FRED R. KOHN, Ph.D.

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SUMMARY

Independent consultant with 20 years of experience in the biotechnology/pharmaceutical industry designing and directing preclinical programs for product development (small molecules, proteins, peptides, monoclonal antibodies, drug delivery systems, cell-based therapies). Broad industry experience in companies ranging in size from start-up biotechnology ventures to large pharmaceutical corporations. Experience as a Project Team Leader responsible for coordination of multidisciplinary product development activities, from early development through late-stage clinical trials. Experience with business development activities, including fund raising, corporate collaborations and evaluation of in-licensing opportunities. Involved in successful regulatory approval and commercialization of a biopharmaceutical product.

Experience includes extensive writing of regulatory documents and interaction with regulatory agencies, research collaborations with academic laboratories, analytical methods development and setup of QA/QC/documentation systems, clinical trial design, monitoring of preclinical and analytical studies at contract facilities, and project management. Knowledge of GLP regulations. Biomedical areas of expertise include oncology, diabetes, autoimmune diseases, inflammation, infectious diseases and pain management. Excellent written and oral communication skills.

EXPERIENCE

2008 - present **Independent Consultant**
Preclinical Development

Consult on all aspects of preclinical drug development, including design and implementation of development plans for pharmacology, pharmacokinetic/ADME and toxicology studies, management of studies at contract facilities, data interpretation, writing of regulatory submissions and interaction with regulatory agencies, and due diligence of in-licensing candidates.

2007 - 2008 **Paramount Biosciences LLC, San Diego, CA**
Vice President, Preclinical Development
Reporting to: Chief Medical Officer

Responsibilities: Evaluated biopharmaceutical products for potential in-licensing. Designed preclinical development plans for in-licensed assets, and managed Contract Research Organizations to implement the plans. Wrote and reviewed regulatory documents. Assisted with transfer of assets and development plans to newly formed biotechnology portfolio companies. Served as Project Team Leader for select assets.

2003 - 2007 **Pfizer Global Research & Development, La Jolla, CA**
Safety Sciences Global Team Lead, Diabetes & Frailty
Reporting to: Senior Director, Safety Testing & Evaluation

Responsibilities: Designed and implemented the preclinical safety strategy for the global diabetes and frailty portfolios (small molecules and monoclonal Abs). Interpreted safety data and wrote preclinical safety sections for regulatory submissions. Served as Safety Sciences single point of accountability on the global diabetes and frailty therapeutic area project teams. Interacted with regulatory agencies. Mentored junior project team members in the therapeutic area. Designed de-risking strategies for safety issues. Served as the resident expert on safety issues associated with competitor compounds in the therapeutic area. Evaluated potential new technologies for licensing/acquisition and possible new targets for internal R&D.

2001 – 2003 **MicroIslet, Inc., San Diego, CA**
Vice President, Preclinical & Clinical Development
Reported to: President/COO

Responsibilities: Designed the preclinical and clinical development plans for a cell-based therapy. Designed the product regulatory strategy. Assisted with development of overall business strategy. Assisted with acquisition of funding. Setup the Scientific and Clinical Advisory Board. Evaluated potential new technologies for licensing/acquisition.

2000 – 2001 **SkyePharma Ltd. (formerly DepoTech Corp.), La Jolla, CA**
Director**,** Project Management
Reported to: President/COO

Responsibilities: Served as company management representative on collaborative projects with corporate partners. Coordinated resources, personnel, budgeting and timelines on such projects. Served as Project Team Leader for an in-house product in mid/late stage clinical development. Directed/designed/monitored later development stage preclinical safety and bioequivalency studies.

1999 – 2000 **Desmos, Inc., La Jolla, CA**
Director**,** Product Development
Reported to: Vice President, R&D

Responsibilities: Directed development of protein-based therapeutics in the periodontal disease area. Designed the preclinical, clinical and regulatory development strategies. Supervised in-house animal studies. Setup the Clinical Advisory Board. Assisted with setup of an in-house GMP manufacturing facility and QA/QC/documentation systems. Assisted with acquisition of funding. Evaluated potential new technologies for licensing/acquisition.

1995 – 1999 **DepoTech Corporation, La Jolla, CA**
Associate Director, Preclinical Development and ***Project Team Leader*** (1997 - 1999)
Reported to: President/COO

Management responsibilities: As head of Preclinical Development: Coordinated all departmental activities. Prepared the departmental budget. Procured laboratory capital equipment. Represented the department in Product Development Teams and management staff meetings. As Project Team Leader: Coordinated all product development activities. Assured the project kept to timeline and budget. Interacted with regulatory agencies, scientific advisors/consultants and potential corporate partners.

Scientific responsibilities: Designed, conducted, supervised/monitored preclinical efficacy, PK and GLP toxicology studies required for product and formulation development. Designed and monitored clinical PK studies. Analyzed preclinical and clinical PK data. Monitored analytical methods validation and PK sample analyses at contract facilities. Reviewed in-house animal research and feasibility study protocols. Collaborated with academic investigators on R&D projects. Wrote preclinical and clinical PK sections of regulatory submissions, Investigator's Brochures, package inserts and patent applications. Presented results at in-house and extramural scientific meetings; published when appropriate. Evaluated potential new products for development.

Personnel management: Supervised one Ph.D. toxicologist and two technical staff.

Senior Scientist, Preclinical Development (1995-1997)
Reported to: Senior V.P., Research, Development & Operations

Responsibilities: As above

1991 – 1995 **XOMA Corporation, Berkeley, CA**
Senior Scientist (Acting Director), Immunology (1994 - 1995)
Reported to: Vice President, Preclinical Science

Management responsibilities: Prepared the departmental budget. Procured laboratory capital equipment. Represented the department in Product Development Team and management staff meetings. Headed the Flow Cytometry Laboratory and as such coordinated its activities as a service provided to scientists in other departments. Trained personnel in handling of biohazardous and radioactive materials and general laboratory safety.

Scientific/research responsibilities: Designed, conducted and supervised studies evaluating efficacy and mechanism of action of monoclonal antibody and protein-based therapeutics in animal models and *in vitro* immunological assays. Developed and characterized novel animal models or adapted pre-existing models for the above purpose (see list below). Presented results at in-house and extramural scientific meetings; published when appropriate. Wrote up results for inclusion in regulatory submissions and patent applications. Identified and evaluated potential new products for acquisition and development.

Personnel management: Supervised one Ph.D. immunologist and three technical staff.

Pharmacologist, Pharmacology & Toxicology (1991 - 1994)
Reported to: Director, Pharmacology & Toxicology

Management responsibilities: Completed performance reviews of direct reports. Member of several Product Development Teams. Designed a laboratory for conducting *in vitro* assays and cell culture experiments.

Scientific/research responsibilities: Designed, conducted and supervised studies evaluating efficacy and mechanism of action of monoclonal antibody and protein-based therapeutics in animal models of sepsis, inflammation and autoimmune diseases. Developed and characterized novel animal models or adapted existing models for the above purpose. Developed ELISA assays for pharmacokinetic and toxicology (immunogenicity) studies. Designed and supervised pharmacokinetic studies. Presented results at in-house and extramural scientific meetings; published in scientific journals.

Gained extensive experience with the following animal models:

- rodent sepsis models (endotoxin and bacterial challenge by various routes)
- rat subcutaneous air pouch acute inflammation model
- rat intestinal ischemia/reperfusion-induced lung inflammation model
- rat collagen- and adjuvant-induced arthritis models
- BB rat diabetes model
- NZB/W mouse systemic lupus erythematosus model
- xenogeneic transplantation of human lymphocytes and leukemic cells into immunodeficient mice

Personnel management: Supervised two to three technical staff.

1987 – 1991 **Terry Fox Laboratory for Hematology/Oncology**
BC Cancer Agency, Vancouver, British Columbia, Canada
Postdoctoral Fellow

- Conducted basic research in the following areas:
  - Regulation of adhesion molecules on human lymphocytes and monocytes and their role in cellular activation during immune/inflammatory responses.
  - Regulation of proinflammatory cytokine production/gene expression in monocytes from normal donors and bone marrow transplant recipients.
- Developed methods to isolate endotoxin-free fibronectin from human plasma and to purify large numbers of unactivated/unprimed monocytes from peripheral blood.
- Gained extensive experience in immune function and cytokine assays, flow cytometry and molecular biology techniques.
- Supervised summer students, co-supervised technical staff and helped manage the laboratory.

1981 – 1987 **University of Minnesota, Minneapolis, MN**
Graduate Student, Pharmacology

- Examined the effects of cyclophosphamide analogs on normal mouse and human hematopoietic stem cells. Discovered that the relative stem cell sparing effect of these chemotherapeutic agents is due to the presence of aldehyde dehydrogenase (an intracellular enzyme that catalyzes the conversion of the active metabolite of cyclophosphamide to an inactive product) in the most primitive hematopoietic cells.
- Established all of the mouse and human hematopoietic colony-forming unit assays from following the literature.
- Established and utilized a murine allogeneic bone marrow transplantation model to evaluate the effect of *ex vivo* treatment of donor marrow with cyclophosphamide analogs on development of acute graft-*vs.*-host disease.

Summer 1981 **GD Searle & Co., Skokie, IL**
Research Assistant, Pharmacology, Antihypertensive Section

- Established a toxicological assay (the mouse wire test) for the preliminary evaluation of toxic effects of novel antihypertensive agents.
- Aided technical staff in conduct of cardiovascular studies using rodent and canine models.

Summer 1975 **Abbott Laboratories, Abbott Park, IL**
Research Assistant, Pharmacology, Anti-Inflammatory Section

- Conducted studies evaluating efficacy of novel anti-inflammatory agents using the Arthus reaction in rats.
- Designed a computer program to analyze and present the data.

EDUCATION

1987 Ph.D. Department of Pharmacology, University of Minnesota, Minneapolis, MN

1980 B.S. Department of Biology, University of Illinois, Champaign/Urbana, IL

AWARDS/HONORS/FELLOWSHIPS

1974 Illinois State Scholar
1974 Edmund J. James Scholar
1981 - 1987 United States Public Health Service Fellowship
1986 Bacaner Award for Basic Research in Pharmacology, Minnesota Medical Foundation

PROFESSIONAL AFFILIATIONS

American Association of Pharmaceutical Scientists
American Association for the Advancement of Science
Drug Information Association

PROFESSIONAL DEVELOPMENT

PERI course on Drug Development
From the Laboratory to Leadership, The Leadership Edge
Leadership and Management Program, UCSD course

BIBLIOGRAPHY

Full Publications:

Kohn FR and Sladek NE. Aldehyde dehydrogenase activity as the basis for the relative insensitivity of murine pluripotent hematopoietic stem cells to oxazaphosphorines. *Biochem Pharmacol* 34: 3465-3471, 1985.

Kohn FR and Sladek NE. Effect of aldehyde dehydrogenase inhibitors on the *ex vivo* sensitivity of murine late spleen colony-forming cells (day-12 CFU-S) and hematopoietic repopulating cells to mafosfamide (ASTA Z 7557). *Biochem Pharmacol* 36: 2805-2811, 1987.

Kohn FR, Landkamer GJ and Sladek NE. Effect of the aldehyde dehydrogenase inhibitor, cyanamide, on the *ex vivo* sensitivity of murine multipotent and committed hematopoietic progenitor cells to mafosfamide (ASTA Z 7557). *Immunopharmacol Immunotoxicol* 9: 163-176, 1987.

Kohn FR, Landkamer GJ, Manthey CL, Ramsay NKC and Sladek NE. Effect of aldehyde dehydrogenase inhibitors on the *ex vivo* sensitivity of human multipotent and committed hematopoietic progenitor cells and malignant blood cells to oxazaphosphorines. *Cancer Res* 47: 3180-3185, 1987.

Kohn FR and Sladek NE. *Ex vivo* treatment of murine splenocyte-supplemented bone marrow inocula with mafosfamide prior to allogeneic transplantation in an attempt to prevent lethal graft-*versus*-host disease without compromising engraftment. *Immunopharmacol Immunotoxicol* 10: 387-398, 1988.

Kohn FR, Grigg ME and Klingemann H-G. Differential regulation of fibronectin receptor subunit gene and cell surface expression in human peripheral blood T lymphocytes. *J Immunol* 146: 1484-1489, 1991.

Klingemann H-G, Kohn FR and Phillips GL. Proliferation of peripheral lymphocytes to interleukin-2 and interleukin-4 after marrow transplantation. *Eur Cytokine Net* 2: 131-136, 1991.

Kohn FR, Grigg ME and Klingemann H-G. Fibronectin receptor subunit (α^5, α^4 and β_1) mRNA and cell surface expression in human peripheral blood B lymphocytes. *Immunol Letters* 28: 27-30, 1991.

Kohn FR and Klingemann H-G. Regulation of fibronectin receptor ($\alpha^5\beta_1$) mRNA expression in human monocytes and monocyte-derived macrophages by activation/differentiation signals. *Exp Hematol* 19: 653-658, 1991.

Klingemann H-G and Kohn FR. Involvement of fibronectin and its receptor in human lymphocyte proliferation. *J Leuk Biol* 50: 464-470, 1991.

Kohn FR, Phillips GL and Klingemann H-G. Regulation of tumor necrosis factor-α production and gene expression in monocytes. *Bone Marrow Transpl* 9: 369-376, 1992.

Kohn FR, Fishwild DM and Kung AHC. Efficacy of an anti-human CD5-ricin A chain immunoconjugate in an improved human peripheral blood lymphocyte-reconstituted severe combined immunodeficient mouse model. *Int J Immunopharmacol* 15: 695-709, 1993.

Kohn FR, Ammons WS, Horwitz A, Grinna L, Theofan G, Weickmann J and Kung AHC. Protective effect of a recombinant amino terminal fragment of bactericidal/permeability-increasing protein in experimental endotoxemia. *J Infect Dis* 168: 1307-1310, 1993.

Full Publications (continued):

Kohn FR, Fishwild DM, Bernhard SL, Better M and Kung AHC. Efficacy of anti-CD5 $F(ab')_2$- and Fab' immunoconjugates in human peripheral blood lymphocyte-reconstituted severe combined immunodeficient mice. *Int J Immunopharmacol* 15: 871-878, 1993.

Lin Y, Kohn FR, Kung AHC and Ammons WS. Protective effect of a recombinant fragment of bactericidal/permeability increasing protein against carbohydrate dyshomeostasis and tumor necrosis factor-α elevation in rat endotoxemia. *Biochem Pharmacol* 43: 1553-1559, 1994.

Ammons WS, Kohn FR and Kung AHC. Protective effects of an N-terminal fragment of bactericidal/permeability-increasing protein in rodent models of gram-negative sepsis: Role of bactericidal properties. *J Infect Dis* 170: 1473-1478, 1994.

Kohn FR and Kung AHC. Role of endotoxin in acute inflammation induced by gram-negative bacteria: Specific inhibition of lipopolysaccharide-mediated responses with an amino terminal fragment of bactericidal/permeability-increasing protein. *Infect Immun* 63: 333-339, 1995.

Kohn FR, Malkmus SA, Brownson EA, Rossi SS and Yaksh TL. Fate of the predominant phospholipid component of DepoFoam™ drug delivery matrix after intrathecal administration of sustained-release encapsulated cytarabine in rats. *Drug Deliv* 5(2): 143-151, 1998.

Yaksh TL, Provencher JC, Rathbun ML and Kohn FR. Pharmacokinetics and efficacy of epidurally delivered sustained release encapsulated morphine in dogs. *Anesthesiol* 90(5):1402-12, 1999.

Yaksh TL, Provencher JC, Rathbun ML, Myers RR, Powell H, Richter P and Kohn FR. Safety assessment of encapsulated morphine delivered epidurally in a sustained-release multivesicular liposome preparation in dogs. *Drug Deliv* 7(1): 27-36, 2000.

Book Chapters/Meeting Proceedings/Reviews:

Kung AHC, Ammons WS, Lin Y and Kohn FR. Efficacy of a recombinant amino terminal fragment of bactericidal/permeability increasing protein in rodents challenged with LPS or *E. coli* bacteria. In: *Bacterial Endotoxins: Basic Science to Anti-Sepsis Strategies. Proceedings of the International Conference on Endotoxins IV* (eds., Levin J, Sturk A, van der Poll T and van Deventer SJH), Wiley-Liss, Inc., New York, 1994.

Elsbach P, Weiss J, Doerfler M, Shu C, Kohn FR, Ammons WS, Kung AHC, Mészáros K, Parent JB, Gazzano-Santoro H, Huang K and Fishwild D. The bactericidal/permeability increasing protein of neutrophils is a potent antibacterial and antiendotoxin agent *in vitro* and *in vivo*. In: *Bacterial Endotoxins: Basic Science to Anti-Sepsis Strategies. Proceedings of the International Conference on Endotoxins IV* (eds., Levin J, Sturk A, van de Poll T and van Deventer SJH), Wiley-Liss, Inc., New York, 1994.

Ammons WS, Kohn FR, Lin Y and Kung AHC. Protective effects of an N-terminal fragment of bactericidal/permeability-increasing protein in endotoxemia and gram-negative sepsis. In: *Novel Therapeutic Strategies in the Treatment of Sepsis*. (ed. Morrison DC), Marcel Dekker, New York, 1996.

Numerous abstracts and presentations at scientific meetings