Glenn D. Prestwich, Ph. D. <u>Clear Solutions Biomedical LLC</u> *Consulting for the Chemical and Life Sciences*

1. Overview

The broad expertise of Clear Solutions Biomedical LLC includes organic synthesis, natural products chemistry, medicinal chemistry, mechanistic enzymology, novel pest control agents, termite biology, insect and mammalian pheromone biochemistry, insect juvenile hormone biochemistry, mammalian and insect steroid metabolism, photoaffinity labeling and intracellular visualization technology. Dr. Prestwich's recent research encompasses the chemical biology of phosphoinositide and lysophosphatidic acid signaling; the chemistry of hyaluronic acid; the development of hyaluronic acid derived biomaterials for reparative medicine, wound repair, 3-D cell culture, drug discovery and evaluation; and the development of new anti-inflammatory drugs based on sulfated glycosaminoglycans.

2. Academic Background

President's Distinguished Professor (Emeritus), Washington State University (2016 - 2021); Founding Director, Spinout Space in Spokane (sp³nw). Presidential Professor of Medicinal Chemistry (Emeritus) and Special Presidential Assistant for Faculty Entrepreneurism at The University of Utah (1996 - 2018), with adjunct appointments in the Departments of Chemistry, Biochemistry, Surgery, and Bioengineering. Educational Background: B.Sc. Honors (1970), Chemistry, California Institute of Technology; Ph.D., Chemistry (1974), Stanford University; Professor of Chemistry and Professor of Molecular and Cell Biology, Stony Brook University (1977-1996). Alfred P. Sloan Research and Dreyfus Teacher-Scholar Awards; 1998 Paul Dawson Biotechnology Award and 2008 Volwiler Research Achievement Award of the American Association of Colleges of Pharmacy; Fellow of the American Institute for Medical and Biological Engineering (2005 current); vSpring v100 Top 100 Utah Entrepreneurs (2005, 2006); TIAA-CREF Greater Good Award (2006); Utah Business Magazine Health Care Heroes (2006); Governor's Medal for Science and Technology (2006); University of Utah Distinguished Scholarly and Creative Research Award (2010); ISHAS Rooster Prize for therapeutic applications of hyaluronan (2010); University of Utah Distinguished Innovation and Impact Award (2014); Fellow of National Academy of Inventors (2014 - current); Fellow of the American Association for Advancement of Science (2018 - current). Previous titles include: Director, NY State Center for Advanced Technology in Medical Biotechnology (1992-1996), Director, Center for Cell Signaling (1997-2002) and Director, Center for Therapeutic Biomaterials (2004 – 2016), both Utah Centers of Excellence. Dr. Prestwich has published over 665 technical papers and book chapters, 90 patents and patent applications (49 issued) and has trained over 72 graduate students and 55 postdocs.

3. Business and Entrepreneurial Experience

Co-founder and Principal Scientific Advisor, Clear Solutions Biotech, Inc. (1992-1998). Co-founder and former CSO of Echelon Biosciences, Inc (1997-2003); co-founder and former CSO, Sentrx Surgical, Inc. (2004-2005); Senior Scientific Advisor, Carbylan BioSurgery, Inc. (Palo Alto, CA); co-founder, former CSO, and science advisor for Sentrx Animal Care, Inc. and Glycosan BioSystems, Inc (both Salt Lake City, UT, 2006 - 2022); co-founder and CSO, GlycoMira LLC and GlycoMira Therapeutics (Salt Lake City, 2008 -); Senior Scientific Advisor, Echelon Biosciences-Frontier Scientific (2008 - current); Science Advisor, BioTime, Inc (2011 - 2014); Co-founder, President & CEO, Metallosensors, Inc. (2011 - 2014). Manager and Science advisor, Deuteria Agrochemicals LLC (2013 - 2018); co-founder, manager and Science Advisor, Deuteria Biomaterials LLC (2013 - 2022). Chief Scientific Officer, Symic Bio, Inc. (2017 - 2019); Consultant, Shasqi, Inc. and Tambo, Inc. (2018 -current); Consultant, C-DOCTOR project on VolumatrixTM (2018 - 2022); Consultant and Science Advisor, Amasa Therapeutics (2016 - current); Consultant and Science Advisor, Rebel Medicine (2020 - current); Consultant and Science & Innovation Advisor, HTL Biotechnology (2019 - current); Consultant, Valitor, Inc (2018 - current); cofounder and President, Matrix Diagnostics Biosystems, Inc. (2020 - current); co-founder and Vice President, Maana Discoveries, Inc. (2021 - current). Scientific Advisory Boards: Clinical Tissue Engineering Center, Cleveland Clinic Foundation (2004 - 2010), Aeterna Zentaris (2005 - 2007), Novozymes Biopolymers (2006 - 2012), Organovo (2007 - 2017), Elastin Specialties (2008-2012), ContraDyn (2008 - 2012), Brickell Biotech (2010 - 2013), Jade Therapeutics (2013-2016); Symic Bio (2014 - 2017); Modern Meadow (2016 - current); University Medical Pharmaceuticals (2013 - 2016). Past multiday consultancies (1978 - current) have included: Allergan, Centre de Recherche Pierre Fabre, Kirin Life Sciences, MedChem, New England Nuclear, Sandoz, Serono Pharmaceutical Research Institute, and Velsicol.

4. Specific Experience in Insect Biochemistry, Growth Regulators, Olfaction and Pheromones

Dr. Prestwich has worked in three major areas of insect biochemistry: steroid biochemistry, olfaction, and hormonal regulation of growth and development. In steroid biochemistry, he documented plant steroid dealkylation pathways and developed inhibitors, and he patented a novel insect-specific pro-pesticide -- a metabolically-activated fluorophytosterol. In

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insect olfaction, he worked on the chemistry and biochemistry of insect olfaction. His expertise includes determination of pheromone structures, chemical synthesis of pheromones and analogs, analytical chemistry, enzymatic degradation of pheromones, synthesis and testing of novel pheromone analogs for insect control by mating disruption, and determination of the molecular biology and biochemistry of pheromone action. In insect developmental biology, he partnered with the Hammock (UC Davis) and Riddiford (U Washington) labs for over twelve years to determine the molecular basis for juvenile hormone action in insects and other arthropods. For each of these three areas, his lab pioneered the synthesis and use of highly tritium labeled steroids, pheromones, juvenile hormones, insect growth regulators -- and their photoaffinity analogs -- to identify proteins in insect antennae that bind, transport, and transduce olfactory signals and to identify molecular targets for juvenile hormone and commercial insect growth regulators. He was awarded the 2002 Silverstein-Simeone Award of the International Society of Chemical Ecology for his lifetime achievements in these fields. From 2013 - 2018, Dr. Prestwich managed Deuteria Agrochemicals LLC to develop deuterium-stabilized insect pheromones for integrated pest management.

5. Specific Experience in Medicinal Chemistry and Bioengineering, Focused on Hyaluronan

Dr. Prestwich was the founding Vice President for Applied Research of the International Society for Hyaluronan Science (ISHAS) from 2004-2008, and is now the current Vice President for Applied Research of ISHAS (2020 -). He initiated research on chemical modification of HA in the early 1990s and phosphoinositides/phospholipids in mid-1990s. Over eighty of his peer-reviewed publications and book chapters and over 20 of his issued patents and patent applications deal with the chemistry and biology of HA and HA-derived products. The focus of this research has been the development of hyaluronic acid derived biomaterials for reparative medicine, wound repair, 3-D cell culture, drug toxicology evaluation, the discovery of anti-cancer drugs. Projects included development of bio-inks for bioprinting and fabrication of biomaterial devices. This research has been resulted in commercial products in research, veterinary medicine, and human clinical use. More recently, sulfated glycosaminoglycans derived from HA are in development as new anti-inflammatory, immune-modulating oncology therapeutics. From 2014-2016, he worked with University Medical Pharmaceuticals for anti-aging formulations containing HA, and with Jade Therapeutics (now Eyegate Therapeutics) for ophthalmic drug delivery using HA hydrogels. Beginning in 2017, he works with several startup companies developing HA-derived or glycosaminoglycan-derived products, including Shasqi, Inc., Valitor, Inc., Amasa Therapeutics, Inc., Glycologix, Inc., Matrix Diagnostics Biosystems, Inc., and Maana Discoveries, Inc. From 2017 - 2022, Dr. Prestwich managed Deuteria Biomaterials LLC to develop deuterium-stabilized "Heavy HA" that was resistant to radical depolymerization. He now is Science and Innovation Advisor in North America for HTL Biotechnology SAS, a global HA supplier.

6. Expert Witness Experience

Declarations, reports, depositions, and courtroom testimony have been provided in over eighteen cases since 2007. Selected specific topics included: (i) patent infringement/invalidity for a synthetic prostanoids used for glaucoma; (ii) patent invalidity in the case of analogs of synthetic phosphoinositides used for drug discovery and cell biology; (iii) patent invalidity in a drug eluting stent case; (iv) whether advertising claims for a functional food product were false and misleading; (v) patent validity and infringement for use of HA for drug delivery; (vi) patent validity and infringement for a crosslinked HA used in treating osteoarthritis; (vii) patent validity via post-grant review (PGR) of a patent for pesticidal compounds; (viii) patent infringement for a plant growth regulator formulation; (ix) *inter partes* review (IPR) and patent infringement of methods analysis of cell-free DNA analysis in blood; (x) false and misleading advertising for an OTC nasal spray; (xi) misappropriation of trade secrets from a university; (xii) misappropriation of trade secrets related to a lipid nutritional supplement; and (xiii) validity of patents related to a deuterium-labeled natural product. Other recently completed cases have involved *inter partes* review and patent infringement & validity for medical devices, diagnostic tests, blood substitutes, HA-based dermal fillers, pharmaceutical compositions, and nutraceutical formulations.