Bradley T. Wyman, Ph.D.

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Objective

To improve human health and wellbeing by translating ideas into effective diagnostics or therapeutic treatments.

Experience

CEO

OThree Consulting LLC, Vineyard, UT

8/15-present

- Helping biotechnology and pharmaceutical companies advance their ideas into life impacting solutions for patients. Clients range from small startup companies to major pharmaceutical companies.
- Conducted due diligence on behalf of investors to evaluate novel technologies for product development. Created comprehensive business plans including proposed paths for: technology development, validation, regulatory approval, technical and business derisking, company structure and financing. Recommendations were used to make final investment decisions.
- Conducted business development to win new opportunities for my client by leveraging my network and facilitating introductions. Coauthored work proposals to help clients win new business.
- Helped a client build business by developing and implementing an electronic media strategy to
 promote the client's internet presence. Made recommendations for developing their website and
 their presence on LinkedIn, Facebook, Twitter, Google+ and YouTube. Also, developed a strategy
 for blogging and publications.
- Developed biomarker strategies and tactical plans in the areas of immuno-oncology, osteoarthritis
 and pulmonary imaging. Conducted literature searches to evaluate optimal technologies and to
 make technical recommendations for biomarker development plans and clinical study endpoints.
 Facilitated introductions to key opinion leaders.
- Generated critical study documentation including protocols, FDA annual reports, clinical study reports (CSR) and preclinical technical reports.
- Analyzed data using Matlab and Excel to mine for trends and confounders in study and preclinical data ressults. Based on the analysis, made recommendations for the next drug study designs.

Chief Scientific Officer (CSO)

BodyQuant Imaging

7/16-4/17

- BodyQuant Imaging is a technology start-up that enables innovation and commercialization of image-derived biomarkers to support precision medicine, personalized wellness and population health applications through evidence based medicine.
- Executive responsibilities include: Identifying and evaluating technology options, establishing and implementing development strategies for technologies showing greatest promise for patient benefit, and being the chief technical representative in promoting BodyQuant's technologies and services to potential investors.

V.P. Clinical Development

ImaginAb, Inglewood, CA

5/14-7/15

- As an Executive Team member, maximized the shareholder return by delivering the corporate
 objectives to advance a portfolio of PET radiolabeled molecular antibody fragments for the
 detection of cancer and immuno-oncology targets. Specific responsibilities included oversight of
 the international preclinical imaging and clinical teams.
- Successfully transitioned the company from a startup stage to a stable growth stage company by implementing Target Asset Profile and Project Management systems. This resulted in tighter focus

- and prioritization of resources, better delineation of goals and reliable team delivery against those goals.
- Accelerated the value of the company's portfolio by developing and executing the phase 2 clinical program for ⁸⁹Zr-Df-IAB2M, a minibody directed against the prostate specific membrane antigen (PSMA) for the diagnosis and detection of metastatic prostate cancer. Responsible for study design, protocol development, vendor and site selection and management, study delivery, oversight of analysis and development of the clinical study reports (CSR). Designed the phase 2 program to balance regulatory, scientific, budgetary and corporate objectives.
- Led the team responsible for the successful writing and subsequent award of a \$3M non-dilutive Small Business Initiative Research (SBIR) grant.

Head, Functional and Structural Neuroimaging	Pfizer, Groton, CT	8/12 - 5/14
Director, Imaging, Molecular Medicine		8/08 - 8/12
Associate Director, Global Clinical Technology		8/05 - 8/08
Manager, Computational Medicine		1/04 - 8/05

- Lead the team responsible for designing and implementing biomarkers for the development of drugs in the neurodegenerative, psychiatric, and pain therapeutic areas including Alzheimer's disease, Parkinson's disease, cerebral amyloid angiopathy, post traumatic stress disorder (PTSD) Huntington's disease, depression, schizophrenia, fibromyalgia, and pain.
- Managed the technological development from concept through deployment of imaging biomarkers for enhancing clinical decision making during Phase I through Phase 4 drug testing. Actively managed programs in the Cardiovascular, Metabolic Disease, Inflammation, CNS, Pain, and Ophthalmology therapeutic areas.
- Responsible for developing and guiding direct reports, academic groups, contract research organizations (CROs) and external alliances to ensure the successful deployment of imaging in clinical studies for decision making. Creatively applied technical and managerial skills to implement strategies, resolve problems and ensure that the imaging endpoints successfully achieved the designed goals.
- Ensured the successful execution of the imaging for multiple early and late phase Alzheimer's disease studies including the phase 3 bapineuzumab program. Worked with key opinion leaders and CROs to ensure proper implementation of safety and efficacy biomarkers including CSF biomarkers, volumetric MRI, florbetapir (AV-45) and ¹¹C-PIB PET.
- Designed, developed and implemented imaging biomarker programs (X-ray and MRI) to support the new drug application (NDA) for tofacitinib (Xeljanz). Studies were conducted in rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis.
- Responsible for the technical execution of multi-year methods study for evaluating existing and exploratory biomarkers for osteoarthritis (approximately \$12M investment). Results from this study were applied to optimize the trial design of a disease modifying osteoarthritis drug.
- Generated cost savings across multiple projects from reducing custom development and creating efficiencies in image management. Led the team responsible for the design and implementation of the repository for storage of large datasets such as images, ECG, EEG, etc. Worked to build consensus across the organization to expand the utility of the system for multiple customers.
- Demonstrated drug safety issues in conjunction with two compound studies that led to a reformulation in one case and early termination in another case preventing the compounds from advancing to more expensive testing. This was accomplished by leading a team responsible for all aspects of implementation and execution of MRI liver fat quantification biomarker substudies.

<u>Director of Development</u> <u>Computerized Medical Systems, Champaign, IL</u> 1/03 - 1/04

- Increased revenue and market share by leading the successful release of several new and updated products. Responsible for development of all aspects of the Image Guidance Division's brachytherapy and external beam radiation treatment planning products for prostate cancer. Led the mechanical, electronic, software, and integration teams.
- Consistently delivered products on schedule and within project constraints by implementing

- rigorous program management methods. Previously, this division had a history of late product delivery.
- Helped expand markets into Europe and Japan by working with Manufacturing to achieve ISO 9001 certification and ensuring all products were developed in conformance with the CE mark regulations and Medical Device Directive (MDD). Opened new U.S. markets by working with Regulatory to obtain 510(k) clearance for new products.
- Significantly improved team effectiveness through process improvement. Increased team visibility and effectiveness by establishing clear and effective communication channels. Increased productivity by automating time consuming tasks and streamlining Quality System Regulation (QSR) processes. Generated better products by improving the requirements gathering process to capture customer needs and to effectively translate them into product features.
- Successfully led the transfer of new products to Manufacturing. Responsible for managing the manufacturing engineering team and ensuring that products were released and produced under Good Manufacturing Practices (GMP).

Senior Research Scientist (Manager)

Insightful Corp., Seattle, WA

4/02 - 1/03 11/00 - 4/02

- **Research Scientist**
- Created new markets by solving unmet customer needs by leading the Medical Imaging Group in the research and development of enabling medical imaging technologies for the next generation of products. Responsible for setting the group's vision (2 direct reports, 4 indirect reports plus numerous external academic, clinical and regulatory contractors).
- Significantly reduced the company's financial outlay for new product development through successful submission of several research contracts and grants. Funding sources included SBIR grants through the National Institute of Health (NIH) and contracts through the National Library of Medicine. Responsible for managing and allocating the \$1.4 million budget.
- Implemented and validated advanced image processing algorithms for the National Library of Medicine's (NLM) ITK Toolkit. The ITK Toolkit is a generalized library of sophisticated image segmentation and registration modules written in C++ that runs on multiple platforms (Windows, Linux, and Solaris).
- Responsible for the FDA 510(k) submission for a class II medical device. Coordinated the efforts of the entire team to produce the application and received approval of all features ahead of the planned product release.
- Served as the Quality Manager responsible for the writing of the quality manual as well as the development, implementation and maintenance of the QSR required for FDA compliance. Developed and implemented a quality system based on the FDA recognized standards AAMI SW68 ("Medical Device Software—Software Life Cycle Processes") and AAMI 14971 ("Medical Devices—Application of Risk Management to Medical Devices").

Senior Research Scientist, MRI

Confirma Inc., Kirkland, WA

9/98 - 9/00

- Developed, implemented and validated image-processing algorithms for automatically segmenting tissues from multi-parametric MRI acquisitions. This technology was developed to improve the physician's ability to locate tumors from MRI.
- Validated the research premises and system performance by leading definitive multi-site animal MRI studies. The studies confirmed that the device performed significantly better than previous methods and was used in the Pre-Market Application (PMA) submission. Based on this data, specific changes were made which further improved the product performance.
- Supported preparation of a class III modular PMA for FDA submission including descriptions of the preclinical trial results and the product technical specifications.

Ph.D. Research Johns Hopkins University, Medical Imaging Lab 9/93 - 9/98

Researched the effects of pacing on heart mechanics using MRI tagging on a canine model. Created mathematical models of heart mechanics from the MR images to evaluate heart physiology under various pacing protocols. These techniques were transferred clinically to non-invasively select the optimal pacing sites in patients with dilated cardiomyopathy

Member of Technical Staff AT&T Bell Laboratories, Naperville, IL 7/88 - 9/93

• Ported automatic speech recognition (ASR) technology from research to develop new commercial applications using assembly and C.

Skills

- Current/Previous Programming Experience: MATLAB, UNIX, Windows, C/C++.
- Language Skills: Some French.
- Additional Education: University of Washington, Biomedical Regulatory Affairs (20 weeks) and Software Program Management, Development and Release (13 weeks).

Awards and Honors

• Elected Secretary/Program Director ISMRM MRI in Drug Development Study Section 2008-2010.

Education

- Ph.D. Biomedical Engineering, Johns Hopkins University, Baltimore, MD, 1999, Thesis: Mechanical Evaluation of the Paced Heart Using High-Resolution MR Tagged Imaging.
- M.S. Electrical Engineering, Northwestern University, Evanston, IL, 1991, Thesis: Optical Image Processing.
- B.S. Cum-Laude with Honors, Electrical Engineering with a math minor, Brigham Young University, Provo, UT, 1988.

Publications

Patents

- V. Chalana, S. Fogarasi, L. Ng, J. Oelund, S. Pathak, S. Racki, B. Sparks, B. Wyman, "System and Method for Mining Quantitative Information from Medical Images", <u>U.S. Patent No.</u> 7,158,692, Jan 2, 2007.
- B.T. Wyman, L. Ng, "A System and Method for Determining Convergence of Image Set Registration", <u>U.S. Patent 7,106,891</u>, Sept. 12, 2006.
- C.L. Stork, B.T. Wyman, "Convolution Filtering of Similarity Data for Visual Display of Enhanced Image", U.S. Patent No. 6,674,880, Jan. 6, 2004.
- M.A. Johnson, S.A. O'Brien, B.T. Wyman, "Voice Messaging System with Voice Activated Prompt Interrupt", <u>U.S. Patent No. 5,155,760</u>, Oct. 13, 1992.
- C.L. Stork, B.T. Wyman, "Dynamic Thresholding of Segmented Data Sets and Display of Similarity Values in a Similarity Image", Filed Nov. 2000.

Papers

- R. Vandenberghe, J.O. Rinne, M. Boada, S. Katayama, P. Scheltens, B. Vellas, M. Tuchman, A. Gass, J.B. Fiebach, D. Hill, K. Lobello, D. Li, T. McRae, P. Lucas, I. Evans, K. Booth, G. Luscan, B.T. Wyman, L. Hua, L. Yang, H.R. Brashear, R.S. Black, Bapineuzumab 3000 and 3001 Clinical Study Investigators, "Bapineuzumab for Mild to Moderate Alzheimer's Disease in Two Global, Randomized, Phase 3 Trials", Alzheimer's Research Therapy, May 2016.
- P.G. Conaghan, M. Østergaard, M.A. Bowes, C. Wu, T. Fuerst, D. van der Heijde, F. Irazoque-Palazuelos, O. Soto-Raices, P. Hrycaj, Z. Xie, R. Zhang, B.T. Wyman, J. D. Bradley, K. Soma, B. Wilkinson, "Comparing the Effects of Tofacitinib, Methotrexate and the Combination, on Bone Marrow Oedema, Synovitis and Bone Erosion in Methotrexate-Naïve, Early Active Rheumatoid Arthritis: Results of an Exploratory Randomised MRI Study Incorporating Semiquantitative and Quantitative Techniques", <u>Ann Rheum Dis</u>, 2016.
- G. Novak, N. Fox, S. Clegg, C. Nielsen, S. Einstein, Y. Lu, I.C. Tudor, K. Gregg, J. Di, P. Collins, B.T. Wyman, E. Yuen, M. Grundman, H.R. Brashear, E. Liu, "Changes in Brain Volume with Bapineuzumab in Mild to Moderate Alzheimer's Disease", <u>J. Alzheimer's Disease</u>, 2016, p. 1123-34.
- B.L. Klaasens, H.C. van Gorsel, N. Khalili-Mahani, J. van der Grond, B.T. Wyman, B. Whitcher, S.A. Rombouts, J.M. van Gerven, "Single-Dose Serotonergic Stimulation Shows Widespread Effects on Functional Brain Connectivity", <u>Neuroimage</u>, Nov. 2015, p. 440-450.
- E. Liu, M.E. Schmidt, R. Margolin, R. Sperling, R. Koeppe, N.S. Mason, W.E. Klunk, C.A. Mathis, S. Salloway, N.C. Fox, D.L. Hill, A.S. Les, P. Collins, K.M. Gregg, J. Di, Y. Lu, I.C. Tudor, B.T. Wyman, K. Booth, S. Broome, E. Yuen, M. Grundman, H.R. Brashear; Bapineuzumab 301 and 302 Clinical Trial Investigators, "Amyloid-β 11C-PiB-PET Imaging Results from 2 Randomized Bapineuzumab Phase 3 AD Trials", Neurology, Aug. 2015, p. 692-700.
- J. Sun, X.Q. Zhao, N. Balu, D.S. Hippe, T.S. Hatsukami, D.A. Isquith, K. Yamada, M.B. Neradilek, G. Canton, Y. Xue, J.L. Fleg, P. Desvigne-Nickens, M.T. Klimas, R.J. Padley, M.T. Vassileva, B.T. Wyman, C. Yuan, "Carotid Magnetic Resonance Imaging for Monitoring

- Atherosclerotic Plaque Progression: A Multicenter Reproducibility Study", <u>Int J.</u> <u>Cardiovascular Imaging</u>, Jan. 2015, p. 95-103.
- K. Subburaj, R.B. Souza, B.T. Wyman, M-P Hellio Le Graverand, , X. Li, T.M. Link, S. Majumdar, "Changes in MR Relaxation Times of the Meniscus with Acute Loading: An In Vivo Pilot Study in Knee Osteoarthritis", <u>J. Magnetic Resonance Imaging</u>, Feb. 2015, p. 536-543.
- M. Marsh, R.B. Souza, B.T. Wyman, M-P Hellio Le Graverand, K. Subburaj, T.M. Link, S. Majumdar, "Differences Between X-ray and MRI-Determined Cartilage Thickness in Weight-Bearing and Non-Weight-Bearing Conditions", <u>Osteoarthritis and Cartilage</u>, Dec. 2013, p. 1876-1885.
- S. Cotofana, B.T. Wyman, O. Benichou, D. Dreher, M. Nevitt, J. Gardiner, W. Wirth, W. Hitzl, C.K. Kwoh, F. Eckstein, R.B. Frobell for OAI Investigators Group, "Relationship Between Knee Pain and the Presence, Location, Size and Phenotype of Femorotibial Denuded Areas of Subchondral Bone as Visualized by MRI", Osteoarthritis and Cartilage, Sept. 2013, p. 1214-1222.
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- D. van der Heijde, Y. Tanaka, R. Fleischmann, E. Ekystone, J. Kremer, C. Zerbini, M.H. Cardiel, S. Cohen, P. Nash, Y.W. Song, D. Tegzova, B.T. Wyman, D. Gruben, B. Enda, G. Wallenstein, S. Krishnaswami, S.H. Zwillich, J.D. Bradley, C.A. Connell, ORAL Scan Investigators, "Tofacitinib (CP-690, 550) in Patients with Rheumatoid Arthritis Receiving Methotrexate Twelve-Month data from a Twenty-Four-Month Phase III Randomized Radiographic Study", <u>Arthritis & Rheumatism</u>, Mar. 2013, p. 559-570.
- B.M. Jedynak, A. Lang, B. Liu, E. Katz, Y. Zhang, B.T. Wyman, D. Raunig, C.P. Jedynak, B. Caffo, J.L. Prince, "A Computational Neurodegenerative Disease Progression Score: Method and Results with the Alzheimer's Disease Neuroimaging Initiative Cohort", NeuroImage, Nov. 2012, p. 1478-1486.
- C. Stehling, R.B. Souza, M.P. Hellio Le Graverand, B.T. Wyman, X. Li, S. Majumdar, T.M. Link, "Loading of the Knee During 3.0T MRI is Associated with Significantly Increased Medial Meniscus Extrusion in Mild and Moderate Osteoarthritis", <u>Eur J Radiol</u>, Aug. 2012, p. 1839-1845.
- K. Subburaj, R.B. Souza, C. Stehling, B.T. Wyman, M.P. Hellio Le Graverand, T.M. Link, X. Li, S. Majumdar, "Association of MR Relaxation and Cartilage Deformation in Knee Osteoarthritis", J Orthop Res, Jun. 2012, p. 919-926.
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- F. Eckstein, M.P. Hellio Le Graverand, H.C. Charles, D.J. Hunter, V.B. Kraus, T. Sunyer, O. Nemirovskyi, B.T. Wyman, R. Buck, A9001140 Investigators, "Clinical, Radiographic, Molecular and MRI-based predictors of Cartilage Loss in Knee Osteoarthritis", <u>Ann Rheum Dis</u>, Jul 2011, p. 1223-1230.
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- W. Wirth, S. Larroque, R.Y. Davies, M. Nevitt, A. Gimona, F. Baribaud, J.H. Lee, O. Benichou, B.T. Wyman, M. Hudelmaier, S. Maschek, F. Eckstein, "Comparison of 1-Year vs. 2-Year Change in Regional Cartilage Thickness in Osteoarthritis Results from 346 Participants from the Osteoarthritis Initiative", Osteoarthritis Cartilage, Jan. 2011, p. 74-83.
- R.B. Souza, C. Stehling, B.T. Wyman, M-P Hellio Le Graverand, X. Li, T.M. Link, S. Majumdar, "The Effects of Acute Loading on T1 rho and T2 Relaxation Times of Tibiofemoral Articular Cartilage", Osteoarthritis Cartilage, Dec. 2010, p. 1557-63.
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- E. Vignon, K.D. Brandt, C. Mercier, M. Hochberg, D. Hunter, S. Mazzuca, K. Powell, B. Wyman, M-P Hellio Le Graverand, "Alignment of the Medial Tibial Plateau Affects the Rate of Joint Space Narrowing in the Osteoarthritic Knee", Osteoarthritis Cartilage, Nov. 2010, p. 1436-40.
- M. Hudelmaier, W. Wirth, B. Wehr, V. Kraus, B.T. Wyman, M-P Hellio Le Graverand, F. Eckstein, "Femorotibial Cartilage Morphology: Reproducibility of Different Metrics and Femoral Regions, and Sensitivity to Change in Disease", <u>Cells Tissues Organs</u>, July 2010, p. 340-50.
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- W. Wirth, R.B. Frobell, R.B. Souza, X. Li, B.T. Wyman, M-P Hellio Le Graverand, T.M. Link, S. Majumdar, F. Eckstein, "A three-Dimensional Quantitative Method to Measure Meniscus Shape, Position, and Signal Intensity Using MR Images: A Pilot Study and Preliminary Results in Knee Osteoarthritis", <u>Magnetic Resonance in Medicine</u>, May. 2010, p. 1162-71.
- R.J. Buck, B.T. Wyman, M-P Hellio Le Graverand, W. Wirth, F. Eckstein, "An Efficient Subset of Morphological Measures for Articular Cartilage in the Healthy and Diseased Human Knee", <u>Magnetic Resonance in Medicine</u>, Mar. 2010, p. 680-90.

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 F. Baribaud, A Gimona M. Hudelmaier, S. Cotofana, F. Eckstein, "Presence, Location, Type
 and Size of Denuded Areas of Subchondral Bone in the Knee as a Function of Radiographic
 Stage of OA Data from the OA Initiative", Osteoarthritis Cartilage, May. 2010. p. 668-76.
- R.J. Buck, B.T. Wyman, M-P Hellio Le Graverand, M. Hudelmaier, W. Wirth, F. Eckstein, "Osteoarthritis may not be a One-Way-Road of Cartilage Loss--Comparison of Spatial Patterns of Cartilage Change Between Osteoarthritic and Healthy Knees", (Selected as paper of the month), Osteoarthritis Cartilage, Mar. 2010, p. 329-35.
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- D.J. Hunter, R.J. Buck, E. Vignon, E. Eckstein, K. Brandt, S.A. Mazzuca, B.T. Wyman, I. Otterness, M-P Hellio Le Graverand, "Relation of Regional Articular Cartilage Morphometry and Meniscal Position by MRI to Joint Space Width in Knee Radiographs", Osteoarthritis Cartilage, Sept 2009, p. 1170-6.
- M-P Hellio Le Graverand, R.J. Buck, B.T. Wyman, E. Vignon, S.A. Mazzuca, K. Brandt, M. Piperno, H.C. Charles, M. Hudelmaier, D.J. Hunter, C. Jackson, V.B. Kraus, T.M. Link, S. Majumdar, P.V. Prasad, T.J. Schnitzer, A. Vaz, W. Wirth, F. Eckstein, "Subregional Femorotibial Cartilage Morphology in Women—Comparison Between Healthy Controls and Participants with Different Grades of Radiographic Knee Osteoarthritis", Osteoarthritis Cartilage, Sept 2009, p. 1177-85.
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