



UNIVERSITY OF HAWAI'I
CANCER CENTER

Population Sciences in the Pacific Program - Cancer Epidemiology
Research Seminar Series

**“Women’s Health: ER Positive Breast Cancer-One
disease, two molecules, two approaches to treatment”**

(Wednesday) October 17, 2018
12 Noon – 1:00 pm



Gary Hattersley, Ph.D.

*Chief Scientific Officer
Senior Vice President
Radius Health, Inc.
Waltham, MA*

**University of Hawai'i Cancer Center
701 Ilalo Street
Sullivan Conference Center**

Light refreshments to follow

GARY HATTERSLEY, PHD

EXECUTIVE SUMMARY

Experienced professional with over 30 years research and development experience in women's health, oncology and musculoskeletal diseases including 25 years of pharmaceutical/biotechnology experience. Extensive leadership experience encompassing early stage drug discovery and research, clinical development from Phase 1 to Phase 3, and post-marketing life cycle management. Demonstrated ability in managing complex projects, working effectively in cross-functional interdisciplinary program teams, and implementing effective strategies leveraging internal and external resources. Supported corporate financing (private and public) with over \$1bn raised, including a successful IPO in 2014. Prominent role for external engagement, including scientific engagement, speaker grand rounds, webcasts (JPM, ASCO, SABCS, ASBMR), earnings calls, investor/analyst events and business development support.

PROFESSIONAL EXPERIENCE

RADIUS HEALTH INC, WALTHAM, USA

SENIOR VICE PRESIDENT, CHIEF SCIENTIFIC OFFICER

2013 TO PRESENT

- Responsible for Radius' oncology and women's health R&D portfolio.
- Accountable for establishing the company's strategic R&D roadmap, including early stage, late stage and life cycle management activities.
- Leads key R&D functions including research, clinical development and operations, medical writing, biometrics and program strategy/management.
- Supported first cycle FDA approval of TYMLOS in the US
- Established post-approval life cycle management program for TYMLOS, including initiation of a Phase 3 male osteoporosis bridging study and development of a non-injectable route of administration, with FDA alignment on Phase 3 bridging studies.
- Advancement of elacestrant, an estrogen receptor targeted small molecule, to a pivotal Phase 3 randomized comparator controlled trial in 2L/3L ER+ metastatic breast cancer.
- Initiation of first in human clinical study with an androgen receptor target small molecule in a novel genetically defined hormone receptor positive breast cancer population.
- Discovery of a new small molecule lead series with potential application in the treatment of endocrine driven cancers (ovarian, endometrial and breast).
- Supported global regulatory interactions for the R&D portfolio including receiving fast-track designation for elacestrant in metastatic breast cancer.
- Core member of Radius' executive leadership team.

SENIOR VICE PRESIDENT, PRECLINICAL DEVELOPMENT

2010 TO 2013

- Leadership role for R&D operations and strategic management.
- Supported the clinical and nonclinical development of abaloparatide including NDA enabling nonclinical pharmacology and safety program.
- Responsible for the continued development of a non-injectable delivery technology in collaboration with 3M.
- Lead all external scientific communications.

VICE PRESIDENT, BIOLOGY

2008 TO 2010

- Managed both external and internal R&D activities, including contract research encompassing pharmacology, nonclinical safety, and CMC.

- Supported selection and development of a novel small molecule androgen receptor modulator with potential utility in women's health, diseases of aging and oncology.
- Supported nonclinical safety studies and clinical development for abaloparatide in postmenopausal osteoporosis.
- Led the evaluation and selection of drug delivery technologies for pipeline programs.

SENIOR DIRECTOR OF RESEARCH 2005 TO 2007

- Led the repositioning of an in licensed small molecule for a new indication (in women's health), including pharmacology, nonclinical safety, manufacturing, and formulation development, leading to an IMPD submission, and subsequent successful Phase II clinical proof of concept study.

DIRECTOR, BIOLOGY AND PHARMACOLOGY 2003 TO 2005

- Led a drug discovery program to develop novel therapeutic agents that activate steroid hormone receptor mediated non-genotropic signaling with potential utility in musculoskeletal disorders.

MILLENNIUM PHARMACEUTICALS, CAMBRIDGE, USA

SENIOR SCIENTIST, METABOLIC DISEASE BIOLOGY 2000 TO 2003.

- Led drug discovery including identification and validation of novel druggable targets and evaluation of NCEs
- Development of drug repositioning technology platform (spun out to GeneLogic Inc)

WYETH RESEARCH, FORMERLY GENETICS INSTITUTE, CAMBRIDGE, USA

PRINCIPLE SCIENTIST/STAFF SCIENTIST/POSTDOCTORAL FELLOW 1993 TO 2000

- Cloning of bone morphogenetic protein and evaluation of therapeutic potential in musculoskeletal diseases

ST GEORGE'S HOSPITAL MEDICAL SCHOOL, LONDON, UK

RESEARCH ASSISTANT, DEPARTMENT OF HISTOPATHOLOGY 1987 TO 1993

- Experimental research into the mechanisms by which osteoclast formation and osteoclastic bone resorption is regulated by hematopoietic modulating cytokines

EDUCATION

PHD

St. George's Hospital Medical School, London, United Kingdom

BSc

University of Hull, United Kingdom

PUBLICATIONS

Bone HG, Cosman F, Miller PD, Williams GC, Hattersley G, Hu MY, Fitzpatrick LA, Mitlak B, Papapoulos S, Rizzoli R, Dore RK, Bilezikian JP, Saag KG. ACTIVEExtend: 24 Months of Alendronate after 18 Months of Abaloparatide or Placebo for Postmenopausal Osteoporosis (2018). J Clin Endocrinol Metab. May 24. doi: 10.1210/jc.2018-00163

McClung MR, Harvey NC, Fitzpatrick LA, Miller PD, Hattersley G, Wang Y, Cosman F. Effects of abaloparatide on bone mineral density and risk of fracture in postmenopausal women aged 80 years or older with osteoporosis (2018). Menopause. 2018 Feb 16. doi: 10.1097

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Doyle N, Varela A, Haile S, Guldborg R, Kostenuik PJ, Ominsky MS, Smith SY, Hattersley G. Abaloparatide, a novel PTH receptor agonist, increased bone mass and strength in ovariectomized cynomolgus monkeys by increasing bone formation without increasing bone resorption" (2018). *Osteoporos Int.* 29(3):685-697.

Bilezikian JP, Hattersley G, Fitzpatrick LA, Harris AG, Shevroja E, Banks K, Leder BZ, Zanchetta JR, Hans D. "Abaloparatide-SC improves trabecular microarchitecture as assessed by trabecular bone score (TBS): a 24-week randomized clinical trial" (2018) *Osteoporos Int.* 29(2):323-328.

Yu Z, He S, Wang D, Patel HK, Miller CP, Brown JL, Hattersley G, Saeh JC "Selective Androgen Receptor Modulator RAD140 Inhibits the Growth of Androgen/Estrogen Receptor-Positive Breast Cancer Models with a Distinct Mechanism of Action" (2017) *Clin Cancer Res* 23(24):7608-7620.

Bihani T, Patel HK, Arlt H, Tao N, Jiang H, Brown JL, Purandare DM, Hattersley G, Garner F. "Elacestrant (RAD1901), a Selective Estrogen Receptor Degradable (SERD), Has Antitumor Activity in Multiple ER+ Breast Cancer Patient-derived Xenograft Models" (2017) *Clin Cancer Res* 23(16):4793-4804.

Jollette J, Attalla B, Varela A, Long GG, Mellal N, Trimm S, Smith SY, Ominsky MS, Hattersley G "Comparing the incidence of bone tumors in rats chronically exposed to the selective PTH type 1 receptor agonist abaloparatide or PTH(1-34)" (2017) *Regul Toxicol Pharmacol* 86:356-365.

Cosman F, Miller PD, Williams GC, Hattersley G, Hu MY, Valter I, Fitzpatrick LA, Riis BJ, Christiansen C, Bilezikian JP, Black D "Eighteen Months of Treatment With Subcutaneous Abaloparatide Followed by 6 Months of Treatment With Alendronate in Postmenopausal Women With Osteoporosis: Results of the ACTIVEExtend Trial" (2017) *Mayo Clin Proc* 92(2):200-210.

Varela A, Chouinard L, Lesage E, Guldborg R, Smith SY, Kostenuik PJ, Hattersley G "One year of abaloparatide, a selective peptide activator of the PTH1 receptor, increased bone mass and strength in ovariectomized rats" (2017) *Bone* 95:143-150.

Varela A, Chouinard L, Lesage E, Smith SY, Hattersley G "One Year of Abaloparatide, a Selective Activator of the PTH1 Receptor, Increased Bone Formation and Bone Mass in Osteopenic Ovariectomized Rats Without Increasing Bone Resorption" (2017) *J Bone Miner Res* 32(1):24-33.

Cosman F, Hattersley G, Hu MY, Williams GC, Fitzpatrick LA, Black DM "Effects of Abaloparatide-SC on Fractures and Bone Mineral Density in Subgroups of Postmenopausal Women With Osteoporosis and Varying Baseline Risk Factors" (2017) *J Bone Miner Res* 32(1):17-23

Hattersley G, Harris AG, Simon JA, Constantine GD "Clinical investigation of RAD1901, a novel estrogen receptor ligand, for the treatment of postmenopausal vasomotor symptoms: a phase 2 randomized, placebo-controlled, double-blind, dose-ranging, proof-of-concept trial" *Menopause* 24(1):92-99.

Miller PD, Hattersley G, Riis BJ, Williams GC, Lau E, Russo LA, Alexandersen P, Zerbini CA, Hu MY, Harris AG, Fitzpatrick LA, Cosman F, Christiansen C "Effect of Abaloparatide vs Placebo on New Vertebral Fractures in Postmenopausal Women With Osteoporosis: A Randomized Clinical Trial" (2016) *JAMA* 316(7):722-733.

Bahar H, Gallacher K, Downall J, Nelson CA, Shomali M, Hattersley G "Six Weeks of Daily Abaloparatide Treatment Increased Vertebral and Femoral Bone Mineral Density, Microarchitecture and Strength in Ovariectomized Osteopenic Rats" (2016) *Calcif Tissue Int* 99(5):489-499.

Hattersley G, T Dean, BA Corbin, H Bahar and TJ Gardella. "Binding Selectivity of Abaloparatide for PTH-Type-1-Receptor Conformations and Effects on Downstream Signaling" (2016). *Endocrinology* 157(1):141-149.

Garner, F, M Shomali, D Paquin, CR Lyttle and G Hattersley. "RAD1901, A Novel, Orally Bioavailable Selective Estrogen Receptor Degradable that Demonstrates Antitumor Activity in Breast Cancer Xenograft Models" (2015). *Anti-Cancer Drugs* 26(9):948-956

Hattersley G, JP Bilezikian, J Guerriero, KM Kumar, JR Zanchetta, CR Lyttle and L St L O'Dea. "Effects of BA058, A Human Parathyroid Hormone-related Peptide Analog, on Bone Mineral Density in Postmenopausal Women with Osteoporosis" (2015). *J Clin Endo and Metab* 100(2):697-706.

Jayaraman A, A Christensen, VA Moser, RS Vest, CP Miller, G Hattersley and C Christian. "Selective androgen receptor modulator RAD140 is neuroprotective in cultured neurons and kainate-lesioned male rats" (2014). *Endocrinology* 155(4):1398-1406.

Miller, CP, M Shomali, CR Lyttle, L O'Dea, H Herendeen, K Gallacher, D Paquin, DR Compton, B Sahoo, SA Kerrigan, MS Burge, M Nickels, JL Green, JA Katzenellenbogen, A Tchesnokov and G Hattersley. "Design, Synthesis, and preclinical characterization of the selective androgen receptor modulator (SARM) RAD140" (2011). *ACS Med Chem Lett.* 2:124-129.

Miller, CP, P Bhaket, N Muthukaman, CR Lyttle, M Shomali, K Gallacher, C Slocum and G Hattersley. "Synthesis of potent, substituted carbazoles as selective androgen receptor modulators (SARMs)" (2010). *Bioorg Med Chem Lett.* 20: 7516-7520.

Zeng C, SA Kerrigan, JA Katzenellenbogen, C Slocum, K Gallacher, M Shomali, CR Lyttle, G Hattersley and CP Miller. "Efficient synthesis of (2R,3S)-2-amino-3-(benzyloxy)-4,4,4-trifluorobutanoic acid (4,4,4-trifluoro-OBn-d-allothreonine)" (2010). *Tetrahedron Letters.* 51: 5361-5363.

Thomopoulos, S, G Hattersley, V Rosen, ML Mertens, L Galatz, GR Williams and L Soslowsky. "The localized expression of extracellular matrix components in healing tendon insertion sites: An in situ hybridization study" (2002). *J Ortho Research*. 20:454-463.

Ladher, RK, VL Church, S Allen, L Robson, NA Brown, G Hattersley, V Rosen, FP Luyten, L Dale and PH Francis-West. "Cloning and expression of the Wnt antagonists SFRP-2 and FRZB during chick development" (2000). *Development*. 218: 183-198.

Gamer, LW, NM Wolfman, AJ Celeste, G Hattersley, R Hewick and V Rosen. "A novel BMP expressed in developing mouse limb, spinal cord and tail bud is a potent mesoderm inducer in *Xenopus* embryos" (1999). *Dev Biol* 208: 222-232.

Wolfman, NM, G Hattersley, K Cox, AJ Celeste, R Nelson, N Yamaji, JL Dube, E DiBlasio-Smith, J Nove, JJ Song, JM Wozney and V Rosen. "Ectopic induction of tendon and ligament in rats by GDFs 5, 6 and 7, members of the TGF β gene family" (1997). *J Clin Invest*. 100:321-330.

Rosen, V, K Cox and G Hattersley. "Bone Morphogenetic Proteins" (1996). In *Principles of Bone Biology*. Ed Bilezikian, Raisz and Rodan. Academic Press.

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Hattersley, G and TJ Chambers. "Bones need SOFAs" (1992). *Current Biology* 2:141-142.

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Brown, JA, CJ Gray, G Hattersley and J Robinson. "Prostaglandins in the kidney, urinary bladder and gills of the Rainbow Trout and European Eel adapted to freshwater and saltwater" (1991). *Gen Comp Endocrinology* 84:328-334.

Hattersley, G, J Owens and TJ Chambers. "Effects of macrophage colony stimulating factor on the formation of osteoclasts and macrophages from op/op hemopoietic tissue in vitro" (1991). *Biochem Biophys Res Comm* 177:526-531.

Hattersley, G and TJ Chambers. "The effects of transforming growth factor beta 1 on the regulation of osteoclastic development and function" (1991). *J Bone and Mineral Res* 6:165-172.

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