

**R. Keith Frank, Ph.D.**  
**President and Chief Executive Officer**  
keithfrank@isotherapeutics.com

**Education**

- 1983 Ph.D. (Organic Chemistry), Rice University, Houston, Texas, 1983.  
Dissertation: "Natural Product Synthesis: Total Synthesis of d,l-Antibiotic 593A; Synthetic Approaches toward Naphthyridinomycin."
- 1978 B.A. (Chemistry), University of California, San Diego, La Jolla, California, 1978.

**Experience**

**IsoTherapeutics Group, LLC**

- 2007 – President and Chief Executive Officer
- 2006 – 2007 President
- 2005 Co-founder

**The Dow Chemical Company, Freeport, TX 1982-2006**

- 2004 to 2006 Application Development Leader, Dowpharma, Synthetics and New Offerings. Project management & prioritization, development of new offerings, and technical management of ChelaMed<sup>sm</sup> Radiopharmaceutical Services.
- 2003 to 2004 Technical Leader, ChelaMed<sup>sm</sup> Radiopharmaceutical Services. Instrumental in launch of this new service offering for Dow. New business development and project management responsibilities. Working with customers to develop biotargeted radiopharmaceuticals.
- 1999 to 2003 Technical Leader, BioTargeted Radiopharmaceuticals, Pharmaceutical Technologies. Led the technical program for bifunctional chelating agents directed toward biotargeted radiopharmaceuticals. This included new business development and project management activities.
- 1996 to 1999 Research Associate, Designed Chemicals Research & Development. Discovery Research. Developed radiotherapy solution for use in implantable brachytherapy device. Designed automated apparatus for radiopharmaceutical production. Radon monitoring and risk assessment. Remediation of thorium-containing waste site.

- 1992 to 1996 Research Leader, Designed Chemicals Research & Development. Discovery Research. Developed anti-gingivitis oral rinse formulation. Designed a radiopharmaceutical for treatment of melanoma. Performed exploratory research in phosphonates for osteoporosis therapy. Experience in consumer product research and radioactive waste remediation.
- 1985 to 1992 Project Leader, Functional Chemicals Research. Designed and synthesized bifunctional chelating agents for the attachment of radionuclides to monoclonal antibodies for use in the diagnosis and treatment of soft tissue cancers. Worked as part of a team to develop and commercialize a therapeutic agent for the treatment metastatic bone cancer. Department coordinator for the design and evaluation of computer systems and software.
- 1984 to 1985 Senior Research Chemist, Organic Process Research Researched and developed new products for metal ion control in the pulp and paper industry.
- 1982 to 1984 Senior Research Chemist, Chlor-Nitrogen Research Conducted exploratory research on the synthesis of amino acids used in the food industry.
- Rice University, Houston, Texas. 1978 to 1983.**
- 1979 to 1983 Graduate Research Fellow under the direction of Dr. Tohru Fukuyama. Synthesis of complex natural products. Completed the first total synthesis of d,l-antibiotic 593A and made substantial contributions to the total synthesis of naphthyridinomycin.
- 1978 to 1979 Graduate Teaching Fellow Responsible for teaching undergraduate organic chemistry laboratory.

**Publications and Presentations**

K.A. Selting; J.C. Lattimer; A.R.Ketring; J. Bryan; D.Crump; J. Simon; R.K. Frank; C.J. Henry, "Hematologic Sparing of Samarium-153-DOTMP, a Novel Bone-Seeking Radiopharmaceutical Agent for the Treatment of Bone Tumors." Presented at American College of Veterinary Radiology 2011 Annual Scientific Meeting, Oct, 2011, Albuquerque, NM.

Jingjie Zhou, Mark Lenox, Theresa Fossum, Keith Frank, Jaime (Jim) Simon, Stan Stearns, Catherine Ruoff, Richard Wendt, Gamal Akabani, "Dosimetry of  $^{90}\text{Y}$  Liquid Brachytherapy in a Dog with Osteosarcoma Using PET/CT;" *J Nucl Med.* 2011; 52 (Supplement 1):129

J. Simón, R. K. Frank, D. Crump, J. Rogers, S. Phillips, S. Ellebracht, W. Erwin, N. Ueno, R. Wendt, "Preclinical Evaluation of Sm-153-DOTMP as a Therapeutic Bone-Seeking Radiopharmaceutical;" *J Nucl Med.* 2011; 52 (Supplement 1):1751

Kim A. Selting; Jimmy C. Lattimer; Alan R. Ketrting; Druce K. Crump; Jaime (Jim) Simon; R. Keith Frank; Carolyn J. Henry; "Samarium-153-DOTMP treatment of spontaneously-occurring bone cancer in dogs as a proof-of-concept model;" *J Nucl Med.* 2011; 52 (Supplement 1):174

C.J. Henry, J.C. Lattimer, K.A. Selting, M. Loy, A. Ketrting, S. Axiak, C.H.M. Souza, D. Tate, R.K. Frank, J. Simon, S. Dodson, S. Stearns, "Intralesional liquid brachytherapy in dogs with appendicular osteosarcoma," *Veterinary Cancer Society*, Austin, TX, Oct. 18, 2009.

Jim Simon, Stan Stearns, Kenneth McMillan, Max Loy, Keith Frank, "Liquid Brachytherapy," 55<sup>th</sup> Annual Meeting, The Society of Nuclear Medicine, New Orleans, LA, June 14-18, 2008

Huma Mohsin, Jonathan Fitzsimmons, Tiffani Shelton, Timothy J. Hoffman, Cathy S. Cutler, Michael R. Lewis, Phillip S. Athey, Gyongyi Gulyas, Garry E. Kiefer, R. Keith Frank, Jaime Simon, Susan Z. Lever, Silvia S. Jurisson, "Preparation and biological evaluation of  $^{111}\text{In}$ -,  $^{177}\text{Lu}$ - and  $^{90}\text{Y}$ -labeled DOTA analogues conjugated to B72.3," *Nuclear Medicine and Biology*, **34**, 493-502 (2007).

Huma Mohsin, Fang Jia, Geethapriya Sivaguru, Michael Hudson, Tiffani Shelton, Timothy Hoffman, Cathy S. Cutler, Alan R. Ketrting, Phillip S. Athey, Jim Simón, R. Keith Frank, Silvia S. Jurisson, Michael R. Lewis, "Radiolanthanide-Labeled Monoclonal Antibody CC49 for Radioimmunotherapy of Cancer: Biological Comparison of DOTA Conjugates and  $^{149}\text{Pm}$ ,  $^{166}\text{Ho}$ , and  $^{177}\text{Lu}$ ," *Bioconjugate Chemistry*, **17**(2), 485-492 (2006).

R. Keith Frank, "Bifunctional Chelants for Protein-Based Therapeutic Radiopharmaceuticals," *Advancing Protein Therapeutics – Inaugural Current Challenges in Protein Therapeutics*, PepTalk Conference, San Diego, CA, January 11-13, 2006.

R. Keith Frank, Philip S. Athey, Gyongyi Gulyas, Garry E. Kiefer, Kenneth McMillan, Jaime Simón, "Chelants for delivery of metal ions," *Polymeric Drug Delivery I – Particulate Drug Carriers*, Svenson, S. (Ed.), *ACS Symposium Series*, Vol. 923, Chapter 20, pp. 282-294, American Chemical Society, Washington, DC, 2006.

Michael R. Lewis, Huma Mohsin, Geethapriya Sivaguru, Fang Jia, Jeffrey N. Bryan, Cathy S. Cutler, Alan R. Ketring, Phillip S. Athey, Jim Simon, R. Keith Frank, Louis J. Theodore, Don B. Axworthy, Silvia S. Jurisson, "Therapeutic Radiolanthanides for Antibody Pretargeting: Comparisons of Delivery Platforms, Dose Rates, and Radiation Energetics," *Pacificchem 2005*, Honolulu, Hawaii, December 15, 2005.

H. Mohsin, G. Sivaguru, F. Jia, J. N. Bryan, C. S. Cutler, A. R. Ketring, P. S. Athey, J. Simón, R. K. Frank, L. J. Theodore, D. B. Axworthy, S. S. Jurisson, M. R. Lewis, "Comparison of Pretarget and Conventional CC49 Radioimmunotherapy Using  $^{149}\text{Pm}$ ,  $^{166}\text{Ho}$  and  $^{177}\text{Lu}$ ," *J. Labelled Cpd. Radiopharm.*, in press.

H. Mohsin, G. Sivaguru, F. Jia, J. N. Bryan, C. S. Cutler, A. R. Ketring, P. S. Athey, J. Simón, R. K. Frank, L. J. Theodore, D. B. Axworthy, S. S. Jurisson, M. R. Lewis, "Comparison of Pretarget and Conventional CC49 Radioimmunotherapy Using  $^{149}\text{Pm}$ ,  $^{166}\text{Ho}$  and  $^{177}\text{Lu}$ ," 16<sup>th</sup> International Symposium on Radiopharmaceutical Chemistry, Iowa City, Iowa, June 24-28 (2005).

J. Tedesco, W. Goeckeler, M. Becker, R. K. Frank, G. Gulyas, S. A. Young, "Development of Optimal Lu-177 Labeled Monoclonal Antibody (7E11) Constructs for Radioimmunotherapy of Prostate Cancer," Abstract submitted to American Society of Clinical Oncology for 2005 Annual Meeting.

Patrick Winter, Phillip Athey, Garry Kiefer, Gyongyi Gulyas, Keith Frank, Ralph Fuhrhop, David Robertson, Samuel Wickline, Gregory Lanza, "Improved paramagnetic chelate for molecular imaging with MRI," *Journal of Magnetism and Magnetic Materials*, **293**, 540-545 (2005).

Gyongyi Gulyas, Christopher R. Adair, Philip S. Athey, R. Keith Frank, Garry E. Kiefer, Kenneth McMillan, Jaime Simón, "Metal Chelates for Diagnostic and Therapeutic Applications," Abstracts of Papers, 228th ACS National Meeting, Philadelphia, PA, August 22-26, 2004.

R. Keith Frank, "Lanthanide Bifunctional Chelating Agents for Biotargeted Pharmaceuticals," 3<sup>rd</sup> Annual Antibody World Summit, Philadelphia, PA, July 19-21, 2004.

G. Sivaguru, H. Mohsin, C. S. Cutler, M. F. Embree, T. D. Shelton, T. J. Hoffman, A. R. Ketring, W. H. Miller, J. Simón, R. K. Frank, S. S. Jurisson, M. R. Lewis, "Radiolanthanide-Labeled Monoclonal Antibody CC49 for Radioimmunotherapy in Tumor-Bearing Mice," 51<sup>st</sup> Annual Meeting, The Society of Nuclear Medicine, Philadelphia, PA, June 19-23, 2004.

Mary F. Embree, Geethapriya Sivaguru, Huma Mohsin, Keith D. Bailey, Leonard H. Manson, Fang Jia, R. Keith Frank, Jaime Simón, Silvia S. Jurisson, Cathy S. Cutler, Alan R. Ketring, Michael R. Lewis, "Production of Pm-149 and Comparison to Ho-166 and Lu-177 for Radioimmunotherapy," Abstracts, 38<sup>th</sup> Midwest Regional Meeting of the American Chemical Society, Columbia, MO, November 5-7, 2003.

R. Keith Frank, Philip S. Athey, Gyongyi Gulyas, Garry E. Kiefer, Kenneth McMillan, Jaime Simón, "Chelants for Delivery of Metal Ions," *Polymeric Materials Science and Engineering*, **89**, 148 (2003).

R. Keith Frank, Philip S. Athey, Gyongyi Gulyas, Garry E. Kiefer, Kenneth McMillan, Jaime Simón, "Chelants for Delivery of Metal Ions," Abstracts of Papers, 226<sup>th</sup> ACS National Meeting, New York, NY, September 7-11, 2003.

Michael R. McDevitt, Dangshe Ma, Jim Simón, R. Keith Frank, David A. Scheinberg, "Design and Synthesis of <sup>225</sup>Ac Radioimmunopharmaceuticals," *Applied Radiation and Isotopes*, **57**(6), 841-847 (2002).

Michael R. McDevitt, Dangshe Ma, Lawrence T. Lai, Jim Simón, Paul Borchardt, R. Keith Frank, Karen Wu, Virginia Pellegrini, Michael J. Curcio, Matthias Miederer, Neil H. Bander, David A. Scheinberg, "Tumor Therapy with Targeted Atomic Nanogenerators," *Science*, **294**(5546), 1537-1540 (2001).

James B. Stubbs, Alan D. Strickland, R. Keith Frank, Jaime Simón, Kenneth McMillan, Jeffery A. Williams, "Biodistribution and Dosimetry of an Aqueous Solution Containing Sodium 3-(<sup>125</sup>I)Iodo-4-Hydroxybenzensulfonate (Iotrex) for Brachytherapy of Resected Malignant Brain Tumors," *Cancer Biotherapy & Radiopharmaceuticals*, **15**(6), 645-656 (2000).

James B. Stubbs, Alan D. Strickland, R. Keith Frank, Jaime Simón, Kenneth McMillan, Jeffery A. Williams, "Biodistribution and Dosimetry of Iotrex, An Aqueous Solution Containing Organically-Bound <sup>125</sup>I for Brachytherapy of Resected Malignant Brain Tumors," *Journal of Nuclear Medicine*, **41**(5), 235P (2000).

Tohru Fukuyama, Leping Li, Alison A. Laird, and R. Keith Frank, "Stereocontrolled Total Synthesis of (+)-Cyanocycline A," *Journal of the American Chemical Society*, **109**, 1587 (1987).

Tohru Fukuyama, R. Keith Frank, Alison A. Laird, "Synthesis of Unsymmetrically Substituted 2,5-Piperazinediones: Regioselective Alkylation of Piperazinedione Derivatives," *Tetrahedron Letters*, **26**(25), 2955 (1985).

Richard Keith Frank, "Natural product synthesis: total synthesis of d,l-antibiotic 593A. Synthetic approaches toward naphthyridinomycin," Rice University, Houston, TX, USA. Avail. Univ. Microfilms Int., Order No. DA8314932. (1983), 246 pp. From: Diss. Abstr. Int. B 1983, 44(2), 495-6.

Tohru Fukuyama, R. Keith Frank, and Charles F. Jewell, Jr., "Total Synthesis of d,l-Antibiotic 593A," *Journal of the American Chemical Society*, **102**, 2122 (1980).

### **Issued Patents**

#### **(US & EP)**

Dana W. Simón, Alan D. Strickland, Jaime Simón, Daniel J. Macey, R. Keith Frank, Kenneth McMillan, "Treatment of osteomyelitis with radiopharmaceuticals," **US Patent 7,045,116** (5/16/2006).

Jaime Simón, R. Keith Frank, Alan D. Strickland, "Radioiodinated sulfonated phenols and process therefore," **US Patent 6,861,044** (3/1/2005).

R. Keith Frank, "Aminoalkylenephosphonates for treatment of bone disorders," **US Patent 6,794,371** (9/21/2004).

R. Keith Frank, Garry E. Kiefer, Jaime Simón, "Actinium-225 complexes and conjugates for targeted radiotherapy," **US Patent 6,670,456** (12/30/2003).

Jaime Simón, Alan D. Strickland, R. Keith Frank, "Radioiodinated sulfonated phenols for the study of renal function," **US Patent 6,506,364** (1/14/2003).

Jaime Simón, R. Keith Frank, Alan D. Strickland, "Radioiodinated sulfonated phenols and process therefore," **US Patent 6,506,363** (1/14/2003).

David A. Wilson, Keith R. Frank, Joseph R. Garlich, Jaime Simón, "Ligand based pharmaceutical for the treatment and/or diagnosis of soft tissue tumors," **Eur. Patent 499,098** (4/17/2002).

Jaime Simón, R. Keith Frank, Alan D. Strickland, "Radioiodinated sulfonated phenols for brachytherapy," **US Patent 6,315,979** (11/13/2001).

Dorothy L. Roerden, R. Keith Frank, "Dicationic and polycationic monoprimary alcohols and derivatives thereof," **US Patent 6,177,577** (1/23/2001).

David A. Wilson, R. Keith Frank, Joseph R. Garlich, Jaime Simón, "Compositions and Method for Soft Tissue Tumors Using Phenolic Carboxylate Metal Complexes," **Eur. Patent 497,356** (8/12/1998).

Jaime Simón, Joseph R. Garlich, R. Keith Frank, Kenneth McMillan, "Frozen Radiopharmaceutical Formulations," **US Patent 5,762,907** (6/9/1998).

David A. Wilson, Joseph R. Garlich, William A. Fordyce, R. Keith Frank, Jaime Simón, William F. Goeckler, Roberta C. Cheng, William J. Kruper, Kenneth McMillan, "Macrocyclic Tetraazacyclododecane Conjugates and Their Use as Diagnostic and Therapeutic Agents," **US Patent 5,756,065** (5/26/1998).

David A. Wilson, Joseph R. Garlich, R. Keith Frank, Kenneth McMillan, Jaime Simón, "Conjugates Possessing Ortho Ligating Functionality for Delivering Therapeutic Radiation Doses to Calcific Tumors and Metastatic Bone Cancer," **US Patent 5,714,631** (2/3/1998).

David A. Wilson, Joseph R. Garlich, R. Keith Frank, Kenneth McMillan, "Conjugates Possessing Ortho Ligating Functionality and Complexes Thereof; Binding to Antibodies; Diagnosis and Therapy of Tumors; Relief of Bone Pain," **US Patent 5,696,239** (12/9/1997).

Jaime Simón, Joseph R. Garlich, Garry E. Kiefer, Kenneth McMillan, Richard Keith Frank, William F. Goeckler, William A. Fordyce, Roberta C. Cheng, William J. Kruper, Sharon A. Baughman, David A. Wilson, "Macrocyclic Ligands and Complexes," **US Patent 5,652,361** (7/29/1997).

Dorothy L. Roerden, R. Keith Frank, "Dicationic and Polycationic Primary Monoalcohols and Their Derivatives for Use in Cationizing Starch Compounds for Papermaking," **US Patent 5,616,800** (4/1/1997).

David A. Wilson, Joseph R. Garlich, Richard K. Frank, Kenneth McMillan, Jaime Simón, "Chelants Possessing Ortho Ligating Functionality and Complexes Thereof," **Eur. Patent 566,166** (9/25/1996).

David A. Wilson, Joseph R. Garlich, Richard K. Frank, Kenneth McMillan, Jaime Simón, "Chelants Possessing Ortho Ligating Functionality and Complexes Thereof," **Eur. Patent 570,022** (7/31/1996).

Joseph R. Garlich, Tipton T. Masterson, R. Keith Frank, "Phytate Antimicrobial Compositions in Oral Care Products," **Eur. Patent 616,520** (5/29/1996).

Robert J. Michalowski, Steven H. Christiansen, R. Keith Frank, Teresa Littleton, Jaime Simón, Walter Vaughn, David A. Wilson, "Process for Removing Metal Ions from Liquids," **US Patent 5,447,603** (9/5/1995).

Roberta C. Cheng, William A. Fordyce, William F. Goeckeler, William J. Kruper, Jr., Richard K. Frank, Joseph R. Garlich, Garry E. Kiefer, Kenneth McMillan, Jaime Simón, David A. Wilson, Sharon Baughman, "Macrocyclic Conjugates and their Use as Diagnostic and Therapeutic Agents," **US Patent 5,435,990** (7/25/1995).

Jaime Simón, Joseph R. Garlich, R. Keith Frank, Kenneth McMillan, "Radiopharmaceutical Formulations, Their Method of Administration and Process of Preparation," **Eur. Patent 462,787** (6/21/1995).

David A. Wilson, Joseph R. Garlich, R. Keith Frank, Kenneth McMillan, Jaime Simón, "Chelants Possessing Ortho Ligating Functionality and Complexes Thereof," **Eur. Patent 367,223** (4/26/1995).

Roberta C. Cheng, William A. Fordyce, William F. Goeckeler, William F. Kruper, Jr., Sharon Baughman, Joseph R. Garlich, Garry Kiefer, Kenneth McMillan, Jaime J. Simón, David A. Wilson, Richard Keith Frank, "Macrocyclic Bifunctional Chelating Agents, Complexes thereof and their Antibody Conjugates," **Eur. Patent 353,450** (3/29/1995).



David A. Wilson, R. Keith Frank, Joseph R. Garlich, Jaime Simón, "Radioactive Compositions for Soft Tissue Tumors," **US Patent 5,342,925** (8/30/1994).

David A. Wilson, Joseph R. Garlich, R. Keith Frank, Kenneth McMillan, Jaime Simón, "Complexes Possessing Ortho Ligating Functionality," **US Patent 5,342,604** (8/30/1994).

Joseph R. Garlich, R. Keith Frank, Jaime Simón, Garry E. Kiefer, David A. Wilson, "Oral Compositions for Inhibiting Plaque Formation," **US Patent 5,320,829** (6/14/1994).

R. Keith Frank, Joseph R. Garlich, Jaime Simón, Garry E. Kiefer, David A. Wilson, "Oral Compositions for Inhibiting Calculus Formation," **US Patent 5,318,772** (6/7/1994).

David A. Wilson, R. Keith Frank, Joseph R. Garlich, Jaime Simón, "Method of Treating and/or Diagnosing Soft Tissue Tumors," **US Patent 5,308,606** (5/3/1994).

Joseph R. Garlich, Tipton T. Masterson, R. Keith Frank, "Phytate Antimicrobial Compositions in Oral Care Products," **US Patent 5,300,289** (4/5/1994).

### **Awards & Honors**

Dow Chemical – Best Published Paper Award, 2003, "Tumor Therapy with Targeted Atomic Nanogenerators," *Science*, **294**(5546), 1537-1540 (2001).

Dow Chemical Special Recognition Award, 2002, "Radiolabeled BLYS, Potentially New Radiopharmaceutical."

Recognized by Proxima Therapeutics, 1999, for work on brain brachytherapy solution.

Gulf Coast Scientist's Excellence in Science Award, 1998 "Development of an <sup>125</sup>I Brachytherapy Solution."

Dow Chemical award, 1997, for FDA approval of Quadramet.

C&M Technical Excellence Award, 1990 "Synthesis of new quaternary ammonia compounds."

Robert A Welch Graduate Foundation, 1979 – 1983.

Harry Boyer Weiser Scholarship Award for Chemical Research, Rice University, 1982.

Rice University Fellowship, 1978 – 1979

## **Professional Organizations**

American Chemical Society, member 1978 – present  
Society of Nuclear Medicine, member 1987 – present  
National Federation of Independent Businesses, member 2007 – present  
BioHouston, associate member 2008 – present  
Texas Dow Organic Discussion Group, member 1988 – 2000, President 1990, 1991

## **Community Activities**

Brazosport Rotary Club, member 2009 - present  
St. Timothy's Episcopal Church, Vestry 2006 – 2010 – Sr. Warden 2010 -2011  
Zoning Board of Adjustment, City of Lake Jackson, 2000 – present, Chairman 2003 – present  
Brazosport Center Stages, Board of Directors 1992-1994, 1998-2001, 2005-2007, Director of Facilities & Vice President of Operations  
Citizen's Bond Task Force, City of Lake Jackson, 2004-2005  
Brazoria County Youth Homes, Board of Directors, 1997 – 2003, President 2002  
St. Timothy's Episcopal Church, Parish Council Evangelism Chair, 1999 – 2000,  
United Way of Brazoria County, Fund Raising Chairman 1997  
United Way of Brazoria County, Budgets and Allocations Committee 1991-1994  
Brazosport Fine Arts Council, Vice President 1990 - 1991  
Little Theatre of Brazosport, Board of Directors 1988 - 1991, President 1990 - 1991  
Brazosport Music Theater, Board of Directors 1986 - 1987  
Brazosport Personal Computer Club, President 1987 - 1989