BIOGRAPHICAL SKETCH

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NAME: **Scott J. Weir, PharmD, PhD**

eRA COMMONS USER NAME (credential, e.g., agency login): SJWEIR

POSITION TITLE: Professor of Cancer Biology

EDUCATION/TRAINING**:** *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	COMPLETION DATE (MM/YYYY)	FIELD OF STUDY
University of Nebraska, Omaha, NE	B.Sc.	05/1979	Biology
University of Nebraska Medical Center, Omaha, NE	Pharm.D.	05/1980	Pharmacy
University of Nebraska Medical Center, Omaha, NE	Ph.D.	03/1986	Pharmacokinetics & Biopharmaceutics

A. Personal Statement

My career in drug discovery and development spans over 38 years. Prior to joining the University of Kansas Medical Center (KUMC) in 2006, I spent 20 years in the pharmaceutical industry, directly contributing to the successful development and registration of over 26 drug products such as Cardizem®, Anzemet®, Pentasa®, Allegra®, Priftin®, and Rifater®. Specifically, I led a division within Research and Development comprised of pharmacology, toxicology, drug metabolism and pharmacokinetics, bioanalytical chemistry, and clinical pharmacology departments, each of which conducted studies necessary to support global registration of drug products.

My major responsibilities at KUMC are focused on translational research. I serve as Associate Director for Translational Research at the University of Kansas Cancer Center (KUCC). My role is to assist researchers in developing and advancing cancer research projects. Specifically, I enable and facilitate the formation of multidisciplinary, multi-organizational project teams as well as mentor teams in project planning, execution, and problem solving. I also currently serve as Interim Director of the KUCC Lead Development and Optimization Shared Resource (LDOSR). LDOSR is comprised of three cores including High Throughput Screening, Medicinal Chemistry, and the Biotechology Innovation and Optimization Center. Together, the LDOSR provides critical research infrastructure necessary to generate and optimize lead candidates directed against cancer drug targets. I also direct the Institute for Advancing Medical Innovation (IAMI) at KUMC. IAMI serves as the product development-focused translational research enterprise for the University and its regional partners. IAMI partners with researchers to translate laboratory and bedside discoveries into therapeutic, diagnostic, and medical device innovations, and using an industry approach, executes product development-focused translational research to de-risk the technologies with the intent of partnering those with promise. Empowered multidisciplinary, multi-organizational project teams are formed with IAMI leadership. Teams are guided to develop milestone-based product development-focused translational research project plans and mentored through project execution. Over the past six years, we have supported advancement of five KU-invented anticancer agents to early phase clinical trials. IAMI currently supports a cancer drug discovery research portfolio of over 30 projects.

Along with Ms Tammy Ham, President and CEO of BioNovus Innovations LLC, I manage a unique public-private partnership CureBridgeCollaborative™. CureBridgeCollaborative™ serves as the vehicle for advancing promising medical innovation technologies arising from our drug discovery research portfolio through early development into early phase clinical trials. To date, the partnership has formed six biotechnology companies focused on developing therapeutic, diagnostic, and medical device technologies arising from University laboratory and bedside discoveries.

Ongoing and recently completed projects that I would like to highlight include:

NIH/NCI R44CA246997
mPI: W. McCulloch & S.J. Weir
09/09/2020 - 08/31/2022
Development of Ciclopirox Prodrug as a Novel Systemic Treatment for High-Risk Non-Muscle Invasive Bladder Cancer
1.2 CYM
Principal Investigator

NIH/NCI P30CA168524
PI: R. Jensen
07/01/22-06/30/27
Cancer Center Support Grant (CCSG) for NCI-designated Cancer Centers
3CYM
Key Personnel

NIH UL1TR002366
PI: M. Castro
07/29/22-06/30/27
Institutional Clinical and Translational Science Award (U54)
1.2 CYM
Co-Investigator

NIH R01 CA214916
PI: T. Iwakuma
03/09/2018 - 02/28/2023
Control of mutant p53 stability via the mevalonate pathway-DNAJA1 axis
0.48 CYM
Principal Investigator

VA 5I01BX004497-03
PI: S. Banerjee
10/01/2019 - 09/30/2023
CCN5 Therapy for Triple Negative Breast Cancer
0.6 CYM

Citations:

1. Hughes, M, Inglese, J, Kurtz, A, Andalibi, A, Patton, L, Austin, C, Baltezor, M, Beckloff, M, Sittampalam, S, Weingarten, M, **Weir, S**: Early Drug Discovery and Development Guidelines: For Academic Researchers, Collaborators, and Start-Up Companies. **NCBI Bookshelf, National Library of Medicine, National Institutes of Health** Bookshelf ID: NBK92015. Epub 2012 May 1. PMID: 22553881 (PMC# not applicable)
2. Tyner JW, Tognon CE, Bottomly D, Wilmot B, Kurtz SE, Savage SL, Long N, Schultz AR, Traer E, Abel M, Agarwal A, Blucher A, Borate U, Bryant J, Burke R, Carlos A, Carpenter R, Carroll J, Chang BH, Coblentz C, d'Almeida A, […] Watts JM, **Weir SJ**, Wiest DL, Winters RM, McWeeney SK, Druker BJ: Functional genomic landscape of acute myeloid leukaemia. **Nature** 2018 Oct;562(7728):526-531. PMC6280667
3. Barohn RJ, **Weir SJ**, Simari RD: Progress in drug discovery in academia and persistent challenges of "the Valley of Death". **Mayo Clin Proc** 2019 Mar;94(3):391-393. PMID: 30832788 (PMC# not applicable)
4. Perry JM, Tao F, Roy A, Lin T, He XC, Chen S, Lu X, Nemecheck J, Ruan L, Yu Z, Dukes D, Moran A, Pace J, Schroeder K, Zhao M, Venkatraman A, Qian P, Li Z, Hembree M, Paulson A, He Z, Xu D, Tran TH, Deshmukh P, Nguyen CT, Kasi RM, Ryan R, Broward M, Ding S, Guest E, August K, Gamis AS, Godwin A, Sittampalam GS, **Weir SJ**, Li L: Overcoming Wnt-β-catenin dependent anticanter therapy resistane in leukemia stem cells. **Nature Cell Biol**. 2020; 22, 689–700. PMID:32313104 (PMC# not applicable)

B. Positions, Scientific Appointments, and Honors

Positions:

2009-Present Director, Institute for Advancing Medical Innovation, KUMC
2006-Present Associate Director, Translational Research, KUCC

2006-2008 Director, Office of Therapeutics, Discovery and Development, KUMC
2005-2006 Executive Director, Preclinical Technologies, Aptuit Inc., Kansas City, MO
1999-2005 Vice President, Early Development and Laboratory Services, Quintiles Inc., Kansas City, MO
1996-1998 Director, Global Pharmacokinetics, Hoechst Marion Roussel, Inc., Kansas City, MO
1994-1996 Acting Vice President, Global Pharmacokinetics, Marion Merrell Dow, Inc. and Hoechst Marion Roussel, Inc., Kansas City, MO
1992-1994 Department Head, Clinical Pharmacokinetics, Marion Merrell Dow, Inc., Kansas City, MO
1988-1992 Team Leader, Clinical Pharmacology, Marion Laboratories, Inc., Kansas City, MO
1986-1988 Pharmacokineticist II, Clinical Pharmacology, Marion Laboratories, Inc., Kansas City, MO.

Scientific Appointments (voluntary unless indicated):
2020-Present Steering Committee, Clinical Trial Transformation Initiative
2018-Present Board of Directors, Leo and Anne Albert Institute for Bladder Cancer Research and Patient Care
2017-Present Chief Scientific Officer, CicloMed LLC, Kansas City, MO
2017-Present Scientific Advisory Board, Myeloproliferative Neoplasm Research Foundation
2016-2018. Scientific Advisory Board, Center for Drug Discovery, Washington University
2015-Present Advisory Board, Midwest Stem Cell Therapy Center, KUMC
2015-2016 Institute of Medicine Working Group on Mapping the Drug Discovery and Development Process
2014-Present External Advisory Committee, University of Kentucky Institute for Clinical and Translational Science (renumeration)
2014-Present Scientific Advisory Board, Family Health International 360 (renumeration)
2013-2016 Clinical Trial Transformation Initiative Patient Engagement Working Group
2013-2014 Co-Chair, NCATS Advisory Council CTSA Working Group on the IOM Report
2012-Present Advisory Committee, T32 Pediatric Clinical Pharmacology Training Program, Children's Mercy Kansas City
2012-2017 Advisory Board, Cures Acceleration Network (CAN), National Institutes of Health (NIH)
2012-2017 Advisory Council, National Center for Advancing Translational Science (NCATS) at NIH
2012-Present Co-Chair, Screen-to-Lead Program Study Section, The Leukemia and Lymphoma Society
2006-Present Steering Committee, Frontiers Institute for Clinical and Translational Research, KUMC
2006-2020 Program Co-Leader, Drug Discovery, Delivery and Experimental Therapeutics Program, KUCC

Professional Memberships:
American Association of Pharmaceutical Scientists
American College of Clinical Pharmacology
American Society of Pharmacology and Experimental Therapeutics
American Association for Cancer Research
American Society of Clinical Oncology

Honors:
2017-Present Kelly Family Foundation IAMI Endowed Professor in Cancer Drug Discovery and Development
2017 Janet Davison Rowley Patient Impact Research Award
2016 Global Genes Rare Champion of Hope Award
2013 Global Genes Rare Champion of Hope Award
2012 The Leukemia and Lymphoma Society Medical Professional Award
2010 Kansas Big Thinker
2006-2017 Frank B. Tyler Cancer Research Professor in Therapeutic Discovery

C. Contributions to Science
I have a proven track record in advancing new drug therapies from the bench to the bedside. Prior to joining the University of Kansas Medical Center (KUMC), I led a drug development division in the pharmaceutical industry for 20 years focused on advancing promising new drug therapies from drug discovery through human and/or clinical proof of concept. My efforts contributed to the successful development, registration, and commercialization of over 25 drug products across a wide range of therapeutic areas. Since joining KUMC, we have established pharmaceutical industry best practices, recruited industry veterans, formed and reorganized supported cores and centers, and established strategic partnerships with industry, academia, government and

disease philanthropy organizations, all focused on supporting the discovery, delivery and clinical evaluation of new drug therapies for the treatment and prevention of cancer and rare diseases afflicting children, adolescents, adults and the elderly.

Drug Discovery and Development in an Industry Setting. Over the course of 20 years, I held positions of increasing responsibility in Research and Development for Marion Laboratories Inc., Marion Merrell Dow Inc., Hoechst Marion Roussel, Aventis Pharmaceuticals, Quintiles Inc, and Aptuit Inc. I was responsible for managing and integrating several departments within this drug development division including pharmacology, toxicology, drug metabolism and pharmacokinetics, bioanalytical chemistry, and clinical pharmacology. During two mergers, I co-led task forces that developed innovative early drug development strategies resulting in the acceleration of development candidates from discovery through clinical proof of concept. During the Hoechst Marion Roussel Inc merger, I led the harmonization and integration of drug metabolism and pharmacokinetics disciplines across the three companies being merged. Drug discovery and development processes developed through these efforts made direct, positive impacts on our efforts to identify failures quickly as well as accelerate winners to late stage drug development. My efforts as well as those of my division contributed to the successful registration and commercialization of over 25 drug products that continue to benefit patients today such as Cardizem CD® and Cardizem Injectable®, Carafate®, Anzemet® Oral and Injectable, Pentasa®, Rifater®, rifapentine, and several Allegra® drug products. Representative publications reflecting my contributions to drug discovery and development in an industry setting are provided below.

1. Dimmitt DC, Choo YS, Martin, LA, Arumugham T, Hahne WF, and **Weir SJ**: Single- and multiple-dose pharmacokinetics of oral dolasetron and its active metabolites in healthy volunteers: part 2. **Biopharm Drug Dispos** 1999 20(1):41-48. PMID: 10086836.
2. Keung A, Reith K, Eller MG, McKenzie KA, Cheng L, **Weir SJ**: Enzyme induction observed in healthy volunteers after repeated administration of rifapentine and its lack of effect on steady-state rifapentine pharmacokinetics: part I. **Int J Tuberc Lung Dis** 1999 3(5):426-36. PMID: 10331733.
3. Robbins-Weilert DK, Giesing DH, **Weir SJ**: Steady-state pharmacokinetics of high-dose diltiazem hydrochloride (Cardizem CD) administered once daily in healthy volunteers. **Am J Ther** 1999 6(4):211-6. PMID: 11329099.
4. **Weir SJ**, Gao Y, Henney HR: Population pharmacokinetics and pharmacodynamics of dalframpridine-ER in healthy volunteers and patients with MS. **Curr Med Res Opin** 2013 29(12):1627-1636. PMID: 23157466.

Drug Discovery and Development in Academia. Since joining KUMC over 15 years ago, I have led efforts to build an end-to-end, integrated drug discovery and development program that translates laboratory and clinical discoveries into medical innovations, developing and executing project plans focused on de-risking those projects, and in doing so, creating data packages that support partnering and real financing of the innovations. The drug discovery and development program capitalizes on the University's research base, leverages R&D infrastructure available within the University, and partners with drug discovery and development service providers and collaborators external to the University, with a singular focus of advancing projects to clinical proof of concept trials. A two-pronged approach is routinely taken in parallel, to discover new therapeutic entities and also, to look for opportunities to repurpose existing drugs. IAMI's first drug product, Epaned™, developed in partnership with Silvergate Pharmaceutics LLC and Children's Mercy Hospital in Kansas City, MO, was approved by FDA in August 2013 and commercially launched in October 2013. The drug discovery and development program established under my leadership is a key differentiator for KUMC's CTSA center as well as its NCI designated Cancer Center. Representative publications reflecting my contributions to academic drug discovery and development are provided below.

1. Ma Y, Baltezor M, Rajewski L, Crow J, Samuel G, Staggs VS, Chastain KM, Toretsky JA, **Weir SJ**, Godwin AK: Targeted inhibition of histone deacetylase leads to suppression of Ewing sarcoma tumor growth through an unappreciated EWS-FLI1/HDAC3/HSP90 signaling axis. **J Mol Med** 2019 Jul;97(7):957-972. PMC6584050
2. Dandawate P, Kaushik G, Ghosh C, Standing D, Ali Sayed AA, Choudhury S, Subramaniam D, Manzardo A, Banerjee T, Santra S, Ramamoorthy P, Butler M, Padhye SB, Baranda J, Kasi A, Sun W, Tawfik O, Coppola D, Malafa M, Umar S, Soares MJ, Saha S, **Weir SJ**, Dhar A, Jensen RA, Thomas SM, Anant S: Diphenylbutylpiperidine antipsychotic drugs inhibit prolactin receptor signaling to reduce growth of pancreatic ductal adenocarcinoma in mice. **Gastroenterology**. 2020 Apr;158(5):1433-1449.e27. doi: 10.1053/j.gastro.2019.11.279. Epub 2019 Nov 29. PubMed PMID: 31786131; PubMed Central PMCID: PMC7103550.

3. Subramaniam D, Angulo P, Ponnurangam S, Dandawate P, Ramamoorthy P, Srinivasan P, Iwakuma T, **Weir SJ**, Chastain K, Anant S: Suppressing STAT5 signaling affects osteosarcoma growth and stemness. **Cell Death Dis**. 2020 Feb 24;11(2):149. doi: 10.1038/s41419-020-2335-1. PubMed PMID: 32094348; PubMed Central PMCID: PMC7039889.
4. Dandawate P, Subramaniam D, Panovich P, Standing D, Krishnamachary B, Kaushik G, Thomas SM, Dhar A, **Weir SJ**, Jensen RA, Anant S: Cucurbitacin B and I inhibits colon cancer growth by targeting the Notch signaling pathway. **Sci Rep**. 2020 Jan 28;10(1):1290. doi: 10.1038/s41598-020-57940-9. PubMed PMID: 31992775; PubMed Central PMCID: PMC6987129.

Discovery and Development of New Treatments for Bladder Cancer. In addition to providing drug discovery and development leadership at KUMC, I am a co-inventor of a promising new treatment for non-muscle invasive bladder cancer (NMIBC). The patented fosciclopirox (CPX-POM) represents potentially the first systemically administered treatment for NMIBC. Following systemic administration, this agent selectively delivers ciclopirox to the entire urinary tract. In vitro and in vivo preclinical proof of principle has been established in human bladder cancer cell lines as well as a validated mouse model of invasive bladder cancer. An investigational new drug application (IND 132545) received FDA clearance to proceed with the first-in-human Phase 1 trial in September 2017. CPX-POM-001 (NCT#03348514) has characterized the safety, dose tolerance, pharmacokinetics and pharmacodynamics of CPX-POM in patients with advanced solid tumors and is currently being evaluated in an expansion cohort of cisplatin-ineligible muscle invasive bladder cancer patients. Issued patents supporting development of CPX-POM as well as publications are provided below.

1. **Weir SJ**, Wood R, Schorno K, Brinker AE, Ramamoorthy P, Heppert K, Rajewski L, Tanol M, Ham T, McKenna MJ, McCulloch W, Dalton M, Reed GA, Jensen RA, Baltezor MJ, Anant, S, Taylor III JA: Preclinical pharmacokinetics of fosciclopirox, a novel treatment for urothelial cancers, in rats and dogs. **J Pharmacol Exp Ther** 2019 Aug;370(2):148-159. doi: 10.1124/jpet.119.257972. Epub 2019 May 21. PMC6614794
2. Penticuff JC, Woolbright BL, Sielecki TM, **Weir SJ**, Taylor III JA**:** MIF family proteins in genitourinary cancer: tumorigenic roles and therapeutic potential. **Nat Rev Urol**. 2019 May;16(5):318-328. doi: 10.1038/s41585-019-0171-9. PMID: 30914802 Review.
3. Chestnut C, Subramaniam D, Dandawate P, Padhye S, Taylor III JA, **Weir SJ**, Anant S**:** Targeting major signaling pathways of bladder cancer with phytochemicals: A review. **Nutr Cancer**. 2020 Dec 11:1-23. doi: 10.1080/01635581.2020.1856895. Online ahead of print.PMID: 33305598
4. **Weir SJ**, Dandawate P, Standing D, Bhattacharyya S, Ramamoorthy P, Rangarajan P, Wood R, Brinker AE, Woolbright BL, Tanol M, Ham T, McCulloch W, Dalton D, Reed GA, Baltezor MJ, Jensen RA, Taylor III JA, Anant S: Fosciclopirox Suppresses Growth of High-Grade Urothelial Cancer by Targeting g-Secretase. **Cell Death Dis**, 2021 May 31;12(6):562. doi: 10.1038/s41419-021-03836-z. PMC8166826

Complete List of Published Work in MyBibliography: (Total Number of Publications = 65)
https://www.ncbi.nlm.nih.gov/myncbi/scott.weir.1/bibliography/public/