

Curriculum Vitae

David Griffith Soergel, Jr., M.D.
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Education:

The Children's Hospital of Philadelphia (Jan 2004-Jan 2005)
Advanced Fellowship in Pediatric Heart Failure and Transplantation

The Johns Hopkins Hospital (July 2000-December 2003)
Fellowship in Pediatric Cardiology

The Johns Hopkins Hospital (Nov. 1997-Aug. 1999)
Residency in Pediatrics

Emory University (July 1996-July 1997)
Internship in Pediatrics

Cornell University Medical College (M.D. 1996)

The Johns Hopkins University (B.A. 1989 with General Honors)

Employment:

Novartis (NYSE: NVS), East Hanover, NJ
August 2017 – Present. Global Development Franchise Head, Cardiometabolic
Responsibilities:

- Manage cardiovascular, renal and metabolic development teams
- Progress post-PoC pipeline in cardiovascular, metabolic and renal diseases to registration and launch
- Replenish CM pipeline with on-strategy assets sourced internally or externally
- Contribute to evidence generation for marketed products (eg ENTRESTO)

Trevena, Inc (NASDAQ: TRVN), King of Prussia, PA
March 2015 – August 2017. SVP, Clinical Development & Chief Medical Officer
September 2012-March 2015. Senior Vice President, Clinical Development
November 2009-September 2012. Vice President, Clinical Development
Responsibilities:

- Built world-class clinical development and medical affairs groups to support development of Trevena's portfolio
- Utilized an innovative hybrid in/out-source model to conduct a phase 3

- program enrolling >1000 patients, saving time and money
- Developed innovative phase 2 programs to efficiently achieve PoC
 - Enabled private and public fund-raising, including an initial public offering, contributing medical expertise in pain and heart failure
 - Partnered with head of research to progress 4 novel compounds into the clinic
 - Led development of clinical strategy and presented to Board and investors
 - Participant in various formal and informal interactions with FDA including type B and C meetings
 - Contributed key content to the granted Breakthrough Therapy designation request for oliceridine
 - Transitioned a virtual medical affairs model to a FTE model with the aim of enhancing awareness of oliceridine in preparation for eventual product launch

Concert Pharmaceuticals (NASDAQ: CNCE), Lexington, MA
July 2008-November 2009. Senior Director, Clinical Development
Multiple therapy areas: infectious diseases (anti-viral and anti-bacterial),
nephrology, women's health, fibrosis, heart failure

Responsibilities:

- Designed and executed clinical studies, predominantly Ph1-2
- Contributed to preparation of regulatory documents
- Interface with KOLs
- Support business development needs to facilitate partnering of assets, including GSK partnership

GlaxoSmithKline, Upper Merion, PA
Jan 2005-June 2008. Director, Discovery Medicine, Cardiovascular and
Urological Center for Excellence in Drug Discovery
Clinical focus: Urology and Women's Health

Responsibilities:

- Participate in Disease Strategy Groups to identify and prioritize targets
- Prepare and submit protocols for internal and external review
- Participate in regulatory meetings and document preparation
- Execute and monitor clinical studies
- GSK Internal Cardiac Safety Panel, GSK Pediatric Network

Children's Hospital of Philadelphia, Philadelphia, PA
Jan. 2004-Jan. 2005. Clinical Associate and Advanced Fellow in Pediatric Heart
Failure and Transplant.

The Johns Hopkins Hospital, Baltimore, MD
July 2000-Dec. 2003. Fellow in Pediatric Cardiology. Individual NRSA-
sponsored (NIH) research in laboratory of Anne Murphy, MD.

Franklin Square Hospital, Baltimore, MD

July 1999-July 2000. Attending Pediatric Hospitalist and Emergency Physician.

Johns Hopkins University School of Medicine, Baltimore, MD
June 1993-June 1994. Howard Hughes Predoctoral Fellow, Department of Neurosciences. Preceptors: Fabio Rupp, Ph.D. and Solomon Snyder, M.D.

National Institutes of Health, NIDDK, Bethesda, MD
June 1989-September 1991. Laboratory Technician and pre-doctoral IRTA fellow, Laboratory of Bioorganic Chemistry. Supervisors: John W. Daly, Ph.D. and Fabian Gusovsky, Ph.D.

Publications:

Fossler MJ, Sadler BM, Farrell C, Burt DA, Pitsiu M, Skobieranda F, Soergel DG. "Oliceridine (TRV130), a Novel G Protein-Biased Ligand at the μ -Opioid Receptor, Demonstrates a Predictable Relationship Between Plasma Concentrations and Pain Relief. I: Development of a Pharmacokinetic/Pharmacodynamic Model." *J Clin Pharmacol*, 58(6):750-761, Jun 2018, PMID: 29412458.

Fossler MJ, Sadler BM, Farrell C, Burt DA, Pitsiu M, Skobieranda F, Soergel DG. "Oliceridine, a Novel G Protein-Biased Ligand at the μ -Opioid Receptor, Demonstrates a Predictable Relationship Between Plasma Concentrations and Pain Relief. II: Simulation of Potential Phase 3 Study Designs Using a Pharmacokinetic/Pharmacodynamic Model." *J Clin Pharmacol*, 58(6): 762-770, Jun 2018, PMID: 29393971.

Singla N, Minkowitz HS, Soergel DG, Burt DA, Subach RA, Salamea MY, Fossler MJ, Skobieranda F. "A randomized, Phase IIb study investigating oliceridine (TRV130), a novel μ -receptor G-protein pathway selective (μ -GPS) modulator, for the management of moderate to severe acute pain following abdominoplasty." *J Pain Res*, 10:2413-2424, Oct 2017, PMID: 29062240.

Cotter G, Davison BA, Butler J, Collins SP, Ezekowitz JA, Felker GM, Filippatos G, Levy PD, Metra M, Ponikowski P, Teerlink JR, Voors AA, Senger S, Bharucha D, Goin K, Soergel DG, Pang PS. "Relationship between baseline systolic blood pressure and long-term outcomes in acute heart failure patients treated with TRV027: an exploratory subgroup analysis of BLAST-AHF." *Clin Res Cardiol*, 107(2): 170-181, Feb 2018, PMID: 28986703.

Thornton S, Valenzuela G, Baidoo C, Fossler MJ, Montague TH, Clayton L, Powell M, Snidow J, Stier B, Soergel D. "Treatment of spontaneous preterm labour with retosiban: a phase II pilot dose-ranging study." *Br J Clin Pharmacol*, 83(10): 2283-2291, Oct 2017, PMID: 28556962.

Pang PS, Butler J, Collins SP, Cotter G, Davison BA, Ezekowitz JA, Filippatos G, Levy PD, Metra M, Ponikowski P, Teerlink JR, Voors AA, Bharucha D, Goin K, Soergel DG, Felker GM. "Biased ligand of the angiotensin II type 1 receptor in patients with acute heart failure: a randomized, double-blind, placebo-controlled, phase IIB, dose ranging trial (BLAST-AHF)." *Eur Heart J*, 38(30):2364-2373, Aug 2017, PMID: 28459958.

Viscusi ER, Webster L, Kuss M, Daniels S, Bolognese JA, Zuckerman S, Soergel DG, Subach RA, Cook E, Skobieranda F. "A randomized, phase 2 study investigating TRV130, a biased ligand of the m-opioid receptor, for the intravenous treatment of acute pain." *Pain*, 157(1): 264-72, Jan 2016, PMID: 26683109.

Felker GM, Butler J, Collins SP, Cotter G, Davison BA, Ezekowitz JA, Filippatos G, Levy PD, Metra M, Ponikowski P, Soergel DG, Teerlink JR, Violin JD, Voors AA, Pang PS. "Heart failure therapeutics on the basis of a biased ligand of the angiotensin-2 type 1 receptor: rationale and design of the BLAST-AHF Study." *JACC HF*, 3(3): 193-201, Mar 2015, PMID: 25650371.

Soergel DG, Subach RA, Burnham N, Lark MW, James IE, Sadler BM, Skobieranda F, Violin JD, Webster LR. "Biased agonism of the mu opioid receptor by TRV130 increases analgesia and reduces on-target adverse effects versus morphine: a randomized, double-blind placebo-controlled crossover study in healthy volunteers." *Pain*, Jun 2014, PMID: 24954166.

Violin JD, Crombie AL, Soergel DG, Lark MW. "Biased ligands at G-protein-coupled receptors: promise and progress" *Trends Pharmacol Sci*, May 2014, PMID: 24878326.

Soergel DG, Ann Subach R, Sadler B, Connell J, Marion AS, Cowan CL, Violin JD, Lark MW. "First Clinical Experience With TRV130: Pharmacokinetics and Pharmacodynamics in Healthy Volunteers." *J Clin Pharmacol*. 54(3):351-7, 2014.

Monasky, MM, DM Taglieri, M Henze, CM Warren, MS Utter, DG Soergel, JD Violin, RJ Solaro. "The β -arrestin biased ligand TRV120023 inhibits angiotensin II-induced cardiac hypertrophy while preserving enhanced myofilament response to calcium." *Am J Physiol Heart Circ Physiol* 305(6):H856-866, 2013.

Soergel, DG, RA Subach, CL Cowan, JD Violin, MW Lark. "First clinical experience with TRV027: pharmacokinetics and pharmacodynamics in healthy volunteers." *J Clin Pharmacol* 53(9):892-899, 2013.

Violin, JD, DG Soergel, G Boerrigter, JC Burnett, MW Lark. "GPCR biased ligands as novel heart failure therapeutics." *Trends Cardiovasc Med* 23(7):242-249, 2013.

Boerrigter, Guido, Michael W. Lark, Erin Whalen, David G. Soergel, Jonathan D. Violin, John C. Burnett. "TRV120027, a novel beta-arrestin biased ligand at the angiotensin II type I receptor, unloads the heart and maintains renal function when added to furosemide in experimental heart failure." *Circ Heart Fail*, 5(5):627-34, 2012.

Boerrigter, Guido, Michael W. Lark, Erin Whalen, David G. Soergel, Jonathan D. Violin, John C. Burnett. "Cardiorenal actions of TRV120027, a novel, β -arrestin-biased ligand at the angiotensin II type I receptor, in healthy and heart failure canines: A novel therapeutic strategy for acute heart failure." *Circ Heart Fail*, 4(6):770-8, 2011.

Soergel, DG, Dimitrios Georgakopoulos, David A. Kass and Anne M. Murphy. "Augmented systolic response to the calcium sensitizer EMD-57033 in a transgenic model with troponin I truncation." *Am J Physiol: Heart and Circulatory Physiol*, 286: H1785-H1792, 2004.

Takimoto, Eiki, David G Soergel, Paul M.L. Janssen, Linda B. Stull, David A. Kass and Anne M. Murphy. "Frequency- and afterload-dependent modulation in vivo by troponin I with constitutively active protein kinase A phosphorylation sites." *Circ Res*. 94: 1-10, 2004.

Kogler, H, Soergel DG, Murphy AM, Marban E. "Maintained contractile reserve in a transgenic model of myocardial stunning." *Am J Physiol: Heart and Circulatory Physiol*, 280 (6): H2623-30, 2001.

Soergel, D.G., T. Yasumoto, J.W. Daly and Fabian Gusovsky: "Maitotoxin effects are blocked by SK&F 96365, an inhibitor of receptor-mediated calcium entry." *Molecular Pharmacology* 41: 487-493 (1992).

Soergel, D.G., F. Gusovsky, T. Yasumoto and J.W. Daly: "Stimulatory effects of maitotoxin on insulinoma HIT cells: role of calcium uptake and phosphoinositide breakdown." *Journal of Pharmacology and Experimental Therapeutics* 255: 1360-1365 (1991).

Gusovsky, F., D.G. Soergel and J.W. Daly: "Effects of mastoparan and related peptides on phosphoinositide breakdown in HL-60 cells and cell-free preparations." *European Journal of Pharmacology* 206: 309-314 (1991).

Post-Graduate Honors:

Memberships:

Fellow, American Academy of Pediatrics; Member, American College of Cardiology, American Medical Association, American Heart Association
Board Certified in General Pediatrics by the American Board of Pediatrics (1999-2013)
Board Eligible, Pediatric Cardiology, December 2003