**Mission-based Good Manufacturing Practice (GMP) Facility**

**Mission:** To accelerate the translation of scientific discoveries into human clinical trials as safely, efficiently, and cost effectively as possible according to high quality standards.

At the Gates Biomanufacturing Facility we collaborate with basic science and clinical investigators to successfully translate laboratory discoveries into early phase clinical trials.

The Gates Biomanufacturing Facility at the University of Colorado Anschutz Medical Campus is a 14,000 square ft. GMP compliant manufacturing facility that provides cell-based therapies and protein biologics for use in preclinical investigations and Phase I and Phase II human clinical trials. The GBF was established in 2015 though partnership with the Gates Center for Regenerative Medicine, University of Colorado Health, Children’s Hospital Colorado, University of Colorado-School of Medicine, and the Gates Frontiers Fund.

"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"
About

Values:
- Safety
- Quality
- Innovation
- Integrity
- Efficiency
- Collaboration

Expertise:
- Cell-Based Therapies
- Protein Biologics
- Quality Assurance
- Quality Control
- Regulatory support

Clients:
- Academic Researchers
- Clinicians
- Early Stage Biotechnology Companies
- Established Pharmaceutical Companies

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.

Services:
- Cell Therapy and Protein product manufacturing, characterization, storage, and distribution
- Cell Therapy and Protein product process development, consultation, and support
  - Batch record creation and refinement
  - Develop manufacturing SOPs
  - Quality manufacturing process and analytical methods
  - Build and activate Bills of Materials and SOPs for orders to manufacture, collect, process, and release products to patients
- Quality Control (assays and testing)
  - Broad analytical platform that can be tailored for specific projects
  - Best in class environmental monitoring program
- Quality Assurance
  - Robust electronic Quality Management System with cross-functional Quality Council
  - Dedicated Quality staff
  - Documented release of each cGMP suite after cleaning and change over for each manufacturing campaign
  - Equipment qualification program
  - Vendor qualification program
- Regulatory (FDA) compliance and support
  - Assist with pre-IND FDA meetings
  - Assist with Chemistry, Manufacturing, and Controls (CMC) section of -IND preparation
  - Audit and review procedures, processes, and test results
  - Assist with labeling requirements
  - Monitor product non-conformances
- Clinical Protocol Support from Facility Medical Director
  - Review clinical protocol
  - Ongoing study management and problem resolution
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 with ISO 5 biological safety cabinets

**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
Ryan Crisman, Ph.D.
Executive Director
- Extensive experience in cell therapy CMC operations including development and cGMP manufacturing from Phase 1 to commercial-ready processes
- Strong CMC regulatory background for early and late phase cell therapy and protein molecules
- Broad experience in protein fermentation, purification, and formulation with expertise in biophysical characterization

Roger Giller, M.D.
Medical Director
- Over 30 years of experience in laboratory research, clinical research and patient care in the fields of human bone marrow transplantation and other forms of cellular therapy
- Founded, then led and maintained regulatory compliance of the Pediatric Bone Marrow Transplant Program at Children's Hospital Colorado / University of Colorado School of Medicine for 23 years (1993 – 2016)
- Extensive patient care and clinical research expertise in hematopoietic stem cell transplantation, pediatric cancer, nonmalignant blood diseases and immunologic disorders
Cell Processing

Matt Seefeldt, Ph.D.
Director of Cell Therapy

- Eighteen years of experience in biotechnology manufacturing, with an emphasis on translating early-stage therapeutics into the clinic.
- Developed six IND-enabling cGMP processes on both microbial derived proteins and cell therapy products. One of those products was successfully scaled to support Phase III clinical studies.
- Successfully completed the build out and GMP preparation of the Gates Biomanufacturing Facility.

- Considered a world expert in protein refolding
- Expert in protein stability and formulation, with specific understanding of the link between aggregates and immunogenicity

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 a minimum of 30 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
- \( \text{CO}_2 \) and \( \text{O}_2 \) controlled incubators
- CliniMACS\textsuperscript{\textregistered} Prodigy System
- Sepax C-Pro Cell Processing 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

Branden Antonio Salinas, Ph.D.
Director of Protein Development and Manufacturing

- 10 years of corporate Process and Product Development experience with therapeutic and industrial proteins
- Early and Late Phase Drug Development experience
- Owner’s Engineering Project Manager for a large Greenfield API Facility
- Expert in protein solubility and stability
- Experienced troubleshooter and technical problem solver, bridging science and engineering to solve yield, quality and process robustness issues

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 a minimum of 30 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 and AKTA protein purification system
- 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

Christopher Garbe, M.S. M.B.A.
Director of Quality
- 20+ years’ experience in the design, qualification and operation of process/analytical development and quality control labs in a cGMP setting
- Leader in internal and external Quality operations for start-up and large pharmaceutical organizations to support recombinant protein, nucleic acid and cellular therapy (CAR-T, TCR, cord blood) products as they progress from pre-IND to clinical trials through commercial approval
- Responsible for the translation and technology transfer of multiple drug substance and drug product manufacture and quality operations within academic, industrial and contract manufacturing settings
- Author of numerous Chemistry, Manufacturing and Control regulatory submissions to support IND/BLA/MAA applications and post-marketing approvals
- B.S. in Chemistry from Rensselear Polytechnic Institute, M.S. in Biochemistry and Molecular Biology from George Washington University, M.B.A. from McCombs School of Business – University of Texas – Austin

Quality Management System (QMS)
- Dedicated Quality Assurance staff
- Q-Pulse – Electronic Quality Management System (EQMS)
  - Supplier qualification and management
  - Personnel management
  - Asset management (maintenance and calibration)
  - Real-time trending and analysis
  - Document Control
  - Real-time equipment monitoring
- Provide 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 and product requirements.
- Material tracking software
- Environmental monitoring trending software

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 microbiologists
- 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

- Cryogenic storage room with ultra-low (-80 °C) freezers, controlled-rate cryopreservation freezers and liquid nitrogen vapor storage freezers
- Freezer sample management database
- Material storage areas for both ambient and temperature-controlled conditions
- Microsoft Dynamics MRP system for materials traceability
Our Partners

Getting Started
To inquire about our capabilities and services please contact one of the individuals below. Based on the information you provide and our “needs analysis” discovery process, we will prepare an implementation plan with scope of work and estimated cost.

Contacts

General Information
- Timothy Gardner, CFO, Business Development - timothy.gardner@ucdenver.edu - 303.884.9056

Technical Evaluation
- Matthew Seefeldt, Ph.D., Director of Cell Therapy - matthew.seefeldt@ucdenver.edu - 303.724.8474
- Branden Antonio Salinas, Ph.D., Director of Protein Development and Manufacturing - branden.salinas@ucdenver.edu - 303.724.9646
- Ryan Crisman, Executive Director - ryan.crisman@ucdenver.edu - 720.771.0749