

S. RUSS LEHRMAN, Ph.D.

PROFESSIONAL OVERVIEW

A leader in the area of Pharmaceutical Sciences with significant accomplishments in Formulation, Analytical Development and Process Chemistry. Strong scientific, managerial, and organizational background applied to the completion of key objectives that support Preclinical and Clinical Development of small and macromolecular candidates.

Key accomplishments include:

- 1) Successful development of solid oral, inhalation, and parenteral formulations including:
 - small molecule for the treatment of early stage rheumatoid arthritis (Phase I - oral),
 - polymer-modified small molecule for the treatment of multiple sclerosis (Phase I - parenteral)
 - partial PPAR- γ agonist candidates for the treatment of Type II diabetes (Phase IIb - oral),
 - fluoroquinolone antibiotic for the treatment of lung infections (Phase II – nebulized aerosol), and,
 - monoclonal antibody used in the treatment of multiple sclerosis, and Crohn's disease (Phase II - parenteral)
 - cytokine and peptide hormones for pulmonary delivery (DPI)
- 2) Structural optimization of growth hormones, growth hormone releasing factor, and anti-VEGF and anti-P-selectin oligonucleotide aptamers to enhance bioavailability and stability
- 3) Preformulation studies (e.g., polymorph and salt selection) of small molecule candidates which maximized product development potential,
- 4) Development and implementation of analytical assays to support research stage development of the proteins and oligonucleotides drug candidates,
- 5) Management of an API CMO for the manufacture of GMP-compliant drug substance
- 6) Manufacture of a Drug Product CMO for the manufacture of GMP-compliant CTM
- 7) Establishment and management of Formulation and Analytical R&D teams to support Pharm Dev

A respected member of the broader professional community often called upon to review manuscripts and present seminars. Active in education as an Adjunct Professor and mentor.

PROFESSIONAL EXPERIENCE

LEHRMAN BIOPHARMA, Los Altos, CA

January 2006 - present

Principal

- Supported early stage biotechnology companies (capital ranging from \$3M to \$30M). Selected accomplishments include:
 - Development of a high-dose aerosol formulation of an antibiotic. This formulation is in clinical development.
 - Identified and managed CROs that provided analytical and formulation support for an orally active protein therapeutic used in the treatment of a GI tract disorder.
 - Defined the ongoing CMC strategy and answered development issues for a virtual, startup company that was seeking to pursue clinical development of a novel diabetes treatment. These efforts helped secure \$23M in Series A Venture Capital and development rights for this candidate.
 - For the newly established company, executed the CMC strategy for the diabetes drug candidate through successful manufacture of kilogram quantities of GMP and GLP compliant Drug Substance, and Clinical Supplies (liquid filled, hard gelatin capsules) for a Phase IIb clinical trial.
 - Transferred analytical assays to these CMOs to support API and DP efforts
 - Expert witness for the plaintiff in a patent infringement case.

1731 Penny Way
Los Altos, CA 94024
(650) 969-0206

ELAN PHARMACEUTICALS, South San Francisco, CA

2003 – 2005

Associate Director, Formulation Development

- Reestablished a Formulation Development Group that supported Preclinical and Clinical Development of new chemical entities identified by R&D operations. Hired personnel and obtained equipment used for screening and identification of solid oral and parenteral dosage forms.
- Developed solid oral tablets and parenteral formulations for Clinical Trials. Provided preformulation support (solubility, stability, polymorphism studies etc.) to these projects. The solid oral tablets contained nanocrystalline drug and the parenteral formulations were manufactured as lyophilized powders and administered by injection following reconstitution.
- Supervised a technical staff of up to seven scientists. Managed their work efforts and professional development.

INHALE THERAPEUTIC SYSTEMS (now Nektar, Inc.), San Carlos, CA

1998 - 2003

Senior Scientist, Pharmaceutical Research.

- Developed dry powder formulations of proteins (3) and small molecules (2).
- Generated new patents applicable to the aerosol delivery of therapeutic proteins.
- Identified and implemented new analytical methods that aid formulation selection of proteins and small molecules.

NEXSTAR PHARMACEUTICALS, INC. (now OSI, Inc.), Boulder, CO

1994 - 1998

Director of Analytical Research

- Established a new Analytical Chemistry unit that supported discovery research and early preclinical development of oligonucleotide drug candidates. These methods have been validated and used in the release of Macugen, a first-in-class therapeutic for the treatment of macular degeneration.
- Conducted the first complete characterization of oligonucleotide aptamers using LC-MS-MS.
- Patented a new class of oligonucleotide prodrugs.
- Provided post-market support for the liposomal formulation of amphotericin B (Ambisome).
- Supervised a technical staff of up to ten scientists. Managed their work efforts and professional development.

THE UPJOHN COMPANY (now Pfizer), Kalamazoo, MI

1985-1994

Research Scientist and Senior Research Scientist

- Established and led scientific efforts to enhance the stability and solubility of growth hormones and growth hormone releasing factors through structural modification. Material patents have been issued covering these efforts.
- Identified structural components that contribute to well-defined partial denaturation and aggregation of bovine and porcine growth hormones.
- Supervised a group of three research associates and two post-doctoral associates to conduct these efforts.
- Elected to the Upjohn Control Academy in 1993. This was an annual award honoring major contributions made by an individual scientist to Upjohn Pharmaceutical Development.

OTHER PROFESSIONAL EXPERIENCE:

UNIVERSITY OF KANSAS, Lawrence, KS

Adjunct Associate Professor of Pharmaceutical Chemistry

1992 - present

HOFFMANN-LA ROCHE, INC., Nutley, NJ

Postdoctoral Associate

NATIONAL CANCER INSTITUTE, Bethesda, MD

Staff Fellow

EDUCATION

UNIVERSITY OF WISCONSIN-MADISON, SCHOOL OF PHARMACY

Ph. D. in Medicinal Chemistry

Dissertation: "Peptide Substrates and Inhibitors for Vitamin K-dependent Carboxylase: Synthesis and Structure Activity Relationships"

MCGILL UNIVERSITY, MONTREAL, QUEBEC

B.Sc. in Chemistry (with distinction)

PROFESSIONAL SERVICES, and SOCIETIES

Services:

- Reviewer for the following journals: *Pharmaceutical Research*; *Journal of Pharmaceutical Science*, *Analytical Biochemistry*, *Biochemistry*, *Biochimica et Biophysica Acta*, *Journal of Chromatography*, and *International Journal of Peptide and Protein Research*, *Journal of Peptide Research*.
- Organizer of the University of Wisconsin Land of Lakes Conferences Pharmaceutical Sciences in 2003 and 2004.
- Chair of the IIR Symposium on Peptide and Protein Formulation Strategies, held in San Francisco, CA, 2002.
- Co-Organizer and Chair of the Well Characterized Biotechnology Pharmaceutical Symposium Workshops in 1999.

Professional Societies:

- American Association of Pharmaceutical Scientists, Biotechnology Section
- American Chemical Society
- American Association for the Advancement of Science
- American Peptide Society

PUBLICATIONS

- 1) **S.R. Lehrman**, "Protein Aggregation: Relevance to Pharmaceutical Development and Disease Pathology", AAPS News Magazine, June, 2008, in press.
- 2) D.Burke, S. Buckley, **S.R. Lehrman**, B. O'Connor, and J. Callaway "Immunoglobulin Formulation and Method of Preparation Thereof", EP 04709508.8-2402, filed October 18, 2006.
- 3) D. Burke, J. Callaway, T. Yednock, **S.R. Lehrman**, S. Buckley, and B. O'Connor, "Immunoglobulin Formulation and Method of Preparation Thereof", PCT/US04/03873 Filing Number: 10/773,406 filed September 2, 2004.
- 4) H.W. Bosch, J.J. Cunningham, S.B. Ruddy, S.C. Wendel, **S.R. Lehrman**, and S. Barrack, "Nanoparticulate Integrin Antagonist Formulations", filed May 20th, 2005.
- 5) H.-K. Chan, A. Clark, M.-C. Kuo, **S.R. Lehrman**, K. Pikal-Cleland, D.P. Miller, R. Vehring, and D. Lechuga-Ballesteros, "Stability of Salmon Calcitonin Spray-Dried Powders for Inhalation", *J. Pharm. Sci.* 93(3), 792-804 (2004).
- 6) C. Stevenson, J.E. Hastedt, **S.R. Lehrman**, H.-S. Chiang, D.B. Bennett, D. Lesikar, B. Yang, D. Gong, and K. Cabot, "Inhaleable Spray-Dried 4-Helix Bundle Protein Powders Having Minimized Aggregation," U.S. Patent 6,838,075, issued January 4, 2005, superceding U.S. Patent 6,569,406, issued May 27, 2003.
- 7) F.C. Richardson, C. Zhang, **S.R. Lehrman**, H. Koc, J.A. Swenberg, K.A. Richardson, and R.A. Bendele, "Quantitation Of 2'-Fluoro-2'-Deoxyuridine And 2'-Fluoro-2'-Deoxycytidine In DNA And RNA Isolated From Rats And Woodchucks Using LC/MS/MS," *Chemical Research in Toxicology* 15(7), 922-926 (2002).
- 8) **S.R. Lehrman**, and S.W. Niewlandt, "dU Site-Directed Cleavage Of Covalent Conjugates," International Patent Application No. PCT/US99/18091, filed August 10, 1999.
- 9) P. Bridonneau, S. Bunch, R. Tengler, K. Hill, J. Carter, W. Pieken, D. Tinnermeier, **S.R. Lehrman**, D.W. Drolet, "Purification Of A Highly Modified RNA-Aptamer. Effect Of Complete Denaturation During Chromatography On Product Recovery And Specific Activity," *Journal of Chromatography B Biomedical Sciences and Applications* 726, 237-47 (1999).
- 10) **S.R. Lehrman**, H.A. Havel, J.L. Tuls, S.M. Plaisted, and D.N. Brems, "Somatotropin Analogs," U.S. Patent # 5,663,305 September, 1997.
- 11) **S.R. Lehrman**, M.E. Lund, E.L. Ulrich, K.A. Farley and W.M. Moseley, "Stable α -Helicity In Linear Growth Hormone Releasing Factor Analogs," in Peptides: Chemistry and Biology, R.S. Hodges and J.A. Smith ed., ESCOM, Leiden, pp. 802-803 (1994).
- 12) **S.R. Lehrman**, M.E. Lund, and J.R. Shifflett, "Enhancing The Conformational Stability Of Growth Hormone Via Site-Directed Mutagenesis: Incorporation of a Metal Binding Site," in Peptides: Chemistry and Biology, R.S. Hodges and J.A. Smith ed., ESCOM, Leiden, pp. 1050-1051 (1994).
- 13) **S.R. Lehrman**, D.M. Evans, M.E. Lund, and G.A. Walker, "Identification and Characterization of an Anti-Isoaspartic Acid Monoclonal Antibody," *Journal of Protein Chemistry* 11, 657 (1992).
- 14) **S.R. Lehrman**, J.L. Tuls and H.A. Havel, "Molecular Characterization of an Aggregate Formed by a Bovine Growth Hormone Folding Intermediate," in Techniques in Protein Chemistry III, Academic Press, Inc., San Diego, pp. 363-371 (1992).
- 15) **S.R. Lehrman**, J.L. Tuls, H.A. Havel, R.J. Haskell, S.D. Putnam, and C-S.C. Tomich, "Site-Directed Mutagenesis To Probe Protein Folding: Evidence That The Formation And Aggregation Of A Bovine Growth Hormone Folding Intermediate Are Dissociable Properties," *Biochemistry* 30, 5777-5784 (1991).
- 16) **S.R. Lehrman**, "Protein Structure," in Fundamentals of Protein Biotechnology, S.Stein, ed., Marcel Dekker Inc., New York, pp. 9-38 (1991).
- 17) **S.R. Lehrman**, H.A. Havel, J.L. Tuls, S.M. Plaisted, and D.N. Brems, "Somatotropin Analogs," International Patent Application No. PCT/US90/03550, filed June 27, 1990.
- 18) **S.R. Lehrman**, J.L. Tuls, and M.E. Lund, "Peptide α -Helicity In Aqueous Trifluoroethanol: Correlations With Predicted α -Helicity And The Secondary Structure Of The Corresponding Regions Of Bovine Growth Hormone," *Biochemistry* 29, 5590-5596 (1990).

- 19) **S.R. Lehrman**, J.L. Tuls, and M.E. Lund, "Molecular Characterization Of bGH Self-Association," in Peptides: Chemistry and Biology, J.E. Rivier and G.R. Marshall ed., ESCOM, Leiden, pp. 571-574 (1990).
- 20) **S.R. Lehrman**, J.L. Tuls, and M.E. Lund, "Determination Of Peptide α -Helicity In Aqueous Trifluoroethanol And Its Use In Studies Of Protein Secondary Structure," in Peptides: Chemistry and Biology, J.E. Rivier and G.R. Marshall ed., ESCOM, Leiden, pp. 669-671 (1990).
- 21) **S.R. Lehrman**, J.L. Tuls, and M.E. Lund, "Conformational Analysis Of Bovine Growth Hormone Fragments Which Correspond To Helical Regions Of The Intact Protein," in Biotechnology in Growth Regulation (ed. R.G. Heap, C.G. Prosser, and G.E. Lemming), Butterworth and Co., London, U.K., pp. 222 (1989).
- 22) **S.R. Lehrman**, T.F. Holzman, C.J. Cole, and D.N. Brems, "Synthesis And Oxidative Properties Of Cysteine-Containing Fragments Of bGH," in Peptides: Chemistry and Biology, G.R. Marshall ed., ESCOM, Leiden, pp. 392-395 (1988).
- 23) **S.R. Lehrman**, H.-W. Lahm, J.D. Hulmes, M. Meidel, and C.H. Li, "The Primary Structure Of Equine Prolactin," *International Journal of Peptide and Protein Research* 31, 544-554 (1988).
- 24) D.N. Brems, S.M. Plaisted, E.W. Kauffman, M.E. Lund, and **S.R. Lehrman**, "Helical Formation In Isolated Fragments Of Bovine Growth Hormone," *Biochemistry* 26, 7774-7778 (1987).
- 25) D.N. Brems, S.M. Plaisted, E.W. Kauffman, and **S.R. Lehrman**, "A Search For Ordered Secondary Structure In Isolated Fragments Of Bovine Growth Hormone," in Protein Structure Folding and Design 2, D. Oxender ed., pp. 151-165 (1987).
- 26) P.R. Langer-Safer, **S.R. Lehrman**, and A.M. Skalka, "v-src Inhibits Differentiation Via An Extracellular Intermediate(s)," *Molecular and Cellular Biology* 5, 2847-2850 (1985).
- 27) M.K. Dhaon, **S.R. Lehrman**, D.H. Rich, J.A. Engelke, and J.W. Suttie, "Derivatives Of 2-Methyl-1,4-Naphthoquinone As Substrates And Inhibitors Of The Vitamin K-Dependent Carboxylase," *Journal of Medicinal Chemistry* 27, 1196-1201 (1984).
- 28) R.L. Levine, and **S.R. Lehrman**, "Identification Of Amino Acid Phenylthiohydantoin By Multicomponent Analysis Of Ultraviolet Spectra," *Journal of Chromatography* 288, 111-116 (1984).
- 29) **S.R. Lehrman**, and C.A. Meyers, "Pth-amino Acid Identification By Multicomponent Analysis Of First And Second Derivative Ultraviolet Spectra," in Peptides: Synthesis-Structure-Function, V. Hruby and D.H. Rich eds., Pierce Chemical Company, Rockford, IL, 755-758 (1983).
- 30) A.B. Roberts, M.A. Anzano, C.A. Meyers, J. Widemann, R. Blacher, Y.-C. Pan, S. Stein, **S.R. Lehrman**, J.M. Smith, L.C. Lamb, and M.B. Sporn. "Purification And Properties Of A Type β -Transforming Growth Factor From Bovine Kidney," *Biochemistry* 22, 5692-5698 (1983).
- 31) **S.R. Lehrman**, D.H. Rich, H.L. Goodman, and J.W. Suttie, "Synthesis Of A Naphthoquinone Tripeptide Which Inhibits Vitamin K-Dependent Carboxylase," in Peptides: Synthesis-Structure-Function, D.H. Rich and E. Gross eds., Pierce Chemical Company, Rockford, IL, 513-516 (1981).
- 32) D.H. Rich, **S.R. Lehrman**, M. Kawai, H.L. Goodman, and J.W. Suttie, "Synthesis Of Peptide Analogs Of Prothrombin Precursor 5-9," *Journal of Medicinal Chemistry* 24, 706 (1981).
- 33) D.H. Rich, **S.R. Lehrman**, M. Kawai, H.L. Goodman, and J.W. Suttie. "Rat Liver Vitamin K-Dependent Carboxylase: Substrate Specificity," in Vitamin K Metabolism and Vitamin K-dependent Proteins, J.W. Suttie ed., University Park Press, Baltimore, Maryland, 471-479 (1979).
- 34) J.W. Suttie, L.O. Geweke, J.L. Finnan, **S.R. Lehrman**, and D.H. Rich, "Effect Of Pyridoxal Phosphate On Vitamin K-Dependent Carboxylase," in Vitamin K Metabolism and Vitamin K-Dependent Proteins, J.W. Suttie ed., University Park Press, Baltimore, Maryland, 450-454 (1979).
- 35) J.W. Suttie, **S.R. Lehrman**, L.O. Geweke, J.M. Hageman, and D.H. Rich, "Requirements For Carboxylation Of Soluble Peptide Substrates And Substrate Specificity," *Biochemical and Biophysical Research Communications* 86, 500-507 (1979).
- 36) J.W. Suttie, J.M. Hageman, **S.R. Lehrman**, and D.H. Rich, "Vitamin K-Dependent Carboxylase: Development Of A Peptide Substrate," *Journal of Biological Chemistry* 251, 5827-5830 (1976).

SELECTED PRESENTATIONS:

Partial list of invited lectures:

S.R. Lehrman, “Non-parenteral Delivery of Macromolecules”, Pharmaceutical Biotechnology Course Lectures (2), at the University of Kansas-School of Pharmacy, Lawrence, KS, 2008.

S.R. Lehrman, “Physical and Chemical Properties of Proteins, DNA and Lipid Bilayers Relevant to their Solid State Behavior”, Solid state stability course lecture, at the University of Kansas-School of Pharmacy, Lawrence, KS, 2008.

S.R. Lehrman, “Pulmonary and Nasal Delivery of Macromolecules”, Pharmaceutical Biotechnology Course Lectures, at the University of Kansas-School of Pharmacy, Lawrence, KS, 2000-2007.

S.R. Lehrman, “Resolving Challenges Of Protein Stability And Solubility Behavior During Formulation Development,” invited Podium Presentation at the **Protein and Peptide Formulation Strategies Symposium**, held in San Francisco, CA, August 2002.

S.R. Lehrman, David Lechuga, Dan Miller, Katherine Pikal-Cleland, Reinhard Vehring, and, Kim Chan, “Protein Stability In Amorphous Powders,” invited Podium Lecture at the **Higuchi Seminar**, held in Lawrence, KS, May 2002.

S.R. Lehrman and Dale Koble (FDA), Workshop on: “Analytical Challenges In Inhalation Formulation,” at the 5th **Well Characterized Biotechnology Pharmaceuticals Symposium**, February, 2001.

S.R. Lehrman, Short lecture series on: “Inhalation Technology: Biotechnology Applications,” at the **University of Kansas**, April, 2000.

S.R. Lehrman, “Characterization Of A Bioactive Aptamer By LC/MS/MS,” podium presentation at the 3rd **Well Characterized Biotechnology Pharmaceuticals Symposium**, January, 1998.

S.R. Lehrman, D. Tinnermeier, L. Roberts, and S. Krivjansky, “Characterization Of Nuclease-Resistant 2'-Modified Oligonucleotides,” podium presentation at the Annual Meeting of the **American Association of Pharmaceutical Scientists**, October, 1996.

S.R. Lehrman, “Preclinical Development Of Bioactive Nucleic Acid Analogs Identified Using Combinatorial Methods,” invited podium presentation at the 29th Annual **Higuchi Research Seminar**, March, 1996.

S.R. Lehrman, “Proteins As Targets For Oligonucleotide Probes,” invited podium presentation at the 8th Annual **California State University Biotechnology Symposium**

S.R. Lehrman, and C.A. Hall, “Ion Exchange Chromatography Of Nucleic Acids: Dissecting The Mechanism Of Column Retention,” podium presentation to the 31st Annual **American Chemical Society Western Regional Meeting** and 4th Annual San Diego Biotech Exposition. October, 1995.