Mission-based Good Manufacturing Practice (GMP) Facility

**Mission:** To help our clients accelerate the translation of their discoveries into human clinical trials as efficiently and cost effectively as possible.

**Expertise:** Cell-based therapies, protein biologics, quality assurance and control

**Services:** Process development, manufacturing scale-up and cGMP/cGTP manufacturing

**Clients:** Academic researchers, clinicians, early stage biotechnology companies and established pharmaceutical companies

**Flexible Approach:** As a mission-based academic Contract Manufacturing Organization (CMO), we engage in each client’s product development project with a vested interest in advancing healthcare in meaningful ways. Processes, from initial laboratory scale and beyond, are refined through the application of our expertise, state of the art equipment and quality management system. We work collaboratively, acting as part of client teams, to meet project objectives, manufacturability requirements and the quality by design paradigm. Our focus and mission is to deliver GMP grade materials ready for human clinical trials.

**Location:** Conveniently located on the University of Colorado Anschutz Medical Campus, which is adjacent to Children’s Hospital Colorado and the University of Colorado Hospital.

“...The Gates Biomanufacturing Facility was able to provide my company with high quality, active, preclinical material under a tight timeline after other CMOs had failed. The team took real ownership of the project and dealt with every challenge professionally, creatively and in a timely fashion. They were an invaluable resource for accelerating the development of our therapeutics.

- Geoff Davis PhD
Angelica Therapeutics
Facilities Overview

Footprint: 14,000 total square feet

Cell Processing:
- Capable of processing minimally manipulated, expanded, and genetically modified cells
- Five ISO 7 class clean rooms

Quality Assurance and Control:
- Dedicated full-time quality staff  
- Electronic Quality Management System (QMS)  
- Process equipment monitored/recorded wirelessly to 24/7 offsite service  
- Key card controlled access

Protein Manufacturing:
- Microbial infrastructure with five- and 50-liter fermenters
- Four ISO 7 and ISO 8 class clean rooms for fermentation, purification, buffer preparation and aseptic fill

Emergency Power systems:
- Uninterruptible power supply
- Generator

Clean Room Design Features
- Single pass air designed for up to 60 air changes per hour
- Dedicated air handler for cGMP cell processing clean rooms
- Dedicated air handler for cGMP protein manufacturing clean rooms
- Pressurization cascade to prevent cross contamination between clean rooms
- Pressurization monitored and alarmed through an automated building management system

1 Exhaust air out  
2 Filtered air in  
3 HEPA filter  
4 Dedicated air handler  
5 Filters covering 20-30% of ceiling  
6 ISO 7 cleanroom space
Thomas Payne, PhD
Director of Cell Processing

- More than fifteen years in cell therapy research and manufacturing
- Conducted research investigating cell therapy approaches for heart failure at University of Pittsburgh, Children's Hospital Pittsburgh of UPMC
- Translated research into multiple human clinic trials at a cell therapy start-up
- Established cell manufacturing processes and test methods for clinical trials

**cGMP/cGTP Cell Processing Clean Rooms**
- Five – ISO 7 class clean rooms capable of processing minimally manipulated, expanded and genetically-modified cells.
- Clean rooms operate at 20-40 air changes per hour with single-pass HEPA-filtered air supplied by a dedicated air-handling unit
- One or two biological safety cabinets per clean room with built-in particulate monitoring probes
- Two cell processing clean rooms are equipped with vented biological safety cabinets for vector handling
- CO₂ and O₂ controlled incubators
- CliniMACS®Prodigy System
- Temperature-controlled centrifuge
- Automated cell counter – trypan blue, fluorescent dye compatible
- Barcode scanner for equipment and materials traceability

**Cell Therapy Process Development Laboratory**
- Equipment mirrors cGMP cell processing equipment for seamless process transfer - 1:1 scale
Protein Manufacturing

Matthew Seefeldt, PhD
Director of Protein Chemistry and Manufacturing

- Built processes from Phase I to Phase III
- Ten years of prior experience working with more than 150 different proteins, of which a majority were “tricky” proteins requiring innovative process steps
- Considered a world expert in protein refolding
- Expert in protein stability and formulation, with specific understanding of the link between aggregates and immunogenicity
- Built processes resulting in upstream high yields, effective purification schemes, and top-end formulation

CgMP Protein Manufacturing Clean Rooms

- Microbial infrastructure – E.Coli
- 50 liter working volume fermenter with sterilization-in-place
- Clean-in-place skid
- Four ISO 7 and ISO 8 clean rooms operating at 20-40 air changes per hour with single-pass HEPA-filtered air supplied by a dedicated air handling unit
- Clean rooms for buffer preparation, clarification, protein purification, and aseptic formulation and fill of bulk drug substance
- Two – 50 liter magnetic mixers for buffer preparation
- Purification - 0.25 to 2 liter column chromatography capability in both gradient and step format
- Ultra-Filtration/Tangential-Flow Filtration

Protein Process Development Laboratory

- Equipment mirrors cGMP processing equipment for seamless process transfer - 1:10 scale
- Two – 5 liter Microbial Fermenters
- Purification: AKTA™ PURE, AKTA™ PRIME
- Shaker/incubator
- Tangential flow filtration system
- Micro fluidizer
- High pressure refolding capability
Quality

Gabriel Orosco, BSME
Director of Quality Assurance

- Worked in multiple regulatory areas with direct FDA/WHO/NB interaction in cGMP audits in biopharmaceuticals, oral solid dose, active implantable, injectable drugs and many medical devices
- Considered an expert in facilities, computer systems, operations and quality assurance in corporate and startup capacities
- Remediated multiple problematic sites to meet best in practice cGMP, including clearance of Warning Letters and 483s

Quality Management System (QMS)

- Dedicated quality assurance staff
- Q-Pulse – EQMS system
  - Supplier quality assurance
  - Personnel management
  - Asset management (maintenance and calibration)
  - Real-time trending and analysis
  - Sharepoint client side portal
  - Real-time equipment monitoring
- Provides oversight of all manufacturing and facility operations through a comprehensive quality management system tailored to meet regulatory requirements for protein-based biologics and cell-based products.
- Strategic development of QMS in technical areas based on customer type
- Material tracking software utilizing barcodes
- Environmental monitoring trending software

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The Gates Biomanufacturing Facility is a valuable resource for the Anschutz Medical Campus. The team was responsive, conducting thorough fermentation and downstream protein purification experiments. The facility’s efficiency in helping us scale our early-stage processes accelerated our ability to conduct preclinical research.

- Jan P. Kraus PhD Professor
  Pediatrics and Cell and Developmental Biology, University of Colorado School of Medicine

Quality Control Laboratory

- State-of-the-art, qualified equipment for environmental and product testing
- Dedicated quality control staff experienced in cellular and protein analytical techniques

Cell Processing

- Real-time thermocycler
  - Gene expression
  - Mycoplasma
- Flow cytometry – ten colors, three lasers
- Automated cell counter – trypan blue, fluorescent dye compatible
- Microscopy – brightfield, phase, fluorescence
- Microplate reader with high-content cell imaging
- ELISA
- Cell-based assays

Protein Manufacturing

- HPLC/UPLC systems
- UV-Vis spectroscopy
- SDS-PAGE
- ELISA and cell-based assays
- Real-time thermocycler
- Residual host cell DNA
- Biophysical and mass spectrometer characterization using CU Anschutz Medical Campus core facilities

Microbiology

- Dedicated microbiologist
- Endotoxin testing
- Bioburden testing
- Mycoplasma testing

- Sterility testing
- Microbial air sampling
- Non-viable particle analyzers
Utilities

- United States Pharmacopoeia (USP)-grade purified water generation and distribution
- USP-grade gas distribution system with redundancy
- USP-grade clean steam
- ISO classified clean compressed air
- Emergency power systems for critical equipment includes a generator and an uninterruptible power supply

Cryogenic and Material Storage

- Centralized, on-site cryogenic and material storage facilities
- Cryogenic storage room with ultra-low (-80 °C) freezers, controlled-rate cryopreservation freezers and liquid nitrogen vapor storage freezers
- Freezer sample management database with barcoding
- Material storage areas for both ambient and temperature-controlled conditions
- Material management database and barcoding for traceability
- Microsoft Dynamics MRP system
- Supplier quality assurance program
**Gates Biomanufacturing Facility**

**Floor Plan**

- Cell Processing Clean Rooms
- Protein Manufacturing Clean Rooms
- Cryogenic & Material Storage
- Utilities
- Quality Control Laboratory
- Cell Processing Development & Scale-up Laboratory
- Protein Process Development Laboratory
- Quality Assurance

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### Our Partners

- uchealth
- School of Medicine, University of Colorado Anschutz Medical Campus
- Children’s Hospital Colorado
- GATES FRONTIERS FUND

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### Getting Started

Based on information provided by the investigator along with our “needs analysis” discovery process, we will prepare an implementation plan with scope of work and estimated cost.

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### Contacts

**General Information**

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**Technical Evaluation**

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- Matthew Seefeldt, PhD, Director of Protein Chemistry & Manufacturing - matthew.seefeldt@ucdenver.edu - 303.724.8474