Fujifilm Diosynth Biotechnologies Texas

Contract Development and Manufacturing Organization

Partners for Life
Advancing tomorrow's medicines.
Global Vision

To be the leading and most trusted global Contract Development and Manufacturing Organization partner in the biopharmaceutical industry.
One Global Company

3 SITES
Billingham, UK
College Station, TX
RTP, North Carolina

~1,200 EMPLOYEES
World Wide

6 LICENSES
For commercial manufacturing

300+ MOLECULES
In process development and/or manufacturing

25+ YEARS
Of Biologics CDMO experience.
What we offer

Preclinical
Gene Expression & Strain / Cell Line Development
Process Invention
Pre-Clinical Manufacture

Phase I
Process Development & Optimization
Analytical & Stability
cGMP Manufacture
Fill/Finish (Viral Products)

Phase II
Process Development & Optimization
Analytical & Stability
cGMP Manufacture
Fill/Finish (Viral Products)

Phase III
Process Characterization
Process Validation
Late Phase cGMP Manufacture
Stability

Regulatory Approval

Launch
Commercial Production
Post-approval Activities
Strong inspection history by the major regulatory agencies
FDBT Manufacturing Facilities, College Station, Texas

National Center for Therapeutic Manufacturing - 152,000 ft²
- Flexible multi product early stage cGMP
- Mobile Clean Rooms
- Work Force Training labs

Texas Biomanufacturing Facility (TBF-100) – 117,000 ft²
- Flexible multiproduct modified open ball room
- 2 x 2000L Single use cell based manufacturing trains installed
- Capacity for 10 additional trains

Flexible Biomanufacturing Facility (FBF-200) – 76,000 ft²
- Simultaneous, multi product viral process manufacturing facility
- Designed for late stage commercial manufacturing
- Mobile Clean Room Technology operating at BSL2+, BSL3 capable.

Final Drug Product Capacity
- Installed and qualified by Q4 2018
FDBT Process Development Lab

- 7000 ft² of BSL-2 laboratory space
- Single use Micro Bioreactors up to 200L Single Use Bioreactors for suspension cultures
- Cell Stacks, Hyperstacks, and I Cellis for adherent cultures
- Full purification and analytical development support
Overview of FDBT PD Department

• **Department**
  – 24 Scientists growing to 30 by year end
  – Virology and Analytical Development
  – Upstream Process Development
  – Downstream Process Development

• **Department Goal**
  – Closed, continuous, single use-based processing, using standardized approach
  – Strong focus on latest technology and innovation
Virus Expertise and Cell Culture Skills

- Executed Adenovirus, AAV, Influenza and Baculovirus programs
- Additional expertise in
  - Flaviviruses, Rota virus, Lentivirus, retrovirus, CMV, Pox virus, HSV and Hep A and B

- Suspension to adherent: Expi293F, A549
- Adherent to suspension: Vero, HEK293
- Suspension Cell lines: HEK293, A549, SF9, EB66 and Daudi
- Adherent: MDCK, Vero, HEK293
- Adapted Cells to Sera-free growth: Vero, MDCK, HEK293
Virus Quantitation Methods

- Plaque Titer
- TCID$_{50}$
- Infectious Center Immunostaining
- HA titer
- Dual color Flow Cytometry titer assays that can show both virus and insert
- Total viral particles
  - NanoSight
  - A$_{260}$
  - HPLC
- Genome copy number (RT) qPCR
Analytical Capabilities

- HPLC
  - Agilent 1260 UHPLC, Agilent 1200 HPLC
  - Hitachi Chromaster HPLC
  - Thermo Dionex UltiMate 3000 UHPLC
- Host Cell DNA
- CE/SDS-PAGE/Western Blot
- ELISA
- PCR/qPCR/dd PCR
- Restriction Analysis
Small-Scale Models: Quality by Design

- DoE, Screening, Design Space
- Parallel cell culture
- Continuous Improvement
- Troubleshooting
Scale-Up and Scale-Down

DASGIP Parallel Bioreactor ± HF (1/200)

Single use Micro Bioreactors
Screening Media, DO, pH, etc (no KLa)
1/1000 scale – reduce costs; increase capacity;

Process development; Continuous Improvement; Troubleshooting;

XDR GMP Single-Use Bioreactors

SUBs from Pilot-Scale Bioreactor ± HF or ATF (Confirmation runs, Tech Transfer, Demonstration, Engineering) to Manufacturing

Private and Confidential
GMP Equivalent Process Pilot-Scale

• 1 x 10 L Bioreactor w/ATF2
• 1 x 50 L Bioreactor ± ATF6
  – Perfusion
  – High Cell Density
• Performed in MCR or PD lab
Adherent 2D vs Fixed Bed 3D Culture

Seeding@1E5/cm²

1xHS36 = 1E10 cells → 100xHS36 = ~1E12 cells

Seeding@3.2E3/cm² → ~1E10 cells

Seeding@3.2E3/cm²
11 day culture = 2.3E5/cm² = ~1.5E12 cells
Key Bioprocess DSP Equipment

- **Chromatography**
  - 1x AKTA Explorer, 2x ÄKTA Avant, 3 x ÄKTA Pure, 3 x ÄKTA Pilot,
  - Column base: BPG, HiScale, XK, INdex, OmniFit,

- **Cell Lysis**
  - 1 x PandaPLUS homogenizer

- **Filtration and clarification**
  - 1 x Spectrum Krosflo, 1 x AKTA Flux S, 3 x Beckman Avanti (lab and demo scale), Custom single use TFF (lab scale and demo), Millipore Millistak depth filter system.

- **Mixer systems**
  - Pall Allegro Mix tanks, LevMix and MagMix systems

- **In-process analytics**
  - SDS-PAGE, HPLC, Nanosight, qPCR, ELISA
At the end of development a lab scale demonstration run is performed

All parameters directly scale to manufacturing scale with same timings

Process transferred to manufacturing by Process Sciences and PD

PD provide ‘on the ground’ for engineering run and provided technical support for the full manufacturing campaign
Summary

- Available GMP manufacture capacity to produce clinical I-III materials and commercial products
  - Flexible facilities with mobile clean room design
  - Single use upstream and downstream process
- Deep understanding of viral products and processes
  - Virology expert
  - Well established process development teams with strong track record within FDB network
- Regulatory knowledge and commercial manufacture experience
  - An integrated global quality organization
  - Conducted >24 Process Characterization projects and completed >10 Process Performance Qualification (PPQ) Campaigns within FDB network

FDBT has a solid foundation and an integrated technical and regulatory network to assure the success of GMP manufacture for clients
• FDBT thanks CPRIT for support with the set up the Process Development Laboratory in College Station.
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