FUJIFILM

Diosynth biotechnologies

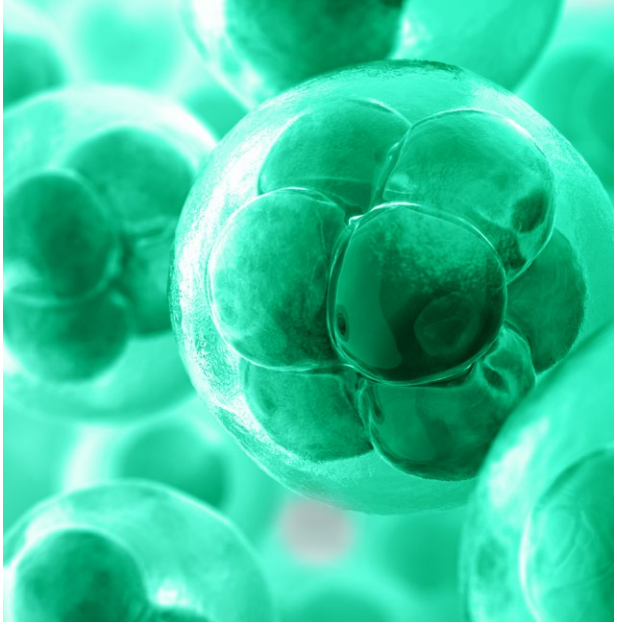
Gene Therapies

Our Experience and Capabilities

Partners for *Life*

Advancing tomorrow's medicines

The Biologics and Gene Therapies CDMO partner for life



Good science, experience and a quality driven approach

Cell Line/Strain Development

As your partner, we help expedite this process by bringing our years of experience and our expression platform technologies for microbial expression, pAVEway™; and platforms and solutions for mammalian expression, Saturn™ and Apollo™ X.

Process Development

At FUJIFILM Diosynth Biotechnologies our Process Development philosophy is driven by designing processes for a wide range of expression systems that result in having phase appropriate product controls that will result in successful process execution during cGMP manufacturing.

cGMP Contract Manufacturing

We offer our partners highly flexible clinical and commercial cGMP facilities for the production, by microbial fermentation and cell culture, of biologics and advanced therapies.

Quality

This is at the heart of everything we do. Quality drives the development and the successful production of your biologics and advanced therapy products from beginning to end, with propriety statistical design tools like RAPTA™ for Laboratory Process Characterization (LPC).

Unique levels of expertise

Virus Technology

- Experience with multiple viruses and virus vectors
  - Attenuated, recombinant
- Generating RVB, MVB, WVB
- Virus titer or genome copy number and total particles determined by orthogonal methods
- Plaque purification
- Virus engineering: purification; inactivation; adaptation to cell lines.

Cell Culture

- Adherent Cells
  - iCellis Nano, HYPERStack-36, CellSTACK
- Suspension Cells
  - 1-200L SUB
- Adaptation Adherent to Suspension
  - HEK293, Vero
- Adaptation Suspension to Adherent
  - SF9, EXPI293, EB66, A549
- Cell culture adaptation to serum free media.

Recombinant Technologies

- Staff is experienced with rDNA technologies including:
  - Transfection
  - Cloning and gene insertion
  - Transduction.

Vaccine Expression Systems

Vaccine Antigen Expression Systems

E. *coli*

CHO

Pseudomonas

Yeasts

Other Mammalian Cells

(HEK-293, Vero, EB66)

Virus Replication Platforms

Typical Hosts:

HEK-293

Per.C6

Sf9/Sf21

CHO

EB66

Vero

MDCK

A549

HeLa

Viruses and Vectors

Adenovirus

Adeno-associated virus (AAV)

Lentivirus (pDNA)

Poxvirus

Baculovirus

Herpesvirus

Picornaviruses

Flaviviruses

Retroviruses

Influenza

cGMP-Ready by Design

Developing a long-term manufacturing ready process for Gene Therapy and Viral Vaccine products can be a challenge. These challenges include selecting the right combination of host/virus systems.

The use of viruses to produce important therapies including gene therapies have become an important modality in the treatment of many disorders. Selecting the right combination will depend mainly on safety, toxicity, and the ability of the host/virus combination to effectively produce the target product.

Typical Viral Vectors

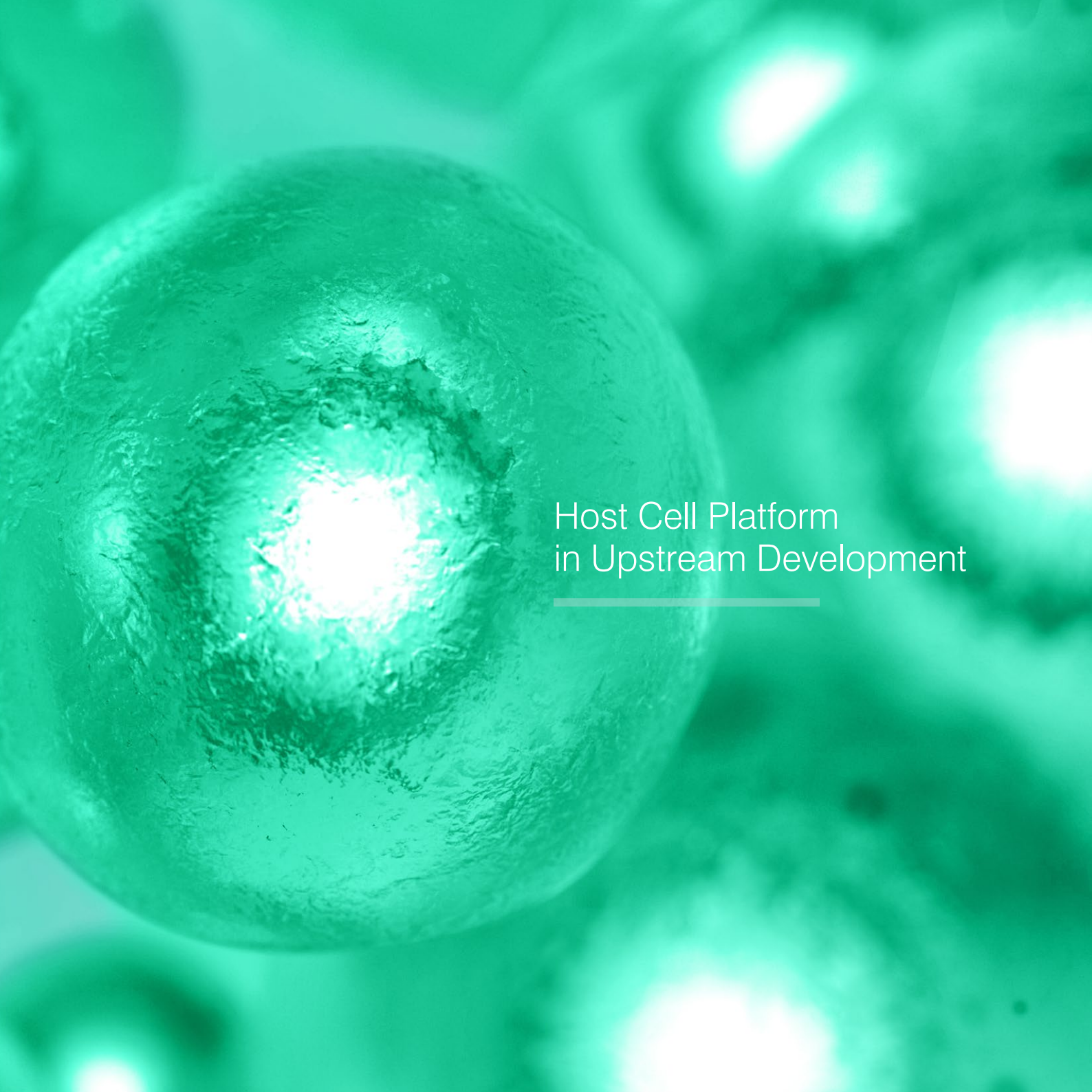
Adenovirus

Adeno-associated virus (AAV)

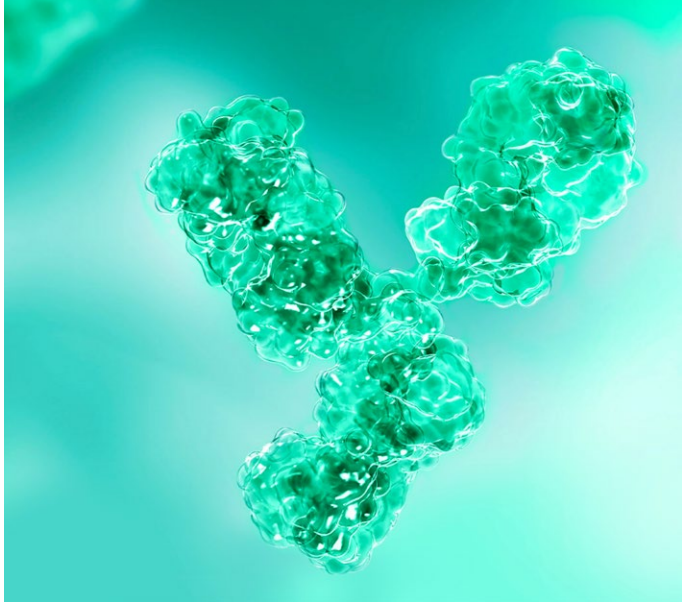
Lentivirus

Poxvirus

Baculovirus



Host Cell Platform in Upstream Development



Host cells have different growth properties, including adherent versus suspension cultures. This may require the evaluation of alternate platforms such as Hyperstacks™, Cell Factory™ systems and/or microcarriers. Some host cells, such as HEK, may have media requirements that can be challenging.

Typical Host Cell Platforms Include:

- **HK-293** - these cells typically serve as excellent plasmids to make AAV virus. Also used in the production of lentiviruses and are typically compatible with suspension processes
- **Per.C6** - human cell line, characterized for the propagation on wInfluenza A and B
- **Sf9/Sf21** - well established systems with regulatory traction
- **CHO** - well proven, characterized, and established host
- **EB66** - typically used for antibody production
- **Vero** - these systems already have regulatory traction with an approved product. However the typical manufacturing challenge is incompatibility with suspension processes
- **MDCK** - typically have good virus growth advantage, adapt well to serum free media.

Advanced Purification

Purification strategies for long term success are important to consider while developing a process. Ultracentrifugation for virus purification is typically not a scalable solution long term.

Evaluation of purification by chromatography should be considered early during process development.

By offering our partners highly flexible clinical and commercial cGMP facilities for their production, either by microbial fermentation and cell culture, or biologics and gene therapies.

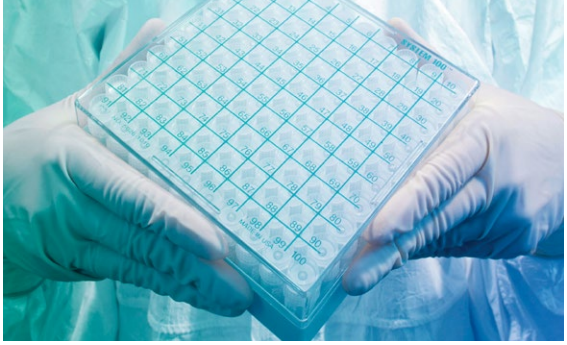
Fill Finish Capabilities

- Early to late phase viral fill capabilities
- State of the art isolator technology to minimize risk to Patient
- Typical batch size from a few hundred to 10k with capability to 25k
- Be able to support multiple container types: vials, syringe, and cartridge.

Analytical Capabilities

Our Analytical Team specializes in development of analytical assays and their qualification to support production and examine expression of our clients' therapeutics and virus vectors.

We continually evaluate how best to utilize analytics for efficient, cost-effective product quality, phase appropriate development and execution of programs. Our Analytical Development philosophy has at its core one main objective: developing and utilizing methods that have built-in success strategies for your Program. Our Virus Analytical Development team is very experienced with the analytical development strategies needed from Monitoring Production to Final Release Potency and Impurity Testing.



Dedicated gene therapy facilities

Our state-of-the-art facilities include:

- The National Center for Therapeutic Manufacturing which is designed for Process Development and Phase I/II GMP production of gene therapies (Viral, Microbial, Plasmid)
- The Flexible BioManufacturing Facility which is designed for cGMP production of Viral and Gene Therapy products, Phase I-III and Commercial.

We are able to offer our partners over 120 years of combined experience in the field of vaccine production and virology.

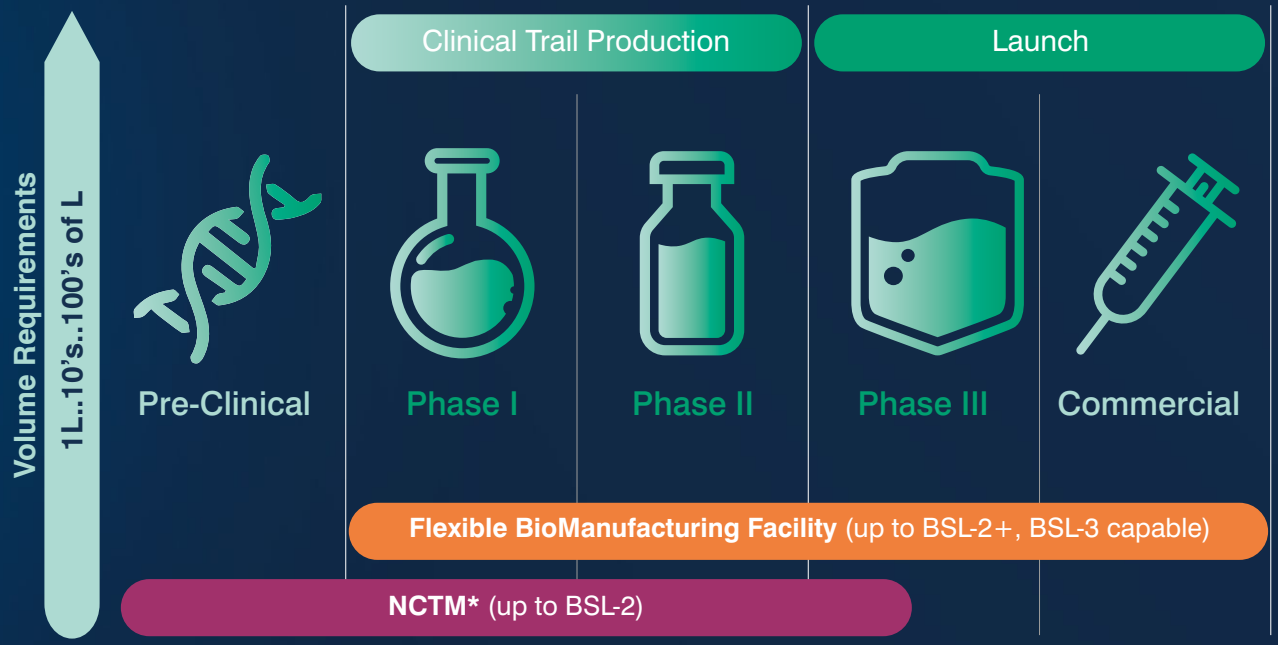
Our team has a vast range of experience in both research and industry. Our aim is to develop processes based on solid science but with manufacturing scale up ability as the end point. This expert knowledge is the foundation of our Process Development capabilities.

Assets for every stage of product lifecycle

Our manufacturing assets will support your full product lifecycle - from pre-clinical development to commercial production.

- Use of Mobile Clean Room Technology
- Fully segregated and self-contained units
- VHP-based cleaning and rapid change-over
- Can connect MCRs together as needed (i.e., Upstream, Recovery, Downstream)
- Near exclusive use of single-use technology, from cell bank to product vial
- Fully functional Process and Analytical development, and Virology sections
- Extensive Quality system, multiple clinical viral and non-viral bulks released
- High-speed robotic viral product fill finish capabilities supporting DP production from early phase to commercial.

Product lifecycle stages



*NCTM = National Center for Therapeutic Manufacturing

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