Charles H. Reynolds
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Experience

2011-present Founder, Gfree Bio, LLC

- Gfree develops and delivers modeling, informatics, and structure-based design capabilities for emerging biotech companies.
- Acting Chief Scientific Officer, PPI Mimics, LLC (2013-2015), and Principal Investigator for NIH STTR Phase I program.
- Other collaborations include: NIH SBIR The Wistar Institute; multiple NIH SBIRs Phelix Therapeutics; NIH STTR Fox Chase Chemical Diversity and Drexel College of Medicine.
- Many successful research/consulting programs for a range of biotech companies.

2009-present Director (Industry Advisory Board) QuantumBio Inc.

- Provide scientific and business development advice to senior management.

2010-2011 Senior Director and Head of Discovery Technologies, Ansaris

- Responsible for scientific computing, proprietary discovery technology, structural biology, and IT. Member of senior management team with significant business development responsibilities.

- Initiated a major update of core computational fragment-based drug design platform. Refocused technology to target small molecule ligands for protein-protein interactions. Updated and improved software (speed, efficiency, user-interface).

- Leadership role in identification and prosecution of an internal target that led to a significant pharma partnering opportunity.

- Executive management of major research collaboration with Novartis.

2000-2010 Research Fellow, Johnson & Johnson Pharmaceutical R&D

- Responsibilities included managing modeling and informatics research teams at the Spring House, PA and La Jolla, CA sites. Managed significant hardware and software budgets across multiple US sites.

- Teams under my direction provided critical support for progression of ten compounds to early development, three compounds to first in human, and one Phase-II candidate. Contributed to carisbamate NDA and European registration for Dacogen®.

- Led development of new discovery methodology at J&J including: informatics tools for fragment-based design, novel protocols for improved crystal-structure refinement, linear interaction energy approaches for ligand optimization, a similarity-based tool for scoring reagents for "drug-likeness," application of linear-scaling quantum calculations to analysis of protein structures, and structure-based ADME-Tox. The latter effort includes a published multi-state homology model for the hERG channel that was employed successfully in multiple discovery programs and was honored in 2008 as a most cited article by Elsevier.

- Migrated J&J Computer-Aided Drug Discovery (CADD) groups to linux-based clusters and workstations, and consolidated CADD software licenses across sites. This effort resulted in a significant improvement in computational capabilities while reducing the overall cost of high-performance computing.

- Member of the New Targets Evaluation Committee for drug discovery. Organized a series of global J&J CADD and structural-biology meetings. Initiated external research collaborations at Penn State, Yale, and the University of Florida. Coordinated J&J's first structural-biology collaboration with DeCode Biostructures (now Emerald).

1995-2000 Research Fellow, **1984-1994** Senior Scientist, Rohm and Haas (now Dow)

- Co-inventor of a new class of ergosterol biosynthesis inhibitor antifungals. Awarded the highest scientific award in the company (Otto Haas Award).

- Led an interdisciplinary team of a dozen scientists tasked with developing new drug therapies and diagnostic aids. This project resulted in a novel nanoparticle-based targeted contrast agent for MR imaging. Roles included developing the concept and selling it to R&D management, leading the team, establishing a collaboration with the University of Pennsylvania Medical School, and developing a market analysis in collaboration with Argonex (a biotechnology company that is now part of Millipore).

2014-present Editorial Advisory Board, ACS Medicinal Chemistry Letters

2013 J.T. Oden Faculty Fellow, ICES, The University of Texas at Austin

2010-present Adjunct Professor, Pennsylvania Drug Discovery Institute

2008-present Member, American Chemical Society Publications Committee

2007-present NIH study sections, BDMA, BCMB, IMST-10, IMST-11, NCI ZCA1

2006-2011 Scientific Advisory Board, Keystone Symposia

2006-2009 Councilor, American Chemical Society

1998-2006 Editorial Advisory Board, Journal of Molecular Graphics and Modeling

1998 Joint postdoctoral research supervisor, University of North Carolina at Chapel Hill

1996-1998 Joint graduate research supervisor, The Pennsylvania State University

1990 Adjunct Professor, The University of Pennsylvania

Additional Experience and Leadership Activities.
2015 National Academy of Sciences STTR program workshop; **2008** Co-organizer, first Keystone Symposium on computer-aided drug discovery; **2006-2009** Advisory Board for NSF sponsored science and math education initiative at Temple University (TU-SMART**);** **2007** Co-organizer, ACS Prospectives Meeting, Advances in Structure-Based Drug Discovery; **2007** Inaugural Keck Foundation Lecture, St. Edward's University**;** **2007** Lecturer, ACS computational chemistry short course**;** **2005** Organizer, ACS Prospectives Meeting, Advances in Structure-Based Drug Discovery; **1999-2000** Rohm and Haas Technology Center Coordinator for Life Sciences; **1998-2000** Membership Committee, ACS Computers in Chemistry Division; **1999** Co-taught a computational chemistry short course (Jan Term) at Austin College; **1997** Chair, ACS Computers in Chemistry Division; **1991-1995** Treasurer, ACS Computers in Chemistry Division; **1989** Faculty, QCPE course.

Education

1984 Ph.D. in Theoretical Organic Chemistry, The University of Texas at Austin, Austin, Texas. Supervisor: Michael J.S. Dewar.
1979 B.A. in Chemistry, Austin College, Sherman, Texas. Honors in Chemistry.

Management Training

2013 Kauffman Institute Entrepreneur Training Program
2002 Johnson & Johnson Management Fundamentals
2001 Johnson & Johnson Manager and the Law
1993 First-Line Leadership
1992 The Leadership Challenge

Awards

2015 Gfree Bio selected as a Kauffman Foundation FastTrac success story
2012 Distinguished Alumni Award, Austin College
2010 Fellow of the American Chemical Society
2007 Standards of Leadership Award, Johnson & Johnson
2007 Platinum Encore Award, Johnson & Johnson (Dacogen® registration in Europe)
2000 Johnson & Johnson Excellence in Science Award (four awarded company wide)
1987 Otto Haas Award, Rohm and Haas (highest award for scientific achievement).
1993 Marion Cox Award, Austin College; **1984** University of Texas Career Development Award; **1983** Robert A. Welch Foundation Pre-doctoral Fellowship, The University of Texas at Austin; **1978** P.S. Wharton Fellowship in chemistry, Austin College; **1978** National Science Foundation Undergraduate Research Scholarship, The University of Texas at Arlington; **1975-1979** Robert A. Welch Undergraduate Chemistry Scholarship.

Publications

Author of approximately 100 papers, chapters, books, and patents

Publications

Reynolds, Charles H. **Ligand efficiency metrics: why all the fuss?** Future Med. Chem. 2015, 7, 1363-1365.

Reynolds, Charles H., **Protein-ligand cocrystal structures: We can do better**, ACS Medicinal Chemistry Letters, 2014. (one of the most read papers in ACS Medicinal Chemistry Letters 2014)

Murray, Christopher W., Daniel A. Erlanson, Andrew L. Hopkins, György M. Keserü, Paul D. Leeson, David C. Rees, Charles H. Reynolds, and Nicola J. Richmond. **Validity of Ligand Efficiency Metrics**. ACS Medicinal Chemistry Letters (2014) 5, 2-5. (One of the most read papers in ACS Medicinal Chemistry Letters 2014)

Martha J. Kelly, Charles H. Reynolds, et al. **Discovery of 2-[3,5-Dichloro-4-(5-isopropyl-6-oxo-1,6-dihydropyridazin-3-yloxy)phenyl]-3,5-dioxo-2,3,4,5-tetrahydro[1,2,4]triazine-6-carbonitrile (MGL-3196), a Highly Selective Thyroid Hormone Receptor β Agonist in Clinical Trials for the Treatment of Dyslipidemia,** Journal of Medicinal Chemistry, 2014, 57, 3912-3923. DOI: 10.1021/jm4019299

Hopkins, A.L.; Keseru, G.M.; Leeson, P.D.; Rees, D.C.; Reynolds, C.H. **The role of ligand efficiency measures in drug discovery**, Nature Reviews Drug Discovery, 2014, 13, 105-121.

Reynolds, Charles, H., **Impact of computational structure-based methods on drug discovery**, Current Pharmaceutical Design, 2014, 20, 3380-3386. DOI: 10.2174/13816128202014052810553 2

Reynolds, Charles H.; Holloway, M. Katharine, **Thermodynamics of ligand binding and efficiency**, ACS Medicinal Chemistry Letters, (2011) 2, 433-437. *One of the top ten accessed papers in ACS Medicinal Chemistry Letters and the Journal of Medicinal Chemistry for 2011and 2012.*

Céline Schalk-Hihi, Carsten Schubert, Richard Alexander, Shariff Bayoumy, Jose C. Clemente, Ingrid Deckman, Renee L. DesJarlais, Keli C. Dzordzorme, Christopher M. Flores, Bruce Grasberger, James K. Kranz, Frank Lewandowski, Li Liu, Hongchang Ma, Diane Maguire, Mark J. Macielag, Mark E. McDonnell, Tara Mezzasalma Haarlander, Robyn Miller, Cindy Milligan, Charles Reynolds, Lawrence C. Kuo, **Crystal structure of a soluble form of human monoglyceride lipase in complex with an inhibitor at 1.35 Å resolution** Protein Science (April 2011) 20, 670–683.

Klon, Anthony E.; Konteatis, Zenon; Meshkat, Siavash N.; Zou, Jinming; Reynolds, Charles H. **Fragment and protein simulation methods in fragment based drug discovery**, Drug Devel. Res. (2011) 72, 1-8.

Yifang Huang, Eric D. Strobel, Chih Y. Ho, Charles H. Reynolds, Kelly A. Conway, Jennifer A. Piesvaux, Douglas E. Brenneman, George J. Yohrling, H. Moore Arnold, Daniel Rosenthal, Richard S. Alexander, Brett A. Tounge, Marc Mercken, Marc Vandermeeren, Michael H. Parker, Allen B. Reitz, Ellen W. Baxter, **Macrocyclic BACE inhibitors: Optimization of a micromolar hit to nanomolar leads**, Bioorganic & Medicinal Chemistry Letters, Volume 20, Issue 10, 15 May 2010, Pages 3158-3160.

Merz, Kenneth M.; Ringe, Dagmar; Reynolds, Charles H., Editors, **Drug design: ligand and structure based approaches**, Cambridge University Press, 2010.

Reynolds, Charles H. **Computer-aided drug design: A practical guide to protein-structure based modeling,** published in Drug design: ligand and structure based approaches, Cambridge University Press, K. M. Merz, D. Ringe, and C. H. Reynolds, editors, 2010.

Zhang, Xiaohua; Gibbs, Alan C.; Reynolds, Charles H.; Peters, Martin B.; Westerhoff, Lance M. **Quantum Mechanical Pairwise Decomposition Analysis of Protein Kinase B Inhibitors: Validating**

a New Tool for Guiding Drug Discovery. J. Chem. Inf. Model. (2010), 50, 651-661.

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Li, Jian; Reynolds, C. H. **A quantum mechanical approach to ligand binding: Calculation of ligand-protein binding affinities for stromelysin-1 (MMP-3) inhibitors**, Canadian Journal of Chemistry, (2009), 87, 1480-1484.

Reitz, Allen B.; Smith, Garry R.; Tounge, Brett A.; Reynolds, Charles H. **Hit Triage Using Efficiency Indices after Screening Compound Libraries in Drug Discovery.** Current Topics in Medicinal Chemistry (2009), 9, 1718-1724.

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Reynolds, Charles H.; Tounge, Brett A.; Bembenek, Scott D. **Ligand binding efficiency: trends, physical basis, and implications.** Journal of Medicinal Chemistry (2008), 51(8), 2432-2438.

Baxter, Ellen W.; Conway, Kelly A.; Kennis, Ludo; Bischoff, Francois; Mercken, Marc H.; De Winter, Hans L.; Reynolds, Charles H.; Tounge, Brett A.; Luo, Chi; Scott, Malcolm K.; Huang, Yifang; Braeken, Mirielle; Pieters, Serge M. A.; Berthelot, Didier J. C.; Masure, Stefan; Bruinzeel, Wouter D.; Jordan, Alfonzo D.; Parker, Michael H.; Boyd, Robert E.; Qu, Junya; Alexander, Richard S.; Brenneman, Douglas E.; Reitz, Allen B. **2-Amino-3,4-dihydroquinazolines as inhibitors of BACE-1 (β -site APP cleaving enzyme): use of structure based design to convert a micromolar hit into a nanomolar lead.** Journal of Medicinal Chemistry (2007), 50(18), 4261-4264. *One of the most accessed articles in JMC for 2007*.

Reynolds, Charles H.; Bembenek, Scott D.; Tounge, Brett A. **The role of molecular size in ligand efficiency.** Bioorganic & Medicinal Chemistry Letters (2007), 17(15), 4258-4261.

Li, Jian; Rajamani, Ramkumar; Tounge, Brett A.; Reynolds, Charles H.. **Mechanistic modeling in drug discovery: MMP-3 and the HERG channel as examples.** Modelling Molecular Structure and Reactivity in Biological Systems, Kevin J. Naidoo, John B. Brady, Martin J. Field, Jiali Gao, and Michael Hahn Editors, The Royal Society of Chemistry (2006) 283-288.

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Reynolds, Charles H.; Editor. **Special Issue: Understanding Protein-Ligand Interactions. (Papers from 2005 National ACS Meeting held in San Diego, California.) [In: J. Mol. Graphics Modell.; 2006, 24(6)].** (2006), 74 pp.

Tounge, Brett A.; Rajamani, Ramkumar; Baxter, Ellen W.; Reitz, Allen B.; Reynolds, Charles H.. **Linear interaction energy models for β -secretase (BACE) inhibitors: Role of van der Waals, electrostatic, and continuum-solvation terms.** Journal of Molecular Graphics & Modelling (2006), 24(6), 475-484.

Reynolds, Charles H.. **Understanding protein-ligand interactions.** Journal of Molecular Graphics & Modelling (2006), 24(6), 413.

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Rajamani, Ramkumar; Reynolds, Charles H. **Modeling the binding affinities of β -secretase inhibitors: application to subsite specificity.** Bioorganic & Medicinal Chemistry Letters (2004), 14(19), 4843-4846.

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Lee, Jung; Reynolds, Charles; Jetter, Michele C.; Youngman, Mark A.; Hlasta, Dennis J.; Dax, Scott L.; Stone, Dennis J.; Zhang, Sui-Po; Codd, Ellen E. **Design and synthesis of novel pyrrolidine-containing bradykinin antagonists.** Bioorganic & Medicinal Chemistry Letters (2003), 13(11), 1879-1882.

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Reynolds, Charles H.; Tropsha, Alexander; Pfahler, Lori B.; Druker, Ross; Chakravorty, Subhas; Ethiraj, G.; Zheng, Weifan. **Diversity and coverage of structural sublibraries selected using the SAGE and SCA algorithms.** Journal of Chemical Information and Computer Sciences (2001), 41(6), 1470-1477.

Cheng, A.; Best, S. A.; Merz, K. M.; Reynolds, C. H.. **GB/SA water model for the Merck molecular force field (MMFF).** Journal of Molecular Graphics & Modelling (2000), 18(3), 273-282.

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Chakravorty, S.; Reynolds, C. H.. **Improved AMBER torsional parameters for the N-N rotational barrier in diacylhydrazines.** Journal of Molecular Graphics & Modelling (2000), Volume Date 1999, 17(5/6), 315-324.

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Reynolds, Charles H.; Hormann, Robert E. **Theoretical Study of the Structure and Rotational Flexibility of Diacylhydrazines: Implications for the Structure of Nonsteroidal Ecdysone Agonists and Azapeptides.** Journal of the American Chemical Society (1996), 118(39), 9395-9401.

Reynolds, Charles H.. **Estimating Lipophilicity Using the GB/SA Continuum Solvation Model: A Direct Method for Computing Partition Coefficients.** Journal of Chemical Information and Computer Sciences (1995), 35(4), 738-42.

Chaubal, Mahesh V.; Payne, Gregory F.; Reynolds, Charles H.; Albright, Robert L. **Equilibria for the adsorption of antibiotics onto neutral polymeric sorbents: experimental and modeling studies.** Biotechnology and Bioengineering (1995), 47(2), 215-26.

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Reynolds, Charles H. **Book Review of Reviews in Computational Chemistry, Vol. I**, J. Am. Chem. Soc. 1992, 114, 5484.

Reynolds, Charles H. **Book Review of Reviews in Computational Chemistry, Vol. II** J. Am. Chem. Soc. 1992, 114, 5484.

Reynolds, Charles H.. **Trihalomethyl cations: relative stability of CX3+ (X = F, Cl or Br).** Journal of the Chemical Society, Chemical Communications (1991), (14), 975-6.

Reynolds, Charles H.. **Relative stabilities of isomeric chlorine-substituted carbocations: the C2H4Cl+ cation.** Journal of the Chemical Society, Chemical Communications (1990), (21), 1533-5.

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Reynolds, Charles H.; Frederick, Clay B. **Calculations on the Reactivity of Biological Nucleophiles** Toxicologist, 1988, 8, 52.

Lynn, Lee L.; Pierce, Thomas H.; Reynolds, Charles H. **AMPAC: Version for IBM Mainframe Computers** QCPE Bull. 1987, 7, 37.

Reynolds, Charles H.; Pierce, Thomas H. **AMPAC (Apollo Version)** QCPE Bull. 1986, 6, 95.

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Dewar, Michael J. S.; Reynolds, Charles H. **Tritium migration in tritiated anisole.** Journal of the American Chemical Society (1982), 104(11), 3244-6.

Patents

D. Keith Hester, Robert J. Duguid, Martha Kelly, Anna Chasnoff, Gang Dong, Edwin L. Crow, Rebecca Taub, Charles H. Reynolds, Duk Soon Choi, Lianhe Shu, Ping Wang **Method of synthesizing thyroid hormone analogs and polymorphs thereof,** Madrigal Pharmaceuticals, Inc., F. Hoffmann-La Roche Ltd., PCT/US2013/060177, Mar 20, 2014.

Baxter, Ellen, Robert Boyd, Steve Coats, Alfonzo Jordan, Allen Reitz, Charles H. Reynolds, Malcolm Scott, and Mark Schulz. "**NOVEL 2-AMINO-QUINAZOLINE DERIVATIVES USEFUL AS INHIBITORS OF ß-SECRETASE (BACE**)." European Patent EP 1776350, issued January 23, 2013.

Baxter, Ellen, Robert Boyd, Steven J. Coats, Alfonzo D. Jordan, Allen B. Reitz, Charles H. Reynolds, Mark Schulz, and Malcolm Scott. "**2-amino-quinazoline derivatives useful as inhibitors of β-secretase (BACE).**" U.S. Patent 8,426,429, issued April 23, 2013.

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Baxter, Ellen, Christopher J. Creighton, Tianbao Lu, Allen B. Reitz, Charles H. Reynolds, Tina Morgan Ross, and Ellen Sieber-McMaster. **6-substituted-thio-2-amino-quinoline derivatives useful as inhibitors of β-secretase (BACE).** U.S. Patent 8,076,358, issued December 13, 2011.

Baxter, Ellen, W. ; Reitz, Allen, B. ; Parker, Michael, H. ; Huang, Yifang ; Ho, Chih, Yung ; Strobel, Eric, D. ; Reynolds, Charles, H. **MACROCYCLE DERIVATIVES USEFUL AS INHIBITORS OF beta-SECRETASE (BACE),** Issued April 26, 2011, US 7,932,261 B2

Reitz, Allen B., Chi Luo, Yifang Huang, Tina M. Ross, Ellen E. Baxter, Brett A. Tounge, Michael H. Parker, Eric D. Strobel, and Charles H. Reynolds. **2-AMINO-3, 4-DIHYDRO-PYRIDO [3, 4-D] PYRIMIDINE DERIVATIVES USEFUL AS INHIBITORS OF BETA-SECRETASE (BACE).** European Patent EP 1966198, issued March 16, 2011.

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Baxter, Ellen ; Reitz, Allen B. ; Maharoof, Umar Saibu Mohomed ; Huang, Yifang ; Creighton, Christopher John ; Reynolds, Charles H. ; Luo, Chi ; Tounge, Brett A. ; Ross, Tina Morgan ; Lu, Tianbao **2-AMINO-QUINOLINE DERIVATIVES USEFUL AS INHIBITORS OF BETA-SECRETASE (BACE)** Issued August 31, 2010, US 7,786,116 B2

Baxter, Ellen E. ; Creighton, Christopher John ; Huang, Yifang ; Luo, Chi ; Parker, Michael H. ; Reitz, Allen B. ; Reynolds, Charles H. ; Ross, Tina Morgan ; Strobel, Eric D. ; Tounge, Brett A. **2-amino-3,4-dihydro-pyrido[3,4-d]pyrimidine derivatives useful as inhibitors of beta-secretase (BACE)** Issued May 12, 2009, US7,531,545 B2

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