CYNTHIA L. STEVENSON

SUMMARY

Manager and pharmaceutical scientist with over 20 years of experience, in a variety of therapeutic areas and drug delivery platforms. Strong leadership experience in pharmaceutical development including 3 successful drug approvals and 7 drug candidates in clinical trials. Strong physical pharmacy skills in both liquids and solids formulation design. Proven experience working with FDA. Strategic planning and strong organizational skills, including infrastructure implementation and change management. Ability to build strong working relationships with executives, managers, advanced career scientists and external organizations

EXPERIENCE

Independent Consultant, 2012-present: Provided all aspects of CMC development for large and small molecule drug candidates, including analytical, regulatory CMC (pre-IND thru CTD, PAI), program management and operations. Wide spectrum of drug delivery experience in controlled release orals, transdermal, inhalation, parenterals and implants. Provided executive management, strategic planning, technical due diligence and fund raising to venture-based companies.

- Pharmaceutical Development
  - Formulation and drug delivery expertise on HIV therapies and contraceptives for non-profit.
  - Expert panel for European advisory firm requiring technical expertise in drug delivery.
  - Seed-stage implantable delivery system company, requiring formulation stabilization strategy, CMC milestones and timeline, reported to VP Pharmaceutical Development.
- Regulatory
  - Established polymer-based drug delivery company (market cap $115M), requiring Pharmaceutical Development, NDA Modules 1,2,3, 4 writing, CTD query response, IND updates and Type B/Type C Briefing Documents, reported to COO and CEO.
  - Established biopharmaceutical company (market cap $62M), requiring strategic planning for CTD submission and introduction of autoinjector, reported to Regulatory and CSO.
  - Seed-stage parenterals company, requiring analytical development and IND writing, reported to CEO.
  - Seed-stage dissolvable microneedle transdermal patch company, requiring regulatory support for pre-IND package, reported to CTO.
- Strategic Planning
  - Established biopharmaceutical company (market cap $603M) requiring technical due diligence for asset/company acquisitions.
  - Canadian proteomics-based CRO, looking to expand mass spectrometry services to later stage pharmaceutical companies, reported to Site Head.

On Demand Therapeutics, 2011-2012 (Vice President, Pharmaceutics): Responsible for the development of an injectable ophthalmic implant, containing multiple laser-activated therapeutic reservoirs, capable of delivering ocular drug therapies to the back of the eye. Lead pharmaceutical, analytical and regulatory activities from invention of delivery designs to pre-IND meeting with FDA. Involved in raising Series A funds and sale of assets, reported to CEO. Funded by InterWest Partners.

Independent Consultant, 2008-2011: Provided strategic planning, portfolio prioritization, competitive intelligence, all aspects of CMC development and drug delivery systems, regulatory CMC (CTD, MAA), program management and organizational design to the pharmaceutical industry.

- Pharmaceutical Development

- Series A1 ocular drug delivery start-up funded by InterWest Partners, requiring support to raise Series A2 funding, creation of key patents and pharmaceutical R&D, reported to CEO.
- Series A pharmaceutical start-up funded by Sofinnova Ventures, requiring Expert Panel technical review of depot product development plans, reported to President R&D.
- Established intelligent implantable device company, requiring formulation and development expertise, reported to VP Manufacturing.

- Regulatory
  - Established Japanese transdermal patch company, requiring RegCMC, query response, and PAI readiness, reported to VP Development.
  - Established oral sustained release drug delivery company (market cap $135 M), requiring RegCMC and PAI readiness for 2 NDAs, reported to head of Regulatory.
  - Established specialty pharmaceutical company, requiring program restart support after CRL.
- Strategic Planning
  - Pure-play oral biotherapeutic start-up funded by Sanderling Ventures, requiring portfolio planning and competitive intelligence, reported to CEO.
  - Seed-stage pharmaceutical start-up requiring competitive intelligence on blood volume expanders, reported to CEO.
  - Established pharmaceutical house (market cap $92 B) requiring Expert Panel strategic input on drug delivery platforms for high volume biologics, reported to Global Marketing.
  - Technical assessment and due diligence for Venture Capital firms.

Ethos Pharmaceuticals, Inc., 2007-2008 (Senior Director, Development): Lead pharmaceutical sciences, reporting to CEO and Chairman of the Board, providing product development for oral and injectable peptidomimetic drug candidates. Recruited by co-founder; funded by USVP and Morgenthaler.

- Identified company portfolio, including strategic therapeutic areas and lead peptidomimetic product targets for clinical proof of concept. Provided competitive intelligence.
- Identified Key Opinion Leaders for Advisory Boards and developed target product profiles.
- Provided Program Management for discovery, pre-clinical and operations teams.
- Built laboratory infrastructure (SOPs, guidelines, templates, data management, QC and QA) and managed CROs/CMOs providing API and analytical services.

Nektar Therapeutics, 2000-2007: Lead product development teams developing small and large molecules. Responsible for formulation development, stability, scale-up, CMC sections of regulatory filings, drug and device specifications, sub-team resources (manufacturing, quality and analytical), budget and work plans.

Director, Product Development (2004-2007)

Direct management of CMC technical leadership for development programs (7 programs).

- Drove Phase I – Phase III programs (tobramycin, ciprofloxacin, amakacin, amphotericin, PEG-dronabinol, PEG-irinotecan, parathyroid hormone) in a wide variety of delivery platforms (DPI, MDI, nebulizer, lyophilized and sterile solution parenterals).
- Delivered formulation design, analytical, stability, specifications, manufacturing process development & scale-up, and RegCMC writing (3 INDs, 1 IMPD, 1 CTA).
- Formulation responsibilities included preformulation, particle design, novel chemical stabilization strategies and characterization of interfacial interactions in sterile solutions, lyophilized powders and pulmonary dry powders.
- Manufacturing responsibilities in-house included spray drying process definition, development, scale-up and tech transfer to Operations for milling, suspension, emulsion and solution preparation methods (g to kg scale).
- Contract manufacturing responsibilities included sterile lyophilized and solution parenterals.

- Delivered accurate development plans to Program Management (work plans, budget, resource allocation, milestones). Integrated drug/device issues to assure seamless product execution.
- Provided strategic input into company restructuring, and designed Drug Development department.
- Implemented the organizational change and defined working interfaces to improve efficiency. Managed $ 8 MM department budget (~35 FTE).
- Assured maintenance of good working relationships with multiple pharmaceutical clients and contract organizations.

Associate Director, Product Development (2001-2004)
Technical leadership and program management for pulmonary delivery of insulin (Exubera®). Member of senior program leadership team, managing $ 50 M budget.

- Provided Program Management and facilitated primary executive communication forum between Nektar and Pfizer (coordinated 5 manufacturing sites). Extensive communications with Pfizer (client), Aventis (API), and Bespak & TechGroup (device).
  - Redesigned working group structures, milestone tracking mechanisms and escalation pathways with Pfizer program management, with the aid of Putnam Associates. Supervised 2 project coordinators.
  - Delivered CMC Publication Strategy to support Pfizer Marketing, and worked with Legal to approve external publications. Managed Competitive Intelligence.
- Primary regulatory point of contact with Pfizer for CMC sections of regulatory filings (CTD, MAA, NDA, Queries).
  - Author for CMC section and editor for Module 2 of CTD. Supervised 2 regulatory staff.
  - Provided leadership for setting API, drug and device specifications.
  - Designed, obtained FDA buy-in and drove successful leachables and extractables strategy for a novel delivery system.
- Lead Development Compliance, Data Management and CMC Readiness groups (~25 FTE). Created insulin development document management system for PAI.
  - Development Compliance provided technical writing, training compliance, lab notebook, laboratory inspections and metrics for Pharmaceutical Development division (~150 FTE).
  - Data Management and CMC Readiness interfaced with QA to assure accuracy and traceability of CTD supporting data, PAI preparation and queries.
- Lead Analytical Development and Material Control departments (~10 FTE).
  - Analytical Development produced chromatography/spectroscopy for non-GMP insulin studies, including elucidation of manufacturing design space during process development (1 kg to 10 kg scale).
  - Resolved API scale-up inconsistencies in solubility and dissolution requirements (protein derived from E. coli) during 4 scale-up exercises, including purification and drying equipment changes (1 g to 100 kg scale).
  - Material Control interfaced with Supply Chain, and delivered leachables, extractables, identity tests, physicochemical characterization and biocompatibility qualification studies.
  - Supplied analytical results to define control space for process validation of molded parts.
  - Guided analytical outsourcing with 9 contract research organizations (Cardinal Health, NAMSA, BAS, QTI), and 3 consultants for drug packaging, device material control and DMF preparation for upstream suppliers ($ 4 MM contract analytical budget).
  - Drove Level 1 post-approval changes for Exubera raw materials.
- Collaborated with Supply Chain to enact quality agreements with upstream suppliers and their suppliers (N-1).
  - Established strategy to place extractables requirements onto supplier C of A, and implemented with Supply Chain organization.

- Spearheaded expiry dates, retest dates, second source supplier and stockpiling plans for critical components.
- Influenced industry practices through PQRI, IPAC-RS and OINDP.

Technical Leader, Product Development (2000-2001)

- Lead preclinical program formulating human growth hormone for pulmonary delivery. Primary technical liaison with Genentech.
- Advanced development of novel surface active excipients. Supervised 4 scientists.
- Characterized cyclosporine thermotropic liquid crystal spray-dried from ethanol.

Alza Corporation, 1994-2000: Lead formulation and analytical teams developing protein drug candidates in implantable pumps (DUROS®) and electrotransport patches (Macroflux®). Manager of ATI Solution Formulation Research and research mass spectrometry laboratory.

Associate Director, Research Scientist, Formulation Development (1999-2000)

Drove late stage product development for the Viadur® Leuprolide Implant.

- Primary author for CMC section of NDA, expert reports and European regulatory activities.
- Took lead in representing CMC section in FDA communications (extractables strategy, query responses, negotiation of final stability specifications).
- Responsible for drug-related communication and integration issues with engineering, manufacturing, toxicology, regulatory and analytical departments, including functionality requirements for a new technology. Managed resource allocations, budgeting and 5 FTE.
- Provided PAI support to war room.
- Managed non-GMP analytical group. Qualified methods and transferred to QC.
- Contributed to process development and scale-up of an aseptic commercial manufacturing line.
- Primary supply chain contact for API and excipients, including vendor selection, qualification and management.
- Drove preformulation and novel formulation efforts for protein solutions (50-400 mg/ml) and suspensions (1%-30% particle loadings) requiring 3-6 months stability under physiological conditions (α-interferon, somatostatin, calcitonin and glucagon-like peptide). GLP-1 formulation for DUROS® implant currently utilized by Intarcia Therapeutics. Designed IP strategies, justified budget and executed milestones.
- Collaborated on strategic task force identifying new corporate product opportunities for sustained release oral tablets, transdermal patches, depot injections and subcutaneous implants. Provided technical support to business development.

Group Leader, Research Scientist, Biopharmaceutical R & D (1996-1999)

Lead formulation and analytical development of the DUROS® Leuprolide Implant.

- Supported aseptic manufacture scale-up, transfer of methods to QC, and setting raw material and final product specifications. Supervised 4 scientists, and matrix team of 10 FTE.
- Contributed to strategic timelines, provided leadership for stability requirements to meet ICH guidelines, impurity/degradation product identification and leachate/migration issues.
- Identified and audited API vendors, and acted as primary contact with Mallinckrodt.
- Primary CMC author for IND, annual reports and amendments.

Lead formulation and analytical development for the Macroflux® transdermal patch, currently utilized by Zosano Pharma.

- Designed insulin gel formulation for the Macroflux® electrotransport transdermal patch.
- Responsible for technology transfer of insulin formulation, manufacture and analytical methods to European pre-IND clinical trials, and provided analytical stability support for clinical trials.

Staff Scientist, Biopharmaceutical R & D (1994-1996)
Co-inventor of DUROS® Implant: designed non-aqueous (DMSO, PG, PEG, alcohols) high concentration (40-50% API) sterile solution formulations in an implantable delivery system.

- Created patents to protect novel formulations and delivery platform.
- Delivered formulation characterization and accelerated stability to assure alleviation of lyotropic liquid crystal formation.

Executed drug delivery feasibility assessments for a calcitonin Technosphere® suspension depot and a spray-dried powder in the PowderJect® needleless injector.

Glaxo, Inc., 1991-1994: Liaison between basic research and development divisions to increase efficiency and shorten development timelines. Safety committee member.

Senior Scientist, Oligomer Development (1992-1994)
Delivered structural characterization, solubility testing, physical stability and preformulation of peptide nucleic acids and phosphorothioate oligonucleotide antisense drug candidates.

Designed permeability screens for peptide and peptidomimetic synthetic combinatorial libraries. Tested oral bioavailability of libraries in Caco-2 cell monolayers and identified transported species, by MS/MS, to develop structure/permeability relationships.

Visiting Scientist, Structural & Biophysical Chemistry (1991-1992)
Characterized the structural stability of growth releasing factor analogs and arctic flounder anti-freeze peptides by monitoring deuterium exchange of amide protons with electrospray LC/MS/MS.

University of Kansas, 1988-1992 (Graduate Student, Pharmaceutical Chemistry): Established the effect of secondary structure (α-helix) on the deamidation rate of Asn, and the structural effects of deamidation on activity of growth releasing factor analogs, by 2D-NMR, LC/MS/MS and CD. Teaching Assistant for Pharmaceutics Lab offered by pharmacy school. Supervised 2 undergraduates.

The Upjohn Company, 1986-1988 (Chemist, Pharmaceutical R & D): Designed and executed preformulation, stability, dissolution testing and sustained-release formulation studies for recombinant bovine somatotropin, including tablets, lyophilized and spray-dried parenterals. Familiar with SOP's and GLP.

Washington University, 1985 (Summer Intern, Pharmacology Department): Synthesized radio-labeled phosphatidylinositol and cultured fibroblast cells to characterize prostaglandin and leukotriene cellular pathways.

Colorado College, 1984-1985 (Assistant, Ornithology Laboratory): Analyzed skin debris samples from endangered peregrine falcons by light and scanning electron microscopy to correlate pollen traces, habitat, pesticide intake, shell thinning and reproduction.

EDUCATION
University of Kansas, Ph.D. Pharmaceutical Chemistry, 1990-1992
University of Kansas, M.S. Pharmaceutical Chemistry, 1988-1990
Colorado College, B.A. Chemistry, 1982-1986

CONTINUING EDUCATION
Leadership Development Program (Center for Creative Leadership, 2006)
DMFs and CMC Section of CTDs (CfPIE, 2006)

Negotiation and Influence Strategies (Stanford Graduate School of Business, 2003)
Legal Aspects of Managing (Cooley Goward LLP, 2003)
US Regulation of Biologics (CCE, 2000)
The FDA Investigator Cometh (Center for Professional Advancement, 1999)
Surviving PAI's (PDA, 1998)
Basic Training in Drug Development (PERI, 1997)
Biologics Approval and Compliance Workshop (RAPS, 1995)

HONORS AND AWARDS
ALZA Special Recognition Award, 1997, 1999
Genentech Predoctoral Fellowship, 1992
NIGMS Biotechnology Training Grant, 1989-1992
Eli Lilly Predoctoral Summer Scholar, 1989
Colorado College Dean's List, 1986
Colorado College Merit Scholarship, 1983

MEMBERSHIPS
Iota Sigma Pi, National Honor Society for Women in Chemistry, 1990-1992
Editorial Board Member for Current Pharmaceutical Biotechnology, 1999-present
Editorial Board Member for Drug Delivery, The Scientific World, 2002-present
Editorial Board Member for ISRN Pharmaceutics, 2011-present

PUBLICATIONS
[26]Reservoir Based Drug Delivery Systems Utilizing Microtechnology. CL Stevenson, JT Santini Jr, R Langer. Advanced Drug Delivery Reviews, **64**, 1590-1602 (2012).

[25]Solid-State Stability of Spray-Dried Insulin Powder for Inhalation: Chemical Kinetics and Structural Relaxation Modeling of Exubera Above and Below the Glass Transition Temperature. N Sadrzadeh, DP Miller, D Lechuga-Ballesteros, N Harper, CL Stevenson, DB Bennett. Journal of Pharmaceutical Sciences, **99**, 3698-3710 (2010).

[24]Advances in Peptide Pharmaceuticals. CL Stevenson. Current Pharmaceutical Biotechnology, **10**, 122-137 (2009).

[23]Trileucine Improves the Dispersibility, Aerosol Performance and Stability of Spray-Dried Powders for Inhalation. D Lechuga-Ballesteros, C Charan, CLM Stults, CL Stevenson, DP Miller, R Vehring, V Tep, MC Kuo. Journal of Pharmaceutical Sciences, **97**, 287-302 (2008).

[22]Peptide Drug Delivery Strategies for the Treatment of Diabetes. N Sadrzadeh, MJ Glembourtt, CL Stevenson. Journal of Pharmaceutical Sciences, **96**, 1925-1954 (2007).

[21]The Design and Performance of the Exubera Pulmonary Insulin Delivery System. NJ Harper, S Gray, J de Groot, JM Parker, N Sadrzadeh, C Schuler, JD Schumacher, S Seshadri, AE Smith, GS Steeno, CL Stevenson, R Taniere, M Wang, DB Bennett. Diabetes Technology and Therapeutics, **9**, 16-27 (2007).

[20]Exubera: Pharmaceutical Development of a Novel Product for Pulmonary Delivery of Insulin. S White, DB Bennett, S Cheu, PW Conley, DB Guzek, S Gray, J Howard, R Malcolmson, JM Parker, P Roberts, JD Schumacher, N Sadrzadeh, S Seshadri, GW Sluggett, CL Stevenson, NJ Harper. Diabetes Technology and Therapeutics, **7**, 896-906 (2005).

[19]Liquid Crystals in Pharmaceutical Systems: The Relevance of Partially Ordered Systems. CL Stevenson, DB Bennett, D Lechuga-Ballesteros. Journal of Pharmaceutical Sciences, **94**, 1861-1880 (2005).

[18]Properties and Stability of a Liquid Crystal Form of Cyclosporine: the First Reported Naturally-Occurring Peptide that Exists as a Thermotropic Liquid Crystal. D Lechuga-Ballesteros, A Abdul-Fattah, CL Stevenson, DB Bennett. Journal of Pharmaceutical Sciences, **92**, 1821-1831 (2003).

[17]Secondary Structure of Cyclosporine in a Spray-Dried Liquid Crystal by FTIR. CL Stevenson, MM Tan, D Lechuga-Ballesteros. Journal of Pharmaceutical Sciences, **92**, 1832-1843 (2003).

[16]Development of a Dedicated Osmotic Implantable System for the Treatment of Prostate Cancer. JC Wright, ST Leonard, CL Stevenson, J Beck, G Chen, J Leonard, R Skowronski. Journal of Controlled Release, **75**, 1-10 (2001).

[15]Characterization of Protein and Peptide Stability in Non-Aqueous Solvents. CL Stevenson. Current Pharmaceutical Biotechnology, **1**, 165-182 (2000).

[14]Solution Stability of Salmon Calcitonin at High Concentration for Delivery in an Implantable System. CL Stevenson, MM Tan. The Journal of Peptide Research, **55**, 129-139 (2000).

[13]Effect of Peptide Concentration and Temperature on Leuprolide Stability in Dimethyl Sulfoxide. CL Stevenson, J Leonard, SC Hall, International Journal of Pharmaceutics, **191**, 115-129 (1999).

[12]Characterization and Comparison of Leuprolide Degradation Profiles in Water and Dimethyl Sulfoxide. SC Hall, MM Tan, J Leonard, CL Stevenson. The Journal of Peptide Research, **53**, 432-441 (1999).

[11]Use of Caco-2 Cells and LC/MS/MS Techniques to Screen Synthetic Peptide Combinatorial Libraries for Permeable Structures. CL Stevenson, PF Augustijns, RW Hendren. International Journal of Pharmaceutics, **177**, 103-115 (1999).

[10]Effect of Gelation on the Chemical Stability and Conformation of Leuprolide. MM Tan, CA Corley, CL Stevenson. Pharmaceutical Research, **15**, 1442-1447 (1998).

[9]Precipitation of Proteins in Supercritical Carbon Dioxide. MA Winters, BL Knutson, PG Debenedetti, HG Sparks, TM Przybycien, CL Stevenson, SJ Prestrelski. Journal of Pharmaceutical Sciences, **85**, 586-594 (1996).

[8]Estimation of Recombinant Bovine Somatotropin Solubility by Excluded-Volume Interaction with Polyethylene Glycols. CL Stevenson, MJ Hageman. Pharmaceutical Research, **12**, 1671-1676 (1995).

[7]The Impact of Biophysical Parameters on the Biological Assessment of Peptide Nucleic Acids, Antisense Inhibitors of Gene Expression. SA Noble, MA Bonham, JE Bisi, DA Bruckenstein, PH Brown, SC Brown, R Cadilla, MD Gaul, JC Hanvey, CF Hassman, JA Josey, MJ Luzzio, PM Myers, AJ Pipe, DJ Ricca, CW Su, CL Stevenson, SA Thomson, RW Wiethe, LE Babiss. Drug Development Research, **34**, 184-195 (1995).

[6]The Mass Spectrometry of Helical Unfolding in Peptides. RJ Anderegg, DS Wagner, CL Stevenson, RT Borchardt. Journal of the American Society for Mass Spectrometry, **5**, 425-433 (1994).

[5]The Effect of Secondary Structure on the Rate of Deamidation of Several Growth Hormone Releasing Factor Analogs. CL Stevenson, ME Donlan, AR Friedman, TM Kubiak, RT Borchardt. International Journal of Peptide and Protein Research, **42**, 497-503 (1993).

[4]Solution Conformation of Leu^{27} hGRF(1-32)NH_2 and its Deamidation Products by 2D NMR. CL Stevenson, ME Donlan, AR Friedman, RT Borchardt. International Journal of Peptide and Protein Research, **42**, 24-32 (1993).

[3]Probing Helical Content of Growth Hormone Releasing Factor Analogs Using Electrospray Mass Spectrometry. CL Stevenson, RJ Anderegg, RT Borchardt. Journal of the American Society for Mass Spectrometry, **4**, 646-651 (1993).

[2]Comparison of Separation and Detection of Techniques for Human Growth Hormone Releasing Factor and the Products Derived from Deamidation. CL Stevenson, RJ Anderegg, RT Borchardt. Journal of Pharmaceutical and Biomedical Analysis, **11**, 367-373 (1993).

[1]Identification and Quantification of Tetrapeptide Deamidation Products by Mass Spectroscopy. CL Stevenson, TD Williams, RJ Anderegg, RT Borchardt. Journal of Pharmaceutical and Biomedical Analysis, **10**, 567-575 (1992).