Paul Abato Ph.D.

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SUMMARY

My services have been retained by a major generic pharmaceutical drug company in a high-profile ANDA case, I was deposed and participated in pretrial preparation.

I have recently provided expert witness consulting services in a case for a nutraceutical company where I have been deposed and gave trial testimony. I have also just been retained by a generic drug company involved in an ANDA case.

I am also presently consulting for an undisclosed pharmaceutical company where I oversee radio-labeled syntheses, of active pharmaceutical ingredients (API) for pharmacokinetic studies as well as the design of stability studies and formulation of the API.

A Ph. D. Medicinal Chemist with over 20 years of experience in the discovery and development of novel human therapeutics in the areas of anti-infective, anti-inflammatory and neurodegenerative diseases.

Contributed significantly to the development of Omadacycline a new antibacterial drug currently in Phase III clinical trials and the discovery of five preclinical candidates for Multiple Sclerosis, Arthritis and Spinal Muscular Atrophy.

I have been involved in all aspects of drug research and development from synthesis/purification, *in-vitro*, *in-vivo* (efficacy, pharmacokinetics and pharmacodynamics) testing, dosing routs, drug formulation, stability studies and the management of CROs. I have co-authored a pre-IND proposal that had a favorable review by the FDA.

EXPERIENCE

Paul Abato Consulting, Providence RI **6/1/14-Present**

Undisclosed Generic Pharmaceutical Company 6/25/18- Present
Independent Expert Witness Consultant

- Provide professional consulting and expert witness services relating to an ANDA case.

Undisclosed Nutraceutical Company 3/1/16- 5/29/18
Independent Expert Witness Consultant

- Deposed for 7h.
- Gave trial testimony for a trial by jury.
- Advised counsel on 2 in progress depositions.
- Provide professional consulting and expert witness services pertaining to patent infringement.
- Coordinated the search for and vetted other experts for the case.
- Coordinated and oversee the chemical analysis of the defendant's contested formulation.
- Preparing expert reports regarding the infringement of contested products over the asserted claims.

Undisclosed Pharmaceutical Company, Cambridge, MA 6/1/17- Present
Pharmaceutical development Consultant

- Coordination of a radiolabeled compound synthesis, stability studies and formulation used in pharmacokinetic studies.
- Assist with CMC of clinical trial material and the intricacies of drug allocation

Major Generic Pharmaceutical Drug Company 4/1/16- 12/19/16
Independent Expert Witness Consultant

- Provided professional consulting and expert witness in connection with Hatch-Waxman ANDA patent infringement litigation in the area of pharmaceutical technology.
- Prepared expert reports regarding the invalidity of plaintiff's patents concerning the reformulation of one of their products.
- Provided compelling arguments based on examples within the prior art, of why it would have been obvious to a person skilled in the art to at least try the formulation in the contested patents with a reasonable expectation of success.
- Prepared reply reports in response to Plaintiff experts' responsive reports in which I reconfirmed my arguments as well as highlighted plaintiff's experts' contradictions and misrepresentations of the prior art.
- I was deposed by the plaintiff's counsel for 7 hours.
- I was also involved with the pre-trial preparation up until the parties settled.

Cemotics LLC, Providence RI 6/01/14- 1/01/16
Pharmaceutical Development Consultant

- Development of Arysphosphonium Salts (APS) as anti-cancer agents. Responsibilities include design of novel compounds, development of screening cascade and medicinal chemistry lead optimization efforts.
- Interact with vendors to facilitate whole cell screening, toxicity, *in vivo* efficacy and ADME.
- Developing a novel treatment for malaria that circumvents resistance, generation of preliminary data through outsourcing with vendors.

Salve University Newport RI, **Rhode Island College** Providence RI **5/1/14-Present**
Professor

- Responsible for teaching Organic Chemistry, Forensic Science and lecture science classes.

Paratek Pharmaceuticals, Boston, MA **8/1/02-6/1/13**
Biotech developing tetracycline therapeutics for anti-infective, anti-inflammatory and neurodegenerative diseases.

Principal Scientist/ Project Coordinator (Project Coordination/Lab work ~ 60%/40%) 01/09 – 06/13

- Project 1: Project Coordinator for Spinal Muscular Atrophy (SMA) program in preclinical development
- Co-authored a pre-IND application for the intrathecal administration of our clinical candidate for Spinal Muscular Atrophy (reviewed by the FDA 1/23/13).
- Responsible for design and development of intrathecal (IT) and intracerebroventricular (ICV) continuous and bolus formulations and dosing protocols for mice, rat and monkey studies.
- Designed and conducted stability studies and formulation studies for continuous dosing efficacy studies to be compatible with Alezet osmotic pumps.
- Worked with cross-functional teams in cell-biology, pharmacology, process chemistry and vendors that supported *in vivo* efficacy studies, DMPK and GLP toxicity studies.
- Responsible for synthesis of new compounds and lead optimization of medicinal chemistry efforts for SMA
- Outsourced and managed preclinical efficacy/PK testing of three compounds at multiple CROs to facilitate pre-clinical toxicity and further PK analysis of our clinical candidate in mice, rat and monkey.
- Contributed to grant writing for NIH and FSMA grants.
- Project 2: Developed a new antibacterial for bacterial resistant respiratory infections in cattle for Elanco. Delivered an efficacious antibacterial compound for subcutaneous bolus dosing which would not tissue stain.
- Worked on additional projects as needed.
- Managed one direct report

Sr Scientist (Project Coordination/Lab work ~ 30%/70%) 01/06 – 01/09

- Worked on areas of anti-inflammation and functioned as the project coordinator for SMA.
- Responsible for synthesis of new derivatives, lead optimization, analysis of results from outsourced and in house *in vitro* studies, whole cell, pharmacology and *in vivo* studies.
- Worked with cross-functional teams in cell-biology, pharmacology, process chemistry as well as vendors that supported *in vitro* and *in vivo* efficacy studies.
- Developed HPLC purification methods for large-scale (6" diameter column) epimer separation of novel tetracycline derivatives previously not possible.
- Managed one direct report.

Scientist II 01/03 – 01/05

- Discovered and developed novel tetracyclines for the treatment of multiple sclerosis (MS) in collaboration with Serono. Delivered three validated pre-clinical tetracycline leads for MS.
- Developed drug formulation procedures that reduced tolerability issues when dosing IP and IV thereby enabling a wider therapeutic window with which to compare compounds using experimental autoimmune encephalomyelitis (EAE) mouse efficacy studies.
- Responsible for synthesis of new derivatives, lead optimization and analysis of results from *in vivo* efficacy
- Worked with cross-functional teams in cell-biology, pharmacology and process chemistry.
- Built a micro reactor to developed an oxidation assay to elucidate the structure activity relationship for tetracycline oxidation/tissue staining, a potentially negative aspect of some tetracyclines. The assay's results correlated with tissue staining *in vivo*.

Scientist I 08/02 – 01/03

- Contributed to the development of pre-clinical candidates for hospital and community acquired severe bacterial infections.
- Optimized synthetic methods and developed purification protocols for two key tetracycline intermediates on a 100g scale. This work removed a huge bottleneck in the production of tetracycline derivatives
- One lead compound is currently in phase III trials (Omadacycline) and a second has completed Phase I.

Eikos Inc., Franklin, MA. **2/1/02 – 8/1/02**

Biotech/material science co developing anti malaria drugs and incorporation of carbon nanotubes into polymers

Scientist I

- Managed all aspects of chemistry at Eikos. Conducted Polymer production reactions using a 50L reactor.
- Developed a solid phase organic synthesis protocol for the production of aminoquinoline antimalarials in support of an SBIR grant.
- Managed three direct reports.

Brown University, Providence RI. **6/01/96 – 2/12/02**

Graduate Researcher, Department of Chemistry; PI Christopher T. Seto

Studied protease inhibitors and developed a novel enzymatic assay for screening catalysts for asymmetric reactions

- Optimized a novel class of protease inhibitors based on a cyclohexanone core
- Developed a protocol for the synthesis of cyclohexanone-based protease inhibitors on solid support.
- Designed and synthesized a 400-member library of these cyclohexanone inhibitors on solid support.
- Developed an enzymatic assay for high-throughput screening of catalysts for asymmetric reactions (see EMDee publication below).
- Developed methodology to conduct assays in a 384 well format to assess inhibition constants for a library of peptidomimetic compounds against various proteases such as cathepsin B, plasmin, papain, trypsin, thrombin and kallikrein
- Monitored reactions by TLC, IR, ^{1}H NMR, ^{13}C NMR, HPLC. Purification by flash chromatography, crystallization, distillation, separation of diastereomers by HPLC and enantiomers by both chiral-GC and chiral-HPLC. Analysis of final compounds ^{1}H NMR, ^{13}C NMR, 2D NMR and MS. Proficient with enzymatic assays and jell electrophoresis.

EDUCATION

Brown University Providence RI. **6/01/96 – 2/12/02**

Ph. D., Chemistry February 2002, Advisor: Prof.Christopher T. Seto

- Thesis Title: The Development of A New Class of Protease Inhibitors and EMDee: A New High-Throughput Enzymatic Method For The Determination of Enantiomeric Excess

Rhode Island College, Providence, RI **9/01/92 - 5/01/96**

BA., Chemistry with a minor in Biology; Awarded Excellence in Organic Chemistry by the American Polymer Society.

SKILLS AND TECHNIQUES

- **Expert Witness Consulting**: Report writing, Deposition experience and pre-trial preparation experience.
- **Medicinal Chemistry**: Discovered multiple clinical candidates
- **Drug Formulation**: Developed stable formulations from hundreds of drugs for preclinical testing.

- **Synthetic Organic Chemistry:** Extensive work with tetracycline natural products pioneering mild reaction conditions suitable for this class of compounds. Cross couplings, transition metal catalysts, formylation, Iodination and peptide coupling reactions to name a few
- **Analytical:** TLC, IR, ^{1}H NMR, ^{13}C NMR, 2D NMR, HPLC and LCMS.
- **Purification:** Analytical and preparative HPLC and Flash chromatography
- **Computer skills:** Microsoft word, Excel, PowerPoint, Photoshop

PATENTS/PUBLICATIONS

Paul Abato and Todd Bowser- **7-Disubstituted-Ph tetracycline compounds for the Treatment of SMA** From PCT Int. Appl (**2013**) WO 2013-US43363, Patent No.WO 2013181391, Priority Appl. No. US 2012-61653262.

"PTK-SMA2, **A novel splice-correcting tetracycline derivative, increases SMN protein expression and significantly improves survival in Type I SMA mice**." Paul Abato, Francine Jodelka, Paul Higgins, Jie-Zhang Hoover, Kevin Klausner, Caroline Dudley, Juan Du, Sujatha Kumar, Michelle Hastings and Todd Bowser. Poster presented at the 2012 Annual Families of Spinal Muscular Atrophy meeting in Bloomington, MN, June 21-23rd **2012**.

Abato, Paul; Bowser, Todd; Higgins, Paul; Verma, Atul; Zhang-Hoover, Jie. **Tetracycline Compounds for the Treatment of Rheumatoid Arthritis and Related Methods of Treatment**. From PCT Int. Appl. (**2010**), WO 2010033939 A1 20100325.

Hastings ML, Berniac J, Liu YH, Abato P, Jodelka FM, Barthel L, Kumar S, Dudley C, Nelson M, Larson K, Edmonds J, Bowser T, Draper M, Higgins P, Krainer AR. **Tetracyclines that promote SMN2 exon 7 splicing as therapeutics for spinal muscular atrophy.** Sci Transl Med. (**2009)** Nov 4;1(5)

Abato, Paul; Assefa, Haregewein; Berniac, Joel; Bhatia, Beena; Bowser, Todd; Grier, Mark; Honeyman, Laura; Ismail, Mohamed; Kim, Oak K.; Nelson, Mark; Pan, Jingwen; Verma, Atul. **Substituted tetracycline compounds for treatment of bacterial infections and neoplasms.** PCT Int. Appl. (**2008**), 224 pp. CODEN: PIXXD2 WO 2008079339 A2 20080703 CAN 149:128685 CAPLUS

Abato, Paul; Assefa, Haregewein; Berniac, Joel; Bowser, Todd; Chen, Jackson; Grier, Mark; Honeyman, Laura **Preparation of 10-substituted tetracycline compounds as antibiotics**. PCT Int. Appl. (**2007**), WO 2007014154 A2 20070201.

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Nelson, Mark L.; Honeyman, Laura; Ismail, Mohamed; Bhatia, Beena; Verma, Atul K.; Warchol, Tadeusz; Bowser, Todd; Berniac, Joel; Mechiche, Rachid; Abato, Paul; Assefa, Haregewein. **Synthesis of diverse tetracycline derivatives via Pd-catalyzed reactions: Creation of a large collection of novel 3rd generation tetracyclines.** Abstracts of Papers, 231st ACS National Meeting, Atlanta, GA, United States, March 26-30, 2006 (**2006**), ORGN-454. CODEN: 69HYEC AN 2006:249168 CAPLUS

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Nelson, Mark L.; Ohemeng, Kwasi; Frechette, Roger; Abato, Paul; Assefa, Haregewein; Bandarage, Upul; Berniac, Joel; Bhatia, Beena; Chen, Jackson; Ismail, Mohamed Y.; Kim, Oak A.; Mathews, Jude; McIntyre, Laura; Nihlawi, Mohammed; Pearson, Andre; Reddy, Laxma; Sheahan, Paul; Sizensky, Emmanuelle; Tourigny, Justin; Verma, Atul K.; Viski, Peter; Warchol, Tadeusz. **Preparation of substituted tetracycline compounds for the treatment of bacterial infections and neoplasms.** PCT Int. Appl. (**2003**), 118 pp. CODEN: PIXXD2 WO 2003079984 A2 20031002 CAN 139:292094 AN 2003:777531 CAPLUS

Paul Abato, Courtney M. Yuen, Jeanne Y. Cubanski, and Christopher T. Seto **Inhibitors of Plasmin that Extend into Both the S and S' Binding Sites: Cooperative Interactions Between S1 and S2.** *JOC.* **2002**, *67*(4), 1184-1191.

Paul Abato and Christopher T. **EMDee: An Enzymatic Method for Determining Enantiomeric Excess.** Seto. *J. Am. Chem. Soc.* **2001**, *123*, 9206-9207.

Paul Abato, Jeffrey L. Conroy, and Christopher T. Seto. **Combinatorial Library of Serine and Cysteine Protease Inhibitors that Interact with Both the S and S' Binding Sites.** *J. Med. Chem.* **1999**, *42*, 4001-4009.

Jeffrey L. Conroy, Paul Abato, Mousumi Ghosh, Mariana I. Austermuhle, Michel R. Kiefer, and Christopher T. Seto**. Synthesis of Cyclohexanone-Based Cathepsin B Inhibitors that Interact with Both the S and S' Binding Sites.,** *Tetrahedron Lett*. **1998**, *39*, 8253-8255.