve library
- Fully human transgenic mice
- SMAB bispecific antibody discovery

Lead Optimization

- Antibody humanization
- Affinity maturation
- Developability assessment
- Bioassay & Bioanalytics

Biologics Development

- Stable pool & material generation
- Cell line development
- Process development
- Analytical development
- GMP manufacturing

PreCLD Cell Pool Development & Developability Assessment

Problems like physical stability and aggregation of biomolecules usually occur in process development and lead to the failure of preclinical development.

GenScript's PreCLD Cell Development & Development Assessment services will help you to know about these potential risks in the beginning of cell line development, which enable you to mitigate potential risk and optimize the process development.

Recommended for

- Bispecific/multivalent antibody and protein projects
- Have multiple candidates ready for CMC and select a best one to move forwards

Service Features

- Evaluate the developability of drug candidates in the same host cell and vector system as CMC to simulate the actual conditions
- Help to identify the possible risk occurred in the process development
- The cell clone can be further developed to stable cell line

Cell Pool Developability Assessment Study

Stability	Analytical methods	Changes from day T_0 to T_{end}		
		Candidate A (Middle cell pool titer)	Candidate B (Middle cell pool titer)	Candidate C (High cell pool titer)
Freeze-thaw	Appereance	Remain the same	Remain the same	Remain the same
Stressful (40℃, 2 weeks)	Appereance	Remain the same	Remain the same	Remain the same
	CE-SDS-NR	Decrease ca. 10%	Remain the same	Remain the same
	SEC-HPLC	Remain the same	Remain the same	Remain the same
	PTM by MS	~ 10% deamidation (not CDR)	~ 10% deamidation (not CDR)	~ 5% Oxidation (not CDR)
	cIEF	Acidic and basic increased	Main peak changed	Acidic and basic increased
	Bioactivity	Remain the same	Remain the same	Remain the same
Acidic Condition (pH3.5, 25°C, 4h)	Appereance	Remain the same	slight suspension	slight suspension
	SEC-HPLC	Decreased ca.70%	Decrease ca.40%	Decrease ca.5%
	PTM by MS	~10% dearmidation (not CDR)	~20% oxidation (CDR)	Remain the same
	cIEF	Remain the same	Main peak changed	Remain the same
	Bioactivity	Remain the same	Decreased	Remain the same

According to this developability assessment, candidate C was chosen and finally succeed in CMC.

ProCLD Cell Line Development Service

Cell line development plays an essential role in drug development. It is the bridge connecting drug discovery and development, and good cell line development service can always save your valuable time and lower your final cost. With extensive understanding of IND-enabling CMC study, GenScript ProCLD cell line development service will provide you the cell lines with shortened timeline and high quality delivery to help you succeed.

Services Features

Key technology driver

Proprietary CHOK1-GenS

- **Royalty-free**
- **Path to commercialization**

Proprietary pGenHT 1.0-DGV expression vector

High throughput clone selection: VIPS, Cellmetric, Cloneselect

Accelerated timeline

Gene synthesis to

Top 6 clones in

14 weeks

Gene synthesis to

Top 1 clones in

18 weeks

High quality delivery

High Quality

- Productivity prior to cell culture, for mAb
  - √ Guarantee: **3g/L**
  - √ Average: **4.35g/L**
  - √ Up to: **8.7g/L**
- Excellent stability in **60-90** generations

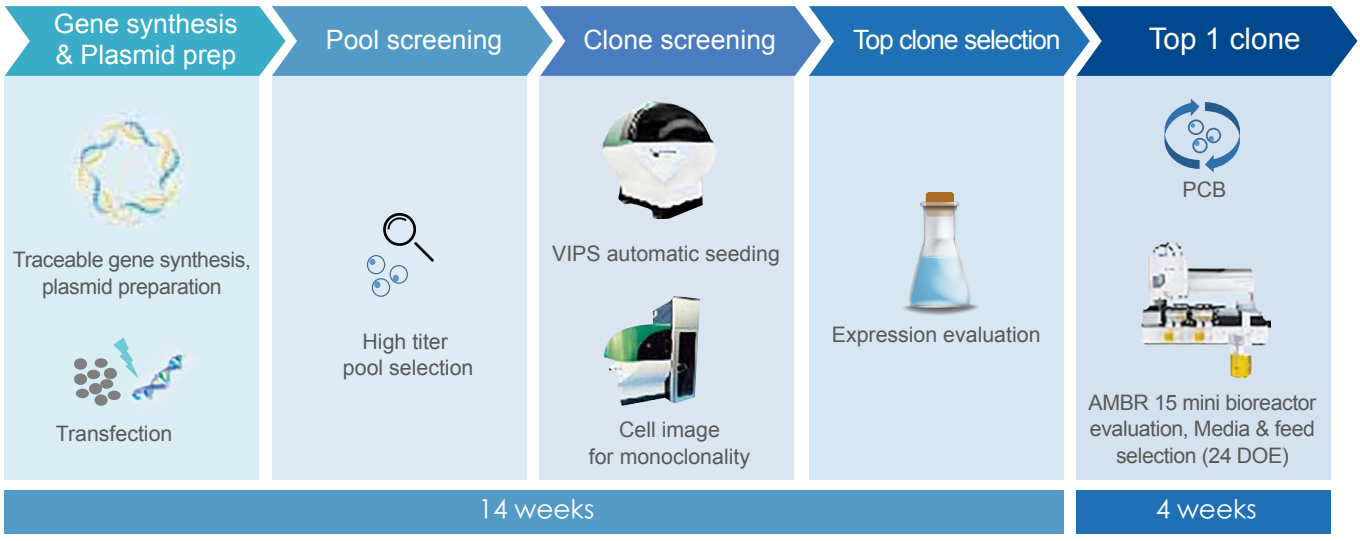
Regulatory Compliance

- Traceable records for host cell and vectors
- Traceable records for cell line development
- Cell image to demonstrate monoclonality

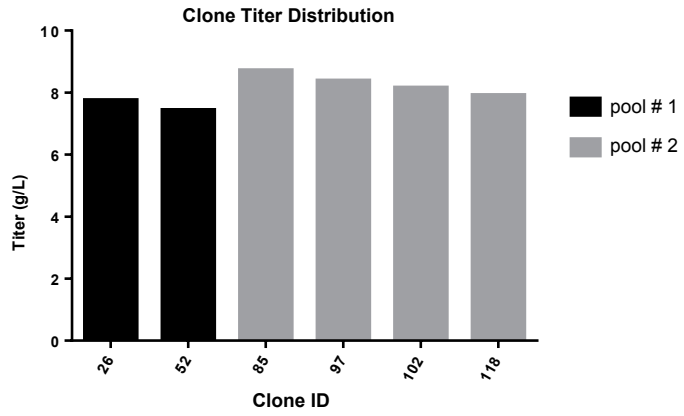
Rich experience

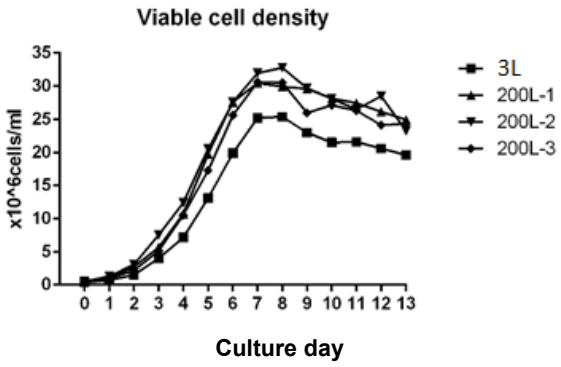
- **>300** cell lines developed
- **>80 projects** for IND filing
- **8** in clinical stage
  - 7 in clinical phase 1
  - 1 in clinical phase 2

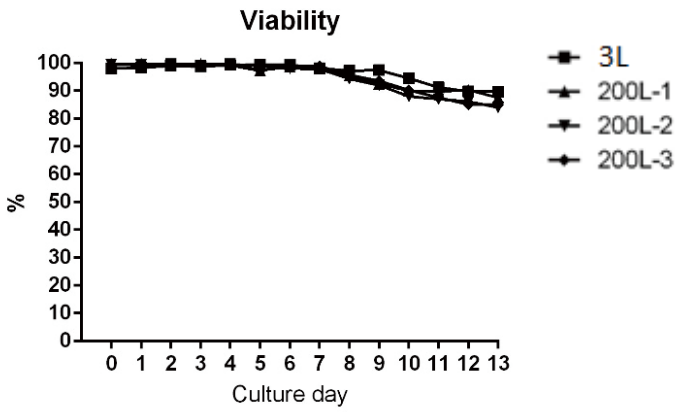
Services Workflow

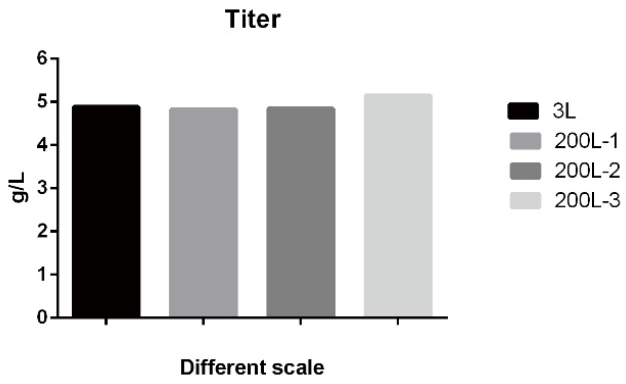


ProCLD shows high titer (up to 8.7g/L) and excellent stability in scale-up









Service Specification

Service	Service Details	Deliverables	Timeline
ProCLD Cell Line Development	• Gene synthesis & plasmid preparation • Cell pool screening • Cell clone screening • Fed-batch evaluation • PCB generation	• Plasmid construct map; • Stable cell line development final report; • 6 PCB	• 14 weeks
	• PCB 60 generation stability study	• Report of stability study	• 14-15 weeks
ProCLD plus Cell Line Development	• Media & Feed screening & ambr 15 mini bioreactor clone evaluation	• Top 1 clone and a back-up clone • Report	• 4 weeks

GMPro Cell Banking Service

The generation of a regulatory-compliant cell bank is an essential element in the biologics manufacturing. GenScript's GMPro cell banking service assures that a uniform and sufficient population of cells are generated and preserved in a secure, controlled and monitored storage environment.

Service Highlights

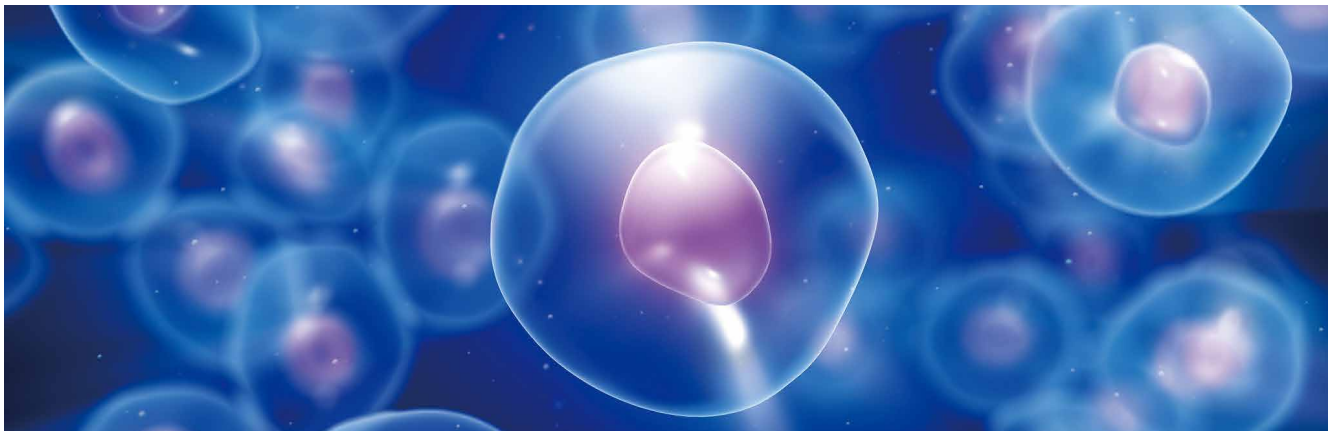
- cGMP-compliant service
- 2 independent liquid nitrogen tanks
- Well established security system
  - 24h CCTV
  - Sound-light alarm & remote alarm function for liquid nitrogen tank
  - Strict authority system
- Excellent documentation system: every "in" and "out" is recorded

Service Specification

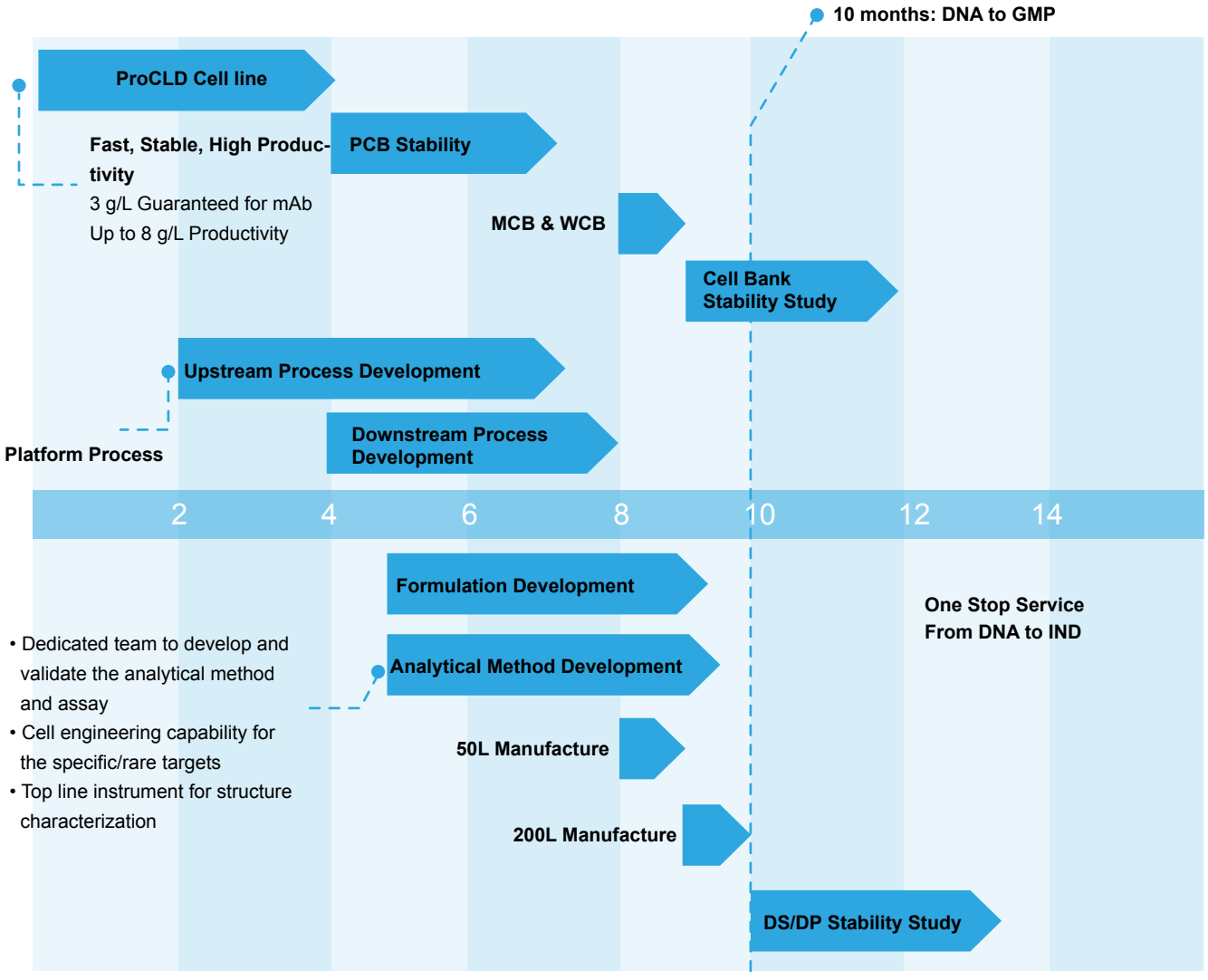
Service		Service Detail	Deliverables	Timeline (week)
GMPro Cell Bank Generation	MCB generation	• GMP batch record prep • MCB generation	200 vials, cell bank records	6
	MCB testing	• MCB cell recovery • Mycroplasma testing	Report	3
	WCB generation	• GMP batch record prep • WCB generation	200 vials, cell bank records	3
	WCB testing	• WCB cell recovery • Mycoplasma testing	Report	3
GMPro Cell Bank Storage	MCB and WCB Storage		Cold chain record	NA

ProIND CMC Service

GenScript builds an integrated platform including stable cell line development, process development, analytical development and GMP manufacturing to accelerate your IND journey. GenScript ProBio provides fed-batch, high density inoculation and perfusion process according to different molecules.



Speed to Clinic: 10 months from DNA to GMP



Process Development

GenScript's comprehensive upstream and downstream process development capabilities, commitment to innovation, and high quality of service make us the ideal partner for the process development of your mammalian cell culture projects. In early clinical phases, speed, flexibility, and expertise are critical to quickly establishing a robust and scalable process. Our experts have the experience and capabilities to develop an optimal process with long-term commercial manufacturing in sight, including:

Cell Culture Process Development

Robust and efficient production processes are crucial to the success of IND-enabling studies and to the preservation of product competitiveness. GenScript's 'Time & Quality-Balanced' process development strategy, including using cell pool samples for purification preliminary development and cell culture process optimization, 3L samples for purification process optimization and formulation development, and 10/50L samples for process scale-up and purification process lock greatly shortens the process development timeline.

Media Screening	• Media adaptation study using cell pool • Identify Top 2 media from platform media to study furtherly
Productivity	

Clone & Media Selection	• Top 12 clones and top 2 media were performed in Ambr 15 • Identify top 1-2 clone conditions to qualify in 3L bioreactors
Quality	

Process Bioreactor	• Top 1-2 conditions were performed in 3L bioreactors with key parameters optimization • Key parameters optimization, e.g., pH, temperature and/or duration
Stability	

10L or 50L Scale-Up	• The locked 3L process was confirmed in 10L or 50L bioreactors • Two 3L satellite bioreactors were performed in parallel
Scalability	

Purification Process Development

GenScript has developed a monoclonal antibody purification platform process that allows clients to quickly establish a production process with an overall recovery rate of around 70% and with acceptable product characteristics, process and product-related impurities. GenScript will customize the processes to meet the unique needs of each client. For example , in the case of biosimilars, GenScript has effective techniques and tools to change the distribution of product glycoforms and charge isomers.

Chromatography	Filtration and Centrifugation	Virus Inactivation and Clearance
• Affinity Chromatography (AC) • Ion-exchange Chromatography(IEX) • Hydrophobic Interaction Chromatography (HIC)	• Deep Filtration • Tangential Flow Filtration (TFF) • Ultrafiltration and Liquor Exchange	• Low pH inactivation and detergent treatment • Nanofiltration (NF) • Chromatography

Analytical Development

Supporting the Full Lifecycle of Biologics Development

Versatile Analytical Procedures	• **General properties:** UV280, AAA, pH, Osmolality, Color, Clarity, etc. • **Structural characterization:** LC-MS, CD, DLS, DSC, etc. • **Product-related impurities:** SEC/CEX/HIC/RP-HPLC, CE-SDS, icIEF, etc. • **Process-related impurities:** HCDNA, HCP, rProteinA, Endotoxin, Bioburden, etc. • **Bioactivities:** ELISA binding and Cell-based assay, ADCC, CDC, ADCP, MLR, Fc-binding
Strong Capability in Method Development	• **Experience of >10 kinds of CMC biologics,** including mAb, bsAb, tsAb, scFv, hILs, coagulation factors, protein complex, and many other specially designed molecules. • **Dedicated cell line engineering team** to develop cell line based on target MOA • **Can start method development as early as possible** (e.g. cell pool stage)
Hardware and Software	• **Powerful instruments:** 2 mass spectrometers (QE Orbitrap and Q-TOF), UHPLC systems of mainstream brands (Agilent/Waters/Thermo), CE systems (PA800 plus, Maurice, etc.), Microplate readers (Molecular Devices) • **Software meets compliance:** Audit trails available, with GMP, GLP, and 21 CFR Part 11 compliance

Bioassay Development

Determining the Biological Potency of Broad Types of Targets

Cell-based Assay Development Capability	• **Dedicated cell line engineering team** to develop cell line based on target MOA • Experience **of >30 targets, multiple off-the-shelf cell line**s to support IND/BLA filing • **In compliance with ICH and USP** to perform method development, optimization and validation. • **Clear background and traceability of cell line,** which is compliant with authority regulation
Different Kinds of Targets	• mAb, bsAb, recombinant protein, cytokine, T-cell engager • Immune checkpoints, tumor-associated antigens, inflammation factors, cytokines, coagulation factors, GPCRs • Anti-cell proliferation, apoptosis, T cell activation, cytokine release, neutralization, etc.
Platforms for Characterization	• ADCC, CDC, ADCP, mixed lymphocyte reaction • Fc-binding • FcγRIIIA (CD16a) 158V, FcγRIIIA (CD16a) 158F, FcγRIIA (CD32a) 131H, FcγRIIA (CD32a) 131R • FcγRI (CD64), FcRn, C1q

Clinical Manufacturing

Early-stage clinical supply of biologic drug substance is produced at state-of-the-art cGMP facilities in Nanjing, China. Your project will be handled by a team of experts with a full range of technologies and analytical tools to not only run the project with the highest flexibility, but also deliver on time with exceptional yields and superior quality.

GenScript Manufacturing Suites

Bio-R&D Center,
Nanjing, China (2x200L)

GMP compliant for IND &
Clinical phase 1 material

USP Applikon 3L/10L
DSP Cytiva AKTA pure/avant/pi-lot/crossflow

USP Cytiva XDR 50L/200L SUB
DSP Cytiva AKTA Process

Bio-MFG Center,
Nanjing, China (6x200L&2x500L)

GMP compliant for Clinical
phase 1 & phase 2 material

USP Thermo fisher/Cytiva 200L/500L SUB
DSP Cytiva AKTA Process / AKTA Ready

GenScript GMP Quality System

Quality Management System

based on ICH and GMP, including 6 sub-systems

Good quality culture from top manager to junior staff

- Experienced team with access to cGMP operation and manufacture know-how
- Reliable GMP facility
  - Physical segregation for each production line
  - Unidirection flow
  - Clean utility meeting global standards
  - All-disposable equipment
  - Automation system
- Quality system compliant to ICH GMP

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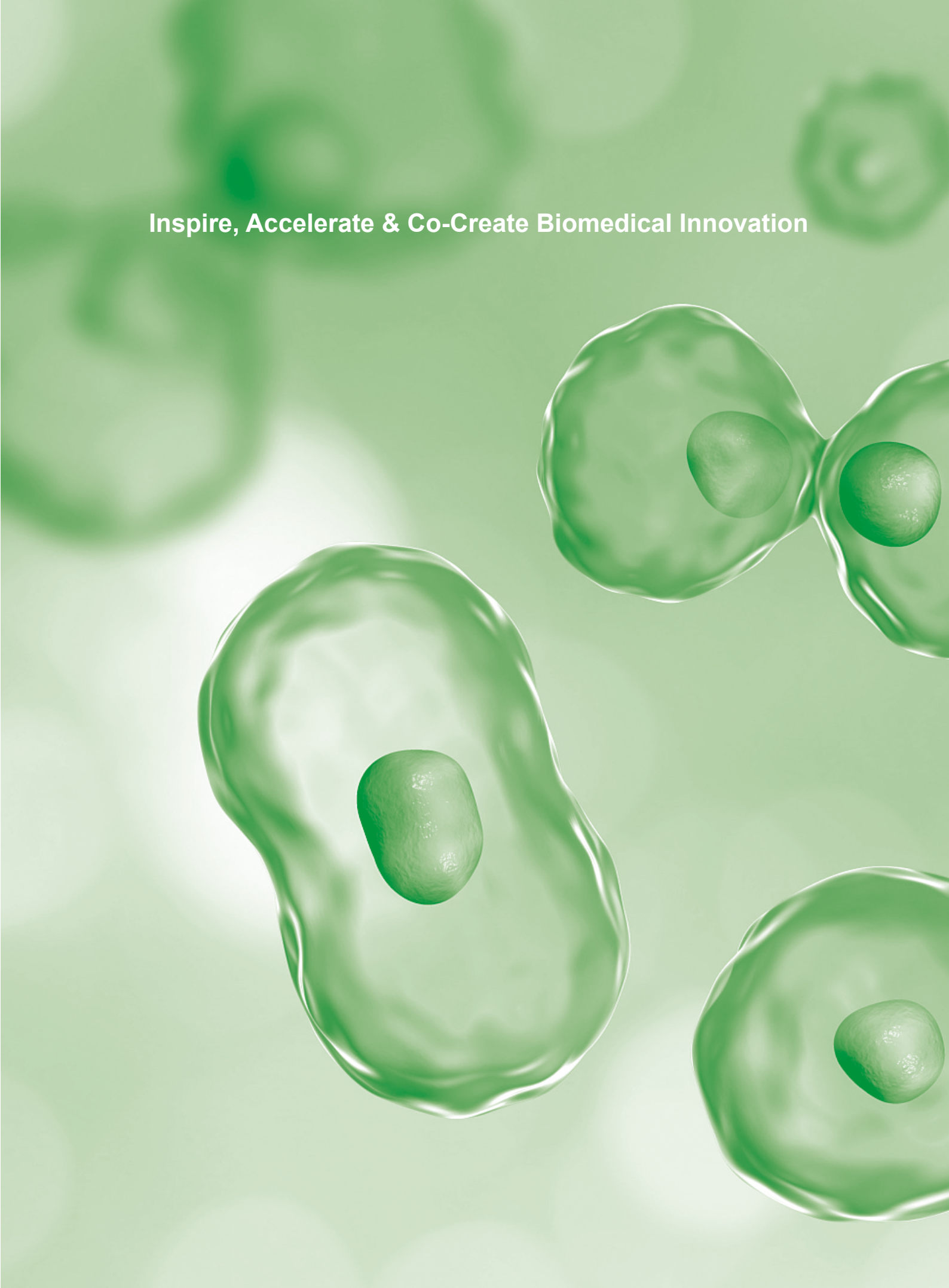

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