Scientist II

SUMMARY

Bolt Biotherapeutics has an exciting opportunity for a highly motivated process development scientist to join our drug development team and play a key role in developing new targeted therapeutics for cancer. The candidate will work closely with other scientists with diverse scientific expertise at a new biotechnology company currently located in Redwood City, CA.

RESPONSIBILITIES

This position, reporting to the Associate Director, Process Development & Manufacturing, will be a key contributor and shall manage Bolt's Process Development & Manufacturing Operations that are performed either internally or contracted externally to CMO's. The candidate will be responsible for the development and implementation of processes to manufacture the Bolt's antibody-based protein drug candidates. In this role, the individual will actively seek to continuously improve operations, perform authorship on regulatory submissions and represent the company on process development & manufacturing related issues. This position can be the project contact for process development and manufacturing related activities with contract manufacturing and other organizations. The incumbent will provide technical or scientific expertise and leadership in the process development and improvement of recombinant proteins (mAb, ADC etc) and scale up and technical transfer to the manufacturing of recombinant proteins. Activities are centered on managing programs /projects for developing and driving unit operations such as filtration, chromatography, formulation, UFDF, conjugation and process trouble shooting.

JOB DUTIES

Process Development

- Development of purification, and UF/DF processes that are scalable, and robust that is transferable to GMP manufacturing operation for production of highquality protein therapeutics for human clinical use
  - Identification of appropriate chromatography and UF/DF steps for purification of a protein therapeutic including resin choice, buffer and filter selection and operating parameters
  - Establishment of proven acceptable ranges and critical processes parameters
  - Evaluation of buffer stability, processing conditions and times
  - Evaluation of appropriate in-process controls and monitoring, including any hold steps
  - Perform gap and risk analysis, as required
- Development of processes and purification support for research proteins and reagents
- Participation in process transfer and troubleshooting
- Design & implementation of process improvements and optimization
- Maintenance of the Process Development Laboratory including general lab organization of lab supplies, equipment and reagents.
- Document activities, as appropriate, in laboratory notebooks and authoring and/or reviewing reports
- Authorship and/or review of Process specifications, in-process testing, master batch records and operating procedures.

Manufacturing

- Management of DS and DP manufacturing schedule and CMOs including availability of raw materials to ensure adequate clinical supply
- Oversee production activities at CMOs and provide technical support and troubleshooting.
- Provide manufacturing solutions and technical expertise to support GMP scale up efforts that lead to sustained manufacturing consistency, robustness, scalability, improved efficiency, and reduced costs.
- Review of executed batch record data.
- Lead, review and/or approve investigations and closure of internal and external OOS/OOT, deviations and excursions and CAPA with QA.

- Generate and/or review Process Validation documentation, including Product Validation Master Plans, Cleaning Validation Plans, and Process Performance Qualification Protocols and Reports.
- Execute action plans independently or as part of the team, or as the technical /project lead for a departmental team.
- Independently prepares and critically edits procedures or technical reports of a complex nature, assimilating information across functional areas, suitable for inclusion in IND, BLA, or equivalent regulatory submission.

Other

- Represent the Organization at internal, external and partner technical meetings and internal or external audits
- Author, review and/or approve portions of the CMC Regulatory Sections
- Liaise with senior management and external partners in technology evaluation and co-development opportunities
- Manage relationships with CROs, CTOs, CMOs and external partners
- Provide input to budgets for Process Development & Manufacturing for approval by executive management.
- Manage activities to time lines to budget
- Develops creative, novel programs to meet departmental objectives.
- Responsible for representing the functional area or capable of leading a cross-functional team to achieve identified objectives.
- Other duties as assigned

JOB REQUIREMENTS

Required

- Educational degrees (BS, MS or Ph.D.) must be relevant to position (e.g., Chemical engineering, bioengineering, Biology, Biochemistry)
- Ph.D. 2+rs, MS with 6+ years, BS with 10+ years of direct experience in process development and relevant, progressive and broad-based CMC experiences supporting the execution of GMP productions. Prior GMP experience is desired. Ph.D. strongly preferred (Depending on the area of assignment, directly related experience or a combination of directly related education and experience and/or competencies may be considered in place of the stated requirements.)
- Extensive hands-on experience in purification at various industrial scales using both non-automated methods and automated FPLC systems, Operational proficiency with AKTA Avant / AKTA Pilot / AKTA Crossflow/AKTA ready, centrifuge and TFF is desired.as well as batch purification, precipitation, filtration (including depth and TFF), concentration, bulk filling, and CIP/SIP operations
- Thorough knowledge of the theory of protein purification and protein chemistry, including the basis of chromatography and other downstream techniques including: column chromatography (IEX, HIC, IMAC, SEC, RP) and membrane chromatography, depth filtration, centrifugation, UF/DF, refold and conjugation, and analytical analysis (Mass Spec, SDS-PAGE, western blots, IEF, UV/Vis spectrophotometry, HPLC, ELISA, HCP, and BCA/Bradford method)
- May lead cross functional teams or represent functional area on cross functional teams.
- Scale down modeling, DOE, and technology and scale up experience
- Experience in a purification process development including resin and condition screening
- Extensive experience in antibody and/or protein conjugations
- Cell culture knowledge and experience, desirable
- Chemistry knowledge and experience, desirable
- Familiarity with standard protein analytical methods and mechanisms of protein instability to achieve desired product quality
- Familiarity and experience with cGMP/GLP, regulation & guidance (e.g. CFR, ICH, WHO, ISO, Part 11, EU Annexes) and working in a GMP environment

- Excellent communication, technical writing, organizational and collaboration skills, self-motivation, prioritization, independence, good decision making, and leadership
- Fill / Finish and lyophilization manufacturing experience desirable
- Experience with IND, IMPD and BLA filings desirable
- Experience managing CMO/CRO's
- Experience management of a developmental laboratory desirable
- Proficient with the use of MS Office software (Excel, word, Powerpoint,Project, Visio) and application software including Unicorn, JMP, mintab, DesignExpert etc).

WORKING CONDITIONS/PHYSICAL DEMANDS

This is a process development position that requires working in a laboratory environment with hazardous chemicals. Protective clothing, gloves and safety glasses are required while working in the lab. Requires the ability to lift containers or instruments (up to 25 pounds) and work standing at a fume hood or lab bench for extended periods.

TRAVEL REQUIREMENTS

Some travel may be required, including domestic and international (10-20%)