Curriculum Vitae

Nicholas Bodor, Ph.D., D.Sc., d.h.c. (multi), HoF

Nicholas Bodor, Ph.D., D.Sc., d.h.c. (multi), HoF

CURRICULUM VITAE

Date of Birth:	February 1, 1939
Address:	10225 Collins Avenue, Apt. 1002-04 Bal Harbour, Florida 33154 USA
Telephone:	(305) 868-8250 (residence) (305) 571-8490 (office; Bodor Laboratories, Inc.)
Married To:	Sheryl Lee Bodor
Children:	Nicole and Erik (Miami); Miklós (Debrecen, Hungary)

EDUCATION:

- R.A. Welch Postdoctoral Fellow
  by invitation of Prof. Michael J. S. Dewar;
  University of Texas at Austin, 1968-1969; 1970-1972

- Doctor in Chemistry
  Babes-Bolyai University, and Supreme Council of Scientific Titles of the Romanian National Academy of Science, 1965

- Diploma in Science (B.S., M.S., Organic Chemistry)
  with special honors - straight A's throughout the five years;
  Bolyai University (Cluj, Romania), 1959

EMPLOYMENT:

- Founder and CEO, Bodor Laboratories, Inc.
  Miami, Florida; Founded in 2006

- Graduate Research Professor Emeritus (active), University of Florida
  Gainesville, Florida; since 2003

- Executive Director, University of Florida Center for Drug Discovery
  J. Hillis Miller Health Science Center, Gainesville, Florida; since 1990

- Affiliate Graduate Research Professor, Dept. of Ophthalmology
  University of Florida College of Medicine, Gainesville, Florida; since 1991

- Affiliate Professor, Dept. of Chemistry
  University of Florida College of Liberal Arts & Sciences
  Gainesville, Florida; since 1990

Previous:

- Chief Scientific Officer, IVAX Corporation
  Miami, Florida; 2003-2005

- Managing Director, IVAX Drug Research Institute, Ltd.
  Budapest, HUNGARY; 1999-2005

- President, IVAX Research Institute, Inc.
  Miami, Florida; 2002-2005

- Senior Vice President, Basic Research & Drug Discovery, IVAX Research, Inc.
  Miami, Florida; 2000-2005

- Graduate Research Professor, Dept. of Pharmaceutics, University of Florida
  College of Pharmacy, Gainesville, Florida; 1991-2003

- Graduate Research Professor, Dept. of Medicinal Chemistry, University of Florida
  College of Pharmacy, Gainesville, Florida; 1983-2003

- V Ravi Chandran PhD Professor in Drug Design and Targeting, University of Florida
  College of Pharmacy, Gainesville, Florida; 2000-2003

- Vice President and Director, Pharmatec, Inc.
  Alachua, Florida; 1983-1992

- Director, Center for Drug Design and Delivery, University of Florida
  J. Hillis Miller Health Science Center, Gainesville, Florida; 1986-1990

- Chairman, Dept. of Medicinal Chemistry, University of Florida
  College of Pharmacy, Gainesville, Florida; 1989-1990

- Professor (1979-1983) and Chairman (1979-1984), University of Florida
  Dept. of Medicinal Chemistry, J. Hillis Miller Health Center, Gainesville, Florida

- Adjunct Professor of Pharmaceutical Chemistry, University of Kansas
  Lawrence, Kansas; 1978-1980

- Adjunct Professor of Medicinal Chemistry, University of Kansas
  Lawrence, Kansas; 1974-1978

- Associate Director of Medicinal Chemistry, INTERx Research Corporation
  Lawrence, Kansas; 1973-1979

- Senior Research Scientist, ALZA Corporation
  Lawrence, Kansas; 1972-1973

- R.A. Welch Postdoctoral Fellow, University of Texas at Austin
  1968-1969 and 1970-1972

- Principal Investigator and Group Leader, Chemical-Pharmaceutical Research Institute
  Cluj, Romania; 1961-1968 and 1969-1970

- Research Investigator and Group Leader, "1 September" Factory
  Satu Mare, Romania; 1959-1961

ELECTED TO:

- Fellow, the World Innovation Foundation; 2002

- Member, Dermatology Advisory Board, Glaxo Wellcome; 1997

- Member, Hungarian Academy of Sciences; 1995

- Fellow, American College of Clinical Pharmacology; 1991

- Fellow, American Association for the Advancement of Science; 1989

- Honorary Member, Panhellinic Association of Pharmacists; 1989

- Honorary Member, Hungarian Chemical Society; 1988

- Fellow, American Association of Pharmaceutical Scientists; 1986

- Fellow, Academy of Pharmaceutical Research and Science; 1983

AWARDS AND HONORS:

- Inducted to the American Chemical Society Hall of Fame (Medicinal Chemistry Division); 2012
- Commander's Cross of the Order of Merit of the Hungarian Republic - presented at the Hungarian Parliament during the national celebration of over 1,000 years of statehood and its Canonized first king, St. Stephen; 2010
- Fabinyi Prize, awarded by the Hungarian Chemical Society (given to eminent scientists living outside Hungary); 2010
- Distinguished Pharmaceutical Scientist Award, American Association of Pharmaceutical Scientists; 2007
- Honorary Doctor of Science Degree, University of Florida; 2005
- Gold Cross of Merit of the Hungarian Republic, awarded by Ferenc Madl, President of Hungary; March 31, 2004
- Volwiler Research Achievement, American Association of Colleges of Pharmacy; 1997
- Professorial Excellence Program Award, University of Florida; 1996
- Leo Friend Award, American Chemical Society; 1996
- The Nagai Foundation Tokyo Fellowship; 1994
- University of Florida Research Achievement Award; 1991
- Doctor Honoris Causa, Medical University of Debrecen, Hungary; 1990
- University of Florida Research Achievement Award; 1990
- Doctor Honoris Causa, Technical University of Budapest, Hungary; 1989
- American Pharmacists Association (APhA) Research Achievement Award in Pharmaceutical and Medicinal Chemistry; 1989
- American Association of Pharmaceutical Scientists Research Achievement Award (the first) in Medicinal and Natural Product Chemistry; 1988
- "The 1984 Florida Scientist of the Year"

OTHER ACADEMIC AND SCIENTIFIC RECOGNITIONS:

- *The Nicholas Bodor Distinguished Lectureship*, University of Florida; established 2014
- *The Nicholas Bodor Professor in Drug Discovery*, University of Florida; established 2007
- Appointed as Graduate Research Professor Emeritus upon retirement from the University of Florida; 2003
- Targeted brain delivery of neuropeptides (as published in *Science*, **257**, 1698-1700, 1992) cited as one of the top 10 medical advances of 1992 by the *Harvard Health Letter*, March 1993 issue
- Appointed Graduate Research Professor, University of Florida; 1983

SERVICE TO ACADEMIA AND INDUSTRY:

- Member, Board of Directors, ALCHEM Laboratories Corp.; 1997-2015 (from inception, to sale to another entity)
- Chairman, Policy Committee of the Florida Center for Heterocyclic Compounds
- Member, Board of Trustees; ARKAT-USA
- Consultant, advisor or Board of Directors member for numerous major pharmaceutical companies and law firms (Taft Law, Schering-Plough, ONO Pharmaceutical Co., Otsuka Pharmaceutical Co., Xenon Vision, Inc., Oculis, Inc., Helene Curtis, Inc., etc.)
- Principal Investigator of numerous National Institutes of Health research grant awards
- Visiting Professor, Hoshi University, Tokyo Japan; 1995
- Visiting Professor, Assiut University, Assiut Egypt; 1984

LECTURES AND CONFERENCES:

- Invited speaker of more than 425 national and international symposia and special lectures (please see separate listing)

- Founder and Organizer of the *Retrometabolism Based Drug Design and Targeting Conference*; international series of symposia held biennially from 1997-2015 (a total of 10 events)

- Name Lectureships given: Hoechst-Roussel Lectureship in Chemistry, Somerville NJ, 1983; Hoshi University Diploma, Tokyo Japan, 1983; Bombay College of Pharmacy Silver Medal, Bombay India, 1984; Nichols Distinguished Symposium, American Chemical Society, Tarrytown NY, 1986; Sigma Xi Lectureship, 1987; University of Saskatchewan College of Pharmacy, Canada, 1998; The Högyes Lecture, Semmelweis University of Medicine, Budapest Hungary, 2000.

EDITORIAL BOARDS:

AAPS Journal
Advanced Drug Delivery Reviews
American Journal of Drug Delivery
Burger's Medicinal Chemistry, 6th Edition
Current Drugs
Current Medicinal Chemistry
Drug Design & Discovery
Expert Opinion on Drug Delivery
Journal of Ocular Pharmacology and Therapeutics
Journal of Pharmacology & Clinical Toxicology
Journal of Pharmacy and Pharmacology
Magyar Kemiai Folyoirat
Open Medicinal Chemistry Journal
Pharmaceutical Research
Pharmaceutical Science Communications
Pharmacy and Pharmacology Communications
STP Pharma Sciences

MEMBERSHIPS:

Academy of Pharmaceutical Scientists (APS)
American Association for the Advancement of Science (AAAS)
American Association of Colleges of Pharmacy (AACP)
American Association of Pharmaceutical Scientists (AAPS)
American Chemical Society (ACS)
American College of Clinical Pharmacology (ACCP)
American Epilepsy Society (AES)
American Pharmacists Association (APhA)
Association for Ocular Pharmacology and Therapeutics (AOPT)
Controlled Release Society (CRS)
Hungarian National Academy of Sciences
International Council of Scientific Unions (ICSU)
International Scientific Advisory Panel of Oxford Molecular Group, PLC
International Union of Pure and Applied Chemistry (IUPAC)
New York Academy of Sciences
Sigma Xi
Worldwide Hungarian Medical Academy (WHMA)

PUBLICATIONS:

- Author/co-author of more than 520 publications (please see separate listing)

PATENTS:

- Inventor on more than 255 patents (please see separate listing)

GRADUATE AND POSTDOCTORAL SUPERVISON:

- Has supervised more than 50 doctoral students and 100 postdoctoral research fellows/associates

LANGUAGES:

- Fluent in English, Hungarian and Romanian;
  Read and write in French, Russian and German

LISTED IN:

American Scientist
Who's Who in America
Who's Who in Frontiers of Science
Who's Who in Science and Technology
Who's Who in Technology Today
Who's Who Worldwide (Platinum Edition)
Ki Kicsoda (Who's Who Worldwide – Hungarian Edition)

Nicholas Bodor, Ph.D., D.Sc., d.h.c. (multi), HoF
BIOGRAPHICAL SKETCH

Dr. Nicholas Bodor is a Graduate Research Professor Emeritus (active) at the University of Florida (UF) College of Pharmacy, Gainesville. He joined the university in 1979 as Professor and Chairman of the Medicinal Chemistry Department, and was promoted to Graduate Research Professor in 1983. He is the Executive Director of the college's Center for Drug Discovery, founded by him in 1986. During his tenure at UF, Dr. Bodor has supervised the training of more than 50 doctoral students and over 100 postdoctoral level research associates and fellows. In February 2000, he took a leave of absence from his academic posts in order to accept a position as Senior Vice President of Basic Research and Drug Discovery at the IVAX Corporation. Dr. Bodor then served as Chief Scientific Officer of the IVAX Corporation, as well as President of the IVAX Research Institute. During this period, he simultaneously led Hungary's Institute for Drug Research as its Managing Director until his retirement from IVAX in October 2005.

Dr. Bodor's main research interests include design of drugs with improved therapeutic index, design of new chemical delivery systems, computer-assisted drug design, drug transport and metabolism, and theoretical and mechanistic organic chemistry. He has published more than 520 research articles, has over 250 patents, and is on the editorial boards of numerous international scientific journals. An internationally recognized leader in drug discovery, design and delivery, he has introduced revolutionary, general, comprehensive drug design and drug targeting concepts known as *retrometabolic drug design* approaches. These concepts strategically combine chemical and enzymatic (metabolic) processes to achieve drug targeting and to produce safe drugs and safe environmental chemicals. The two major classes of the retrometabolic drug design concepts contain *"chemical drug targeting systems" (CDS)* and the *"soft drugs" (SD).* Each of these large classes contains various subclasses, based on the different design rules. The design concepts incorporated in the soft drug approaches were used by Dr. Bodor to develop a *general and comprehensive* program, including a *computerized expert system* which can be used to design all potential and possible metabolites and the corresponding safe active soft drugs or chemical delivery systems. The soft steroid Loteprednol Etabonate, designed by Dr. Bodor, is on the market in the U.S. and other countries. Other drugs designed by him using the retrometabolic concepts are in advanced clinical development.

Dr. Bodor received his B.S./M.S. degree in Organic Chemistry in 1959 at Bolyai University in Transylvania, and his Ph.D. degree in 1965 from the University of Babes-Bolyai, Cluj and the Romanian National Academy of Sciences. He was a Group Leader at the Pharmacochemical Research Institute in Romania until 1968, when he was offered an R. A. Welch Fellowship at the University of Texas in Austin, where he worked in the field of theoretical organic chemistry with Dr. Michael J. S. Dewar, the first Robert A. Welch Research Chair. In 1972 he became a Senior Research Scientist at ALZA Laboratories in Lawrence, Kansas, which later became INTERx Research Corporation, where he was Director of Research, as well as an Adjunct Professor at the University of Kansas until 1978.

Among his many honors, Dr. Bodor is an elected Fellow of the Academy of Pharmaceutical Sciences, American Association of Pharmaceutical Scientists, American Association for the Advancement of Science, and American College of Clinical Pharmacology. He is also an Honorary Member of the Hungarian Chemical Society and the Panhellenic Society of Pharmacists. Among other honors, Dr. Bodor has been named "The 1984 Florida Scientist of the Year" and received the first AAPS Research Achievement Award in Medicinal and Natural Product Chemistry in 1988, as well as the APhA Research Achievement Award in Pharmaceutical and Medicinal Chemistry in 1989. In 1994 he was named the first recipient of the Nagai Foundation Tokyo International Fellowship. He was named by the American Chemical Society as the 1996 recipient of the Leo Friend Award in recognition of his article entitled, "Design of Biologically Safer Chemicals," published in *Chemtech*, October 1995. He is the first College of Pharmacy faculty member to receive a Professorial Excellence Award, given by the University of Florida in 1996. The AACP selected Dr. Bodor as the recipient of the 1997 Volwiler Research Achievement Award. In April 2000, he was named the V. Ravi Chandran Professor in Drug Design and Targeting of the UF College of Pharmacy, the first recipient of this endowed professorship. In February 2002, he was elected a Fellow of the World Innovation Foundation. An honorary Doctor of Science degree was conferred upon Dr. Bodor by the University of Florida in 2005. In 2007, the American Association of Pharmaceutical Scientists awarded Dr. Bodor with the Distinguished Pharmaceutical Scientist Award. Dr. Bodor was inducted in to the American Chemical Society's Hall of Fame, Medicinal Chemistry Division in August 2012. He received the title "Graduate Research Professor Emeritus" upon his retirement from the University of Florida in 2003 and remains an active part of its College of Pharmacy through, among other things, a Distinguished Professorship named the *Nicholas Bodor Professor in Drug Discovery* (established in 2007) and the *Nicholas Bodor Distinguished Lectureship* (introduced in 2014).

In addition to the honors above, Dr. Bodor has received the highest levels of recognition from his home country of Hungary for his scientific achievements and leadership of the Budapest-based Institute for Drug Research. In 1989 he received an honorary Doctor of Science degree from the Technical University of Budapest, and then was awarded the Doctor Honoris Causa degree from the Medical University of Debrecen in 1990. In 1995 he was elected to the Hungarian National Academy of Sciences. Ferenc Madl, President of Hungary, awarded Dr. Bodor the Gold Cross of Merit of the Hungarian Republic in 2004. In 2010 he received the prestigious Fabinyi Prize of the Hungarian Chemical Society, which is given to scientists living outside Hungary whose outstanding scientific accomplishment have contributed to the reputation of the HCS. In August 2010 at the national celebration of Hungary's over 1,000 years' statehood and its canonized first king, St. Stephen, Dr. Bodor was awarded at the Hungarian Parliament, the Commander's Cross of the Order of Merit of the Hungarian Republic, a prestigious award of civil merit.

Dr. Bodor and his wife Sheryl call Miami their primary residence. He founded Bodor Laboratories, Inc. in 2006, and works there with his son Erik and daughter Nicole (who hold PhD/MBA and PhD degrees, respectively, in the relevant fields) to further develop his drug design strategies to the marketplace. His oldest son Miklós (an MD, PhD) is Chairman of the Clinical Pharmacology Department at the Medical University in Debrecen, Hungary.

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SUMMARY OF SCIENTIFIC INTERESTS AND ACHIEVEMENTS

Combining an interest in a wide variety of scientific fields with a wealth of originality, Dr. Bodor has contributed to almost every conceivable aspect of the pharmaceutical sciences, including basic theory, practical drug discovery and development, to taking drugs designed by him through clinical development and FDA approval. His invention of the retrometabolic drug design concept is based on the mechanism of drug action in various tissues and aims at improving the therapeutic index to diminish unwanted side effects. This general concept uses drug metabolism information to design parent drugs whose metabolism and distribution can be controlled to target and eliminate the drug in order to increase efficacy and eliminate undesirable side effects. These approaches represent systematic methodologies that, in addition to thoroughly integrating structure-activity (SAR) and structure-property (SPR) relationships, structure-metabolism (SMR) relationships are also developed and used in the drug design. The retrometabolic drug design loop combines two complementary but distinctly different concepts, the (i) *chemical delivery systems* (CDS) and (ii) *soft drugs* (SD) approaches. In general, a CDS is *inactive* by design and is enzymatically *activated* stepwise to produce the active drug *only* (or preferentially) at the target site/organ. At the other end of the retrometabolic design loop are the soft drugs. A SD *is an active drug*, designed in such a way to be *deactivated* in a predictable and controllable way after it achieves its therapeutic role.

A striking example of a CDS introduced by Dr. Bodor is the *brain targeting of drugs* based on a redox targetor system, such as 1,4-dihydrotrigonelline $\leftrightarrow$ trigonelline salt. The structurally similar, ubiquitous $NAD^+ \leftrightarrow$ NADH redox coenzyme system assures oxidation of the initial lipophilic drug targetor conjugate to the hydrophilic, inactive quaternary form due to the unique architecture of the blood-brain barrier (BBB) and is *locked-in* the brain, but is quickly eliminated from the whole body. Thus, further enzymatic liberation of the drug takes place essentially only in the brain, in a sustained manner.

Dr. Bodor's Soft Drug (SD) approach is particularly well-suited for applications in which a targeted effect is desired, but systematic side effects are to be avoided. One method of the soft drug principle is to apply the *inactive metabolite approach*. The design starts with an inactive metabolite of a known drug which is then chemically modified (activated) to produce an isosteric/isoelectronic analogue of the active drug which then, when applied at the site of need, will perform the desired function. However, when it is absorbed or reaches the systemic circulation, it will be deactivated to the very metabolite the design started from. By design this deactivation takes place by hydrolytic enzymes and avoids the usual oxidative metabolic processes. Dr. Bodor is sole inventor of the soft drug Loteprednol Etabonate, an ophthalmic corticosteroid that is used in suspensions against eye inflammation (for instance, after cataract surgery) and allergic diseases. His involvement carried through to all phases --- from design, through clinical development and FDA approval in 1998. It is currently sold in five different

products (Lotemax™, Alrex™, Zylet™, as well as two subsequent Lotemax™ gel and ointment products) and considered one of the most important and safest eye drugs on the market. Together with a second generation of soft corticosteroids such as etiprednol dicloacetate, it is also being developed for a full spectrum of other possible applications, such as nasal spray for rhinitis, inhalation products for asthma, and topical cream for dermatological applications. Another eye-specific drug invented by Dr. Bodor is betaxoxime, which is inactive when administered but becomes active in the eyes after converting, by design, an oxime into a ketone function, followed by its stereospecific reduction.

At the time of its introduction, the idea of designed-in metabolism represented a significant novelty and was against mainstream thinking of the time that instead focused on minimizing or entirely eliminating drug metabolism. Since then, Dr. Bodor's retrometabolic drug design concepts have ignited research in academia and industry. The importance of this field is reflected by the fact that its review in the 7th edition of *Burger's Medicinal Chemistry, Drug Discovery and Development* requires a full chapter with close to 200 chemical structures and 675 references and the book "*Retrometabolic Drug Design and Targeting*" (2012) is fully dedicated to the subject.

The novelty and importance of Dr. Bodor's CDS approach led to having its first applications published in *Science* in 1975, 1981 and 1983. Its later extension to the targeted brain delivery of neuropeptides by molecular packaging was listed as one of 1992's top 10 medical advances for medical progress by the *Harvard Health Letter*. Other types of CDSs invented by Dr. Bodor target drugs to the eye are of considerable interest as they allow site- and stereo-specific delivery of β-blockers by exploiting differential enzyme distributions. The administered, inactive β-amino-ketoxime is converted to the corresponding ketone by oxime hydrolase, an enzyme with preferential activity in the eye that was first identified by Dr. Bodor and then stereo-specifically reduced to the active alcohol form.

In addition to Loteprednol Etabonate, other drugs designed using the SD approach include soft β-blockers (Adaprolol, Esmolol/Breviblock™, Landiolol/Onoact™); soft opioid analgetics (Remifentanil/Ultiva™); soft Ca^{+}channel blockers (Clevidipine/Cleviprex™); soft soft E_2 analogs at Yale Univ.; novel soft cytokine inhibitors at Janssen Pharm.; soft immunosuppresants (soft cyclosporine A analogs at Enanta Pharm., soft tacrolimus analogs at Novartis); and soft benzodiazepines at GlaxosmithKline. A compelling benefit of Dr. Bodor's concepts is that they have resulted in design of drugs that combine maximum effectiveness and safety, allowing a far greater number of patients to be treated by them. These concepts also allow design of drugs to fill previously-unmet needs. For example, Sofpironium Bromide, a topical soft anticholinergic designed by Dr. Bodor, is currently being developed both in the USA and Japan for treatment of hyperhidrosis.

Dr. Bodor has published more than 520 research articles, many of them on drug design and formulation tools which have garnered high interest and use in the scientific community. In particular, four of his publications on novel models to predict Log P and Log W have been

collectively cited more than 570 times. A pioneer of the use of MO calculations in drug design and delivery and the development and use of semi-empirical MO calculations in drug design, he defined novel computer-enabled systems to allow the design of soft drug and other improved drug candidates using rules-based and MO assessments. He is an innovator in the use of cyclodextrins and solubilizing excipients, and pioneered cyclodextrins for traditional and non-traditional (buccal) administration routes. He is an inventor on more than 250 patents, with numerous additional worldwide patent applications currently pending for such uses as treatment of hyperhidrosis, myopia, COPD and sialorrhea.

The progress in these various related fields has been reviewed biennially at an international series of symposia Dr. Bodor founded in 1997 entitled, *The Retrometabolism Based Drug Design and Targeting Conference*. He organized a total of ten of these meetings between 1997 and 2015 and in addition to Florida, the venues have included Japan, Hungary and Austria.

Nicholas Bodor, Ph.D., D.Sc., d.h.c. (multi), HoF

INVITED PRESENTATIONS

1. March 1978, Lake Ozark, MO; 11th Higuchi Research Seminar.
2. May 1978, Osaka, JAPAN; Otsuka Pharmaceutical Co.
3. May 1978, Osaka, JAPAN; Kanebo, Ltd.
4. May 1978, Tokyo, JAPAN; Sankyo, Ltd.
5. June 1978, Aberdeen Proving Ground, MD; Edgewood Arsenal.
6. November 1978, Chicago, IL; Abbott Laboratories.
7. January 1979, Kalamazoo, MI; Upjohn Company.
8. March 1979, Lake Ozark, MO; Ayerst Laboratory.
9. April 1-6, 1979, Honolulu, HI; ACS/CSJ Computer Assisted Drug Design Symposium.
10. April 1979, Palo Alto, CA: Syntex Research.
11. June 1979, Raleigh, NC; Decontamination of Chemical Agents ARO Special Meeting.
12. November 1979, Philadelphia, PA; McNeil Laboratories.
13. November 1979, London, ENGLAND; Chemical Society – Royal Society.
14. November 1979, London, ENGLAND; University of London.
15. November 1979, Birmingham, ENGLAND; University of Birmingham.
16. February 1980, Bloomfield, NJ; Schering-Plough.
17. March 1980, Lake Ozark, MO; 13th Higuchi Research Seminar.
18. April 1980, Skokie, IL; G.D. Searle Co.
19. April 1980, Skokie, IL; APhA National Meeting.

20. August 24-29, 1980, Las Vegas, NV; ACS Symposium, “Soft Drugs: Strategies for Design of Safer Drugs.”

21. August 1980, Las Vegas, NV; Gordon Research Conference on Medicinal Chemistry.

22. November 3-15, 1980, Reston, VA; ARO Conference on Defense Against Chemical Agents, “Acceleration of Deactivation of Chemical Agents.”

23. December 8, 1980, Ann Arbor, MI; University of Michigan, “The Soft Drug Approach: Strategies for the Design of Safer Drugs.”

24. December 9, 1980, Ann Arbor, MI; Warner Lambert, “The Soft Drug Approach: Strategies for the Design of Safer Drugs.”

25. February 23, 1981, Washington, D.C.; National Institute for Aging, “Soft Drugs.”

26. March 15-18, 1981, Lake Ozark, MO; 14th Higuchi Research Seminar.

27. April 12-17, 1981, Atlanta, GA; FASEB Symposium on Drug Center Systems, “The Prodrug Approach to Controlled Delivery.”

28. August 3-7, 1981, New London, NH; Gordon Research Conference on Medicinal Chemistry.

29. August 25-28, 1981, Noordwijkerhout, THE NETHERLANDS; IUPAC-IUPHAR Symposium, “Strategy in Drug Research.”

30. October 20-21, 1981, Indianapolis, IN; Lilly Research Company.

31. November 27-28, 1981, Montpellier, FRANCE; Clin Midy Research Center Symposium, “Drug Metabolism and Drug Design: Quo Vadis?”

32. December 6-14, 1981, Osaka, JAPAN; Otsuka Pharmaceutical Co.

33. December 7, 1981, Kyoto, JAPAN; Kyoto University.

34. January 10-11, 1982, Painesville, OH; Diamond Shamrock.

35. January 25, 1982, Clifton, NJ; American Cyanamid Company.

36. February 15-16, 1982, Hillside, NJ; Bristol Myers.

37. February 22, 1982, Boston, MA; Gillette Company.

38. March 15-17, 1982, Lake Ozark, MO; 15th Higuchi Seminar.

39. March 29, 1982, Painesville, OH; Diamond Shamrock.

40. March 31, 1982, Groton, CT; Pfizer Company.

41. April 1, 1982, Aberdeen Proving Ground, MD; Edgewood Arsenal.

42. May 6, 1982, Austin, TX; University of Texas.

43. May 25, 1982, Chicago, IL; Abbott Laboratories, "Brian-Specific Delivery of Drugs."

44. December 1982, Osaka, JAPAN; Fujisawa Pharmaceutical Co.

45. December 1982, Hiroshima, JAPAN; Umezawa Research Institute, "Brain-Specific Delivery of Drugs."

46. December 1982, Kyoto, JAPAN; University of Kyoto, "Soft Drugs."

47. March 13-16, 1983, Lake Ozark, MO; 16th Higuchi Research Seminar.

48. April 25, 1983, Skokie, IL; G.D. Searle.

49. May 6, 1983, San Francisco, CA; University of California at San Francisco.

50. September 29, 1983, Somerville, NJ; Hoechst-Roussel.

51. October 19, 1983, Gainesville, FL; University of Florida Frontiers of Science, "Strategies to Design Safe Drugs."

October 25-November 15, 1983, JAPAN:
52. Tokyo; Sankyo, Ltd.
53. Tokyo; Hoshi University, Special Lecture.
54. Tokyo; Snow Brand Milk Products.
55. Tokyo; Toyo Jozo Co., Ltd.
56. Osaka; Takeda Chemical Industries, Ltd.
57. Osaka; Fujisawa Pharmaceutical Co.
58. Osaka; Tanabe Co., Ltd.
59. Osaka; Sumitomo Company.
60. Osaka; Otsuka Pharmaceutical Co.
61. Osaka; Yoshitomi Company.

62. Hiroshima; Hiroshima University, Key Lecture at Drug Design and Metabolism Symposium.
63. Kyoto; ONO Pharmaceutical Co.
64. Kyoto; Kyoto University – Japanese Pharmaceutical Association.
65. Takata; Wakunaga Pharmaceutical Co.

66. December 7, 1983, Boston, MA; New England Nuclear.

67. December 8, 1983, Detroit, MI; Warner Lambert.

68. December 14,1983, Gainesville, FL; University of Florida Endocrinology Seminar.

69. January 1984, Assiut, EGYPT; University of Assiut Lecture Series.

70. January 1984, Milan, ITALY; Recordati Pharmaceutica e Chimica.

71. January 1984, Basel, SWITZERLAND; Sandoz, Inc.

72. January 28, 1984, Bombay, INDIA; Bombay College of Pharmacy, International Symposium Celebrating its 25th Anniversary.

73. February 1, 1984, New Delhi, INDIA; Indian Pharmaceutical Association Satellite Seminar on Advances in Drug Delivery Systems.

74. February 1984, Osaka, JAPAN; One Pharmaceuticals.

75. February 1984, Osaka, JAPAN; Yoshitomi Company.

76. February 1984, Osaka, JAPAN; Fujisawa Pharmaceutical Co.

77. March 11-14, 1984, Lake Ozark, MO; 17th Higuchi Research Seminar.

78. April 19, 1984, Arlington, VA; NIH Special Study Section on “Boronate, Redox and Related Compounds as Vital Reagents.”

79. May 15, 1984, Boston, MA; American Chemical Society, NE Section, Invited Lecture.

80. July 26, 1984, Miami, FL; Key Pharmaceuticals.

81. July 30-August 3, 1984, New London, NH; Gordon Conference on Medicinal Chemistry.

82. August 26-31, 1984, Philadelphia, PA; American Chemical Society Symposium on Drug Design and Discovery.

83. September 27, 1984, Gainesville, FL; University of Florida Department of Chemistry.

84. October 28-31, 1984, Philadelphia, PA; American Pharmaceutical Association Academy of Pharmaceutical Sciences Symposium on Theory and Application of Bioreversible Carriers to Drug Design.

85. November 1, 1984, West Chester, PA; SmithKline and Beckman Corporation.

86. November 9, 1984, Gainesville, FL; Engineering Advisory Council.

87. February 21-22, 1985, Austin, TX; University of Texas.

88. March 10-13, 1985, Lake Ozark, MO; 18th Higuchi Research Seminar.

89. March 18, 1985, Tokyo, JAPAN; Tokyo University – Pharmaceutical Society of Japan (Divisional).

90. March 19, 1985, Tsukuba, JAPAN; Eisai Company.

91. March 20, 1985, Osaka, JAPAN; Takeda Pharmaceutical Co.

92. March 21, 1985, Osaka, JAPAN; Sumitomo Pharmaceutical Co.

93. March 22, 1985, Hiroshima, JAPAN; Hiroshima University – Pharmaceutical Society of Japan (Divisional).

94. March 23, 1985, Osaka, JAPAN; ONO Pharmaceutical Co.

95. March 25, 1985, Tokushima, JAPAN; Otsuka Pharmaceutical Co.

96. March 26, 1985, Kyoto, JAPAN; Biwako Research Institute.

97. March 27, 1985, Osaka, JAPAN; Nihon Medi-Physics.

98. April 21-25, 1985, Anaheim, CA; Federation of American Societies for Experimental Biology (FASEB).

99. May 7, 1985, Cincinnati, OH; Proctor & Gamble.

100. May 8, 1985, Raleigh-Durham, NC; Burroughs-Welcome.

101. May 30, 1985, Magnolia, AR; Medicinal Chemistry Symposium.

102. June 10, 1985, Budapest, HUNGARY; National Academy of Science.

103. June 20, 1985, Milan, ITALY; Recordati Industria Chimica e Farmaceutica S.P.A.

104. June 24, 1985, Geneva, SWITZERLAND; Arcopharma.

105. July 4, 1985, London, ENGLAND; The Institute of Cancer Research and London University College Hospital.

106. July 22-25, 1985, Plymouth, NH; Gordon Conference on Drug Metabolism.

107. September 16, 1985, Philadelphia, PA; McNeil Pharmaceutical Co.

108. September 17, 1985, Kingsport, TN; Eastman Chemical Co.

109. September 25, 1985, Belfast, IRELAND; Queen's University of Belfast, Symposium on Prodrugs, Biochemical Society.

110. September 27, 1985, Reykjavik, ICELAND; University of Iceland.

111. September 30, 1985, Copenhagen, DENMARK; Lunbeck A/C.

112. October 1, 1985, Helsingborg, SWEDEN; Leo Pharmaceuticals.

113. October 3, 1985, London, ENGLAND; University College Hospital.

114. November 7, 1985, Kalamazoo, MI; Upjohn Company.

115. December 3, 1985, Rochester, NY; Eastman Kodak Company.

116. March 9-12, 1986, Lake Ozark, MO; 19th Higuchi Research Seminar.

117. April 4, 1986, Tarrytown, NY; ACS Nichols Distinguished Symposium.

118. May 19, 1986, Edgewood, MD; Edgewood Arsenal Conference.

119. May 20, 1986, Baltimore, MD; Nova Pharmaceutical Co.

120. June 15-19, 1986, Chapel Hill, NC; ACS Medicinal Chemistry Symposium.

121. July 29-August 13, 1986, Budapest, HUNGARY; Conference on the Role of Hungarians in Science and Technology in the World; National Academy of Science of Hungary; Central Research Institute for Drug Research.

122. August 15, 1986, Budapest, HUNGARY; Chinoin Pharmaceutical Co.

123. September 12, 1986, Castres Cedex, FRANCE; Pierre Fabre Research Center.

124. September 14-18, 1986, West Berlin, GERMANY; IX International Symposium on Medicinal Chemistry.

125. September 19, 1986, Helsingborg, SWEDEN; Leo Pharmaceutical Co.

126. September 29-30, 1986, Tokushima, JAPAN; Otsuka Research Institute.

127. October 1, 1986, Hiroshima, JAPAN; Hiroshima University.

128. October 2, 1986, Osaka, JAPAN; Takeda Chemical Industries.

129. October 3, 1986, Osaka, JAPAN; Sumitomo Pharmaceutical Co.

130. October 4, 1986, Kyoto, JAPAN; Kyoto University.

131. October 6, 1986, Tokyo, JAPAN; Hoshi University and Kanto Division of Japanese Pharmaceutical Society.

132. October 7, 1986, Tokyo, JAPAN; Tokyo University.

133. October 7, 1986, Tokyo, JAPAN; Snow Brand Milk Industries.

134. October 8, 1986, Tsukuba, JAPAN; Eisai Company.

135. October 8, 1986, Tsukuba, JAPAN; Tsukuba Research Institute.

136. October 9, 1986, Osaka, JAPAN; Fujisawa Pharmaceuticals.

137. October 10, 1986, Osaka, JAPAN; ONO Pharmaceutical Co.

138. November 2-6, 1986, Washington, D.C.; American Association of Pharmaceutical Scientists.

139. November 18-21, 1986, Edgewood, MD; Edgewood Arsenal Conference.

140. January 12-15, 1987, New York, NY; New York Academy of Sciences.

141. February 10, 1987, Gainesville, FL; Sigma Xi, "Concepts to Design Safer Drugs."

142. March 14-18, 1987, Lake Ozark, MO; 20th Higuchi Research Seminar.

143. March 30-April 3, 1987, Washington, D.C.; Federation of American Societies for Experimental Biology (FASEB).

144. April 2, 1987, Milan, ITALY; Recordati Industria Chimica e Farmaceutica S.P.A.

145. April 3, 1987, Paris, FRANCE; Delagrange, Inc.

146. April 3-13, 1987, Budapest, HUNGARY; Institute for Drug Research and Hungarian Academy of Sciences.

147. April 20-21, 1987, Bloomfield, NJ; Schering Corporation.

148. May 20-23, 1987, Frankfurt, GERMANY; Hoechst AG and Cassella Riedel Pharma GmbH.

149. June 4-7, 1987, Boston, MA; American Association of Pharmaceutical Scientists.

150. June 7-12, 1987, Madison, NJ; Residential School in Medicinal Chemistry of Drew University.

151. June 23-25, 1987, Washington, D.C.; NIH Special Study Section.

152. July 29, 1987, New York, NY; Pfizer Co.

153. August 3-7, 1987, New London, NH; Gordon Conference on Medicinal Chemistry.

154. September 21, 1987, Takasaki, JAPAN; Upjohn Company.

155. September 22, 1987, Tokyo, JAPAN; Eisai Company.

156. September 24, 1987, Osaka, JAPAN; Takeda Pharmaceutical Co.

157. September 25, 1987, Osaka, JAPAN; ONO Pharmaceutical Co.

158. September 26, 1987, Hiroshima, JAPAN; Hiroshima University.

159. September 28, 1987, Osaka, JAPAN; Osaka University.

160. September 29, 1987, Tokushima, JAPAN; Otsuka Pharmaceutical Co.

161. October 17, 1987, Budapest, HUNGARY; Chinoin Pharmaceutical Co.

162. October 22, 1987, Munich, GERMANY; Cyanamid Company.

163. October 22, 1987, Frankfurt, GERMANY; Hoechst AG.

164. October 23, 1987, Frankfurt, GERMANY; Merck.

165. October 26, 1987, London, ENGLAND; May & Baker.

166. November 17-20, 1987, Edgewood, MD; 1987 Scientific Conference on Chemical Defense Research.

167. December 2-7, 1987, Honolulu, HI; JUC PHARM SCI ’87.

168. December 10, 1987, Raleigh, NC; Burroughs-Wellcome and Glaxco.

169. December 17, 1987, Beaverton, OR; Tektronix.

170. February 3-4, 1988, Chicago, IL; Hayes & Griffith.

171. February 7-9, 1988, New York, NY; Pfizer Co.

172. February 25-27, 1988, Austin, TX; Dewar Symposium.

173. March 12-16, 1988, Lake Ozark, MO; 21st Higuchi Research Seminar.

174. March 16-18, 1988, Lexington, KY; University of Kentucky.

175. April 26, 1988, Palo Alto, CA: Syntex.

176. April 27, 1988, Palo Alto, CA; Alza.

177. April 28, 1988, San Francisco, CA; Genentech.

178. May 6, 1988, Gainesville, FL; College of Pharmacy Development Advisory Board.

179. May 29-June 4, 1988, Jerusalem ISRAEL; International Conference on Pharmaceutical Science, ‘Structure-Pharmacokinetic Relationships,”

180. June 22, 1988, Philadelphia, PA; HGP, Inc.

181. July 14, 1988, Newark, NJ; Johnson & Johnson.

182. August 12-19, 1988, Budapest, HUNGARY; Xth International Symposium on Medicinal Chemistry.

183. October 24-25, 1988, Newark, NJ; Johnson & Johnson.

184. October 30-November 3, 1988, Orlando, FL; Annual Meeting of the American Association of Pharmaceutical Scientists (AAPS).

185. January 27, 1989, Miami, FL; Schering-Plough Corporation.

186. March 12-15, 1989, Lake Ozark, MO; 22nd Higuchi Research Seminar.

187. April 8-11, 1989, Anaheim, CA; APhA Annual Meeting.

188. May 11-16, 1989, Thessaloniki, GREECE; Aristotelian University Postgraduate Seminar on Medicinal Chemistry.

189. May 29-30, 1989, Osaka, JAPAN; ONO Pharmaceutical Co.

190. May 31-June 1, 1989, Tokushima, JAPAN; Otsuka Pharmaceutical Co., Ltd.

191. June 2, 1989, Tokyo, JAPAN; Upjohn Company.

192. August 12-19, 1989, Budapest, HUNGARY; XIth International Symposium on Medicinal Chemistry.

193. August 21-25, 1989, Budapest, HUNGARY; Conference, The Role of Hungarians in the Scientific & Technological Progress of the World, “Recent Advances in the Design of Safer Drugs.”

194. September 14-15, 1989, Bethesda, MD; APhA End-of-Summer Symposium, “Chemically Designed Targeted Drug Delivery System.”

195. September 20-21, 1989, Morgantown, WV; West Virginia University Dept. of Chemistry Symposium, “Site-Specific Chemical Delivery System.”

196. October 22-26, 1989, Atlanta, GA; American Association of Pharmaceutical Scientists Annual Meeting, “Concepts in the Design of Safer Drugs.”

197. November 3-7, 1989, Phoenix, AZ; Preuss Foundation Seminar, “Role of the BBB in the Therapy of Brain Tumors,”

198. November 23, 1989, Kyoto, JAPAN; ONO Pharmaceutical Co., “Site-Specific Drug Delivery.”

199. November 24, 1989, Osaka, JAPAN; Otsuka Pharmaceutical Co., Ltd., “Soft Drugs.”

200. November 27, 1989, Tokyo, JAPAN; Japan Tobacco Company, “Novel Strategies in Drug Design.”

201. December 1, 1989, London, ENGLAND; IBC Conference on Recent Advances I Site-Specific Chemical Delivery Systems, “Role of Prodrugs and Soft Drugs in Drug Delivery and targeting Systems.”

202. December 4, 1989, Debrecen, HUNGARY, Medical University of Debrecen, Redox Systems of Drugs to the Brain.”

203. December 11-15, 1989, Maui, HI; American College of Neuropsychopharmacology, “Clinical Utilization of Redox Drug Combinations.”

204. February 12-14, 1990, Memphis, TN; College of Pharmacy, University of Tennessee, “Novel Strategies to Design Safer Drugs.”

205. February 15-16, 1990, Cleveland, OH; College of Pharmacy, Case Western University, “Site-Specific Chemical Delivery Systems.”

206. February 25-28, 1990, Reno, NV; AAPS Western Regional Meeting, “Brain-Specific Delivery of Peptides and Related Compounds.”

207. March 1, 1990, Palo Alto, CA; Syntex Co., “Novel Strategies in Drug Design and Delivery.”

208. March, 10-14, 1990, Lake Ozark, MO; Higuchi Research Seminar, “Delivery of Peptides to the Brain.”

209. March 31-April 8, 1990, Bath, ENGLAND; The Biochemical Society, “Design Strategies for Safer Drugs.”

210. July 1-6, 1990, Amsterdam, THE NETHERLANDS; XIth International Congress of Pharmacology, “Drug Targeting by Site-Specific Chemical Delivery Systems.”

211. July 16-18, 1990, Tokyo, JAPAN; Fifth Japanese-American Conference on Pharmacokinetics and Biopharmaceutics, “Novel Site-Specific Chemical Drug Delivery Systems.”

212. July 18-19, 1990, Kyoto, JAPAN; ONO Pharmaceutical Co., “Brain Delivery of Peptides.”

213. July 22-23, 1990, Tokushima, JAPAN; Otsuka Pharmaceutical Co., “Brain Delivery of Neuropeptides and Related Compounds.”

214. July 25-26, 1990, Osaka, JAPAN; Fujisawa Pharmaceutical Co., “Delivery of Peptides to the Brain.”

215. July 26, 1990, Osaka, JAPAN; Nihon Medi-Physics, “Technetium Chelates.”

216. August 22, 1990, Debrecen, HUNGARY; Hungarian Pharmaceutical Society, “Recent Advances in the Design of Safer Drugs.”

217. August 23, 1990, Budapest, HUNGARY; Federation of European Biochemical Societies, “Recent Advances in Site-Specific Chemical Delivery Systems.”

218. November 4-8, 1990, Las Vegas, NV; AAPS Annual Meeting, “Pharmacological Evaluation of Alprenolone Oxime - A New Potential Antiglaucoma Agent.”

219. February 6, 1991, Gainesville, FL; University of Florida College of Medicine, Division of Cardiovascular Medicine, “Roundtable Discussion: A New Site-Specific Endovascular Drug Delivery Catheter System.”

220. April 4, 1991, Charleston, SC; AAPS Regional Meeting, “Topical Drug Targeting by Chemical Delivery Systems and Soft Drugs.”

221. April 9, 1991, Osaka, JAPAN; Takeda Chemical Industries, Ltd., “Recent Advances in Chemical-Enzymatic Targeting of Drugs.”

222. April 10, 1991, Osaka, JAPAN; Otsuka Pharmaceutical Co., Ltd., “Recent Advances in Chemical-Enzymatic Targeting of Drugs.”

223. April 11-12, 1991, Osaka, JAPAN; ONO Minase Research Institute.

224. April 15, 1991, Tokyo, JAPAN; Eisai Tsukuba Research Laboratories.

225. April 16, 1991, Tokyo, JAPAN; Japan Tobacco Company, “Novel Soft Drugs.”

226. April 18, 1991, Suwon, SOUTH KOREA; Ajou University, “Design of Soft Drugs.”

227. April 19, 1991, Suwon, SOUTH KOREA; Korean Drug Delivery Symposium, “Brain-Specific Drug Delivery.”

228. April 22, 1991, Suwon, SOUTH KOREA; Korea Research Institute of Chemical Technology, “Design of Soft Drugs.”

229. May 6, 1991, Dallas, TX; Alcon Laboratories, Inc., “Enzymes in the Eye.”

230. May 10, 1991, Gainesville, FL; Florida School of Applied Molecular Orbital Theory, “Molecular Orbitals and Drug Design.”

231. May 21, 1991, Jamaica, NY; St. John’s University College of Pharmacy and Health Related Professions, “Chemical-Enzymatic Drug Targeting.”

232. June 6, 1991, San Diego, CA: Gensia Pharmaceutical Co., “Metabolism-Based Drug Design.”

233. June 7, 1991, La Jolla, CA: Agouron Pharmaceutical Co., “Rational Design of Drugs Based on Metabolic Considerations.”

234. July 8-13, 1991, Amsterdam, THE NETHERLANDS; Controlled Release Society Symposium, Chemical Delivery Systems for Brain Targeting of Drugs.”

235. July 12, 1991, Basel, SWITZERLAND; F. Hoffmann-La Roche AG, “Strategies to Design Safer Drugs.”

236. July 24, 1991, Tampa, FL; Bausch & Lomb, Inc.

237. August 17-22, 1991, Budapest, HUNGARY; 33rd IUPAC Congress, “Drug Discovery by Retrometabolism – Concepts and Applications.”

238. September 30-October 1, 1991, East Brunswick, NJ; Technology Management Group Conference on Pharmaceutical Markets in Imaging Agents and Related Products, “Targeted Chemicals for Imaging (Brain and Heart).”

239. October 13-16, 1991, Atlanta, G; American College of Clinical Pharmacology Meeting, “Topical Drug Targeting by Chemical Delivery and Soft Drugs.”

240. October 30, 1991, Gainesville, FL; UF College of Pharmacy Honors Seminar Course in Pharmaceutical Research, “Metabolism-Based Drug Design.”

241. November 226-28, 1991, Tokyo, JAPAN; ONO Pharmaceutical Co.

242. November 28, 1991, Itami, JAPAN; Senju Pharmaceutical Company, Drug Design Based on Retrometabolism Concepts."

243. November 29, 1991, Osaka, JAPAN; Otsuka Pharmaceutical Co., Ltd.

244. December 6, 1991, London, ENGLAND; IBC Conference-Drug Delivery III, "Drug Targeting by Chemical Delivery and Soft Drugs."

245. January 22-24, 1992, Gainesville, FL; UF Short Course on Surface Science in Pharmaceutical Technology, "Drug Targeting by Chemical Delivery and Soft Drugs."

246. February 8-12, 1992, King of Prussia, PA; CAChe Scientific Conference, "Chemistry by Design."

247. March 26-27, 1992, Baltimore, MD; Johns Hopkins Oncology Center, "Novel Methods of Drug Design."

248. May 15, 1992, Tokushima, JAPAN; Otsuka Pharmaceutical Co., "Recent Advances in Retrometabolic Drug Design."

249. May 18, 1992, Osaka, JAPAN; Japan Tobacco Company.

250. May 19, 1992, Itami, JAPAN; Senju Research Company.

251. May 20, 1992, Kyoto, JAPAN; ONO Pharmaceutical Co.

252. May 24-29, 1992, Jerusalem, ISRAEL; Second Jerusalem Conference on Pharmaceutical Sciences and Clinical Pharmacology, "Chemical-Enzymatic Approaches to Drug Targeting: Retrometabolism Concepts."

253. May 25, 1992, Rehovot, ISRAEL; Pharmos, Ltd.

254. June 1-4, 1992, Budapest, HUNGARY; Hungarian Academy of Sciences, "Recent Results in Retrometabolic Drug Design."

255. June 8-10, 1992, Tarrytown, NY; Conference on Topical Glucocorticoids with Increased Benefit/Risk Ratio, "Chemical Variability of Glucocorticoid Molecules: Application of the Soft Drug Concept to Topical Anti-inflammatory Agents."

256. July 22-24, 1992, Washington, D.C.; NIH Drug Discovery Groups for Alzheimer's Disease, "Brain Targeting of Peptides."

257. August 12, 1992, Miami, FL; IVAX Corporation, “Novel Soft Drugs.”

258. September 10, 1992, Madrid, SPAIN; 12th World Computer Congress, “Computer-Aided Drug Design: A Neural Network Approach.”

259. September 15-17, 1992, Washington, D.C.; American Colleges of Clinical Pharmacology, “Development of New Corticosteroids.”

260. September 18, 21 and 23, 1992, Gainesville, FL; (UF) Frontiers of Human Knowledge (university-wide honors course), “Drug Design and Discovery Based on Retrometabolism Concepts.”

261. October 9-11, 1992, Leiden, THE NETHERLANDS; Symposium on Drug Transport to the Brain: Concepts and Strategies, “The Application of Chemical Delivery Systems for Brain Targeting of Drugs.”

262. October 13-14, 1992, Gainesville, FL; UF Faculty Honors Course, “In Search of Magic Bullets.”

263. November 15-19, 1992, San Antonio, TX; AAPS Annual Meeting, “Brain Targeting of Peptides.”

264. November 19-20, 1992, Fort Worth, TX; Alcon Laboratories, Inc., “Chemical Delivery Systems for the Eye.”

265. December 1, 1992, Chicago, IL; Helene Curtis, Inc., “Novel Soft Anticholinergic Compounds.”

266. February 20-22, 1993, Miami, FL; IVAX Corporation, “Soft Drugs for the Treatment of Asthma.”

267. February 24, 1993, Raleigh, NC; Cato Research, Ltd., “Soft Steroids for the Treatment of Colitis.”

268. March 5-8, 1993, Amelia Island, FL; Pharmos Corp., “Soft Ophthalmic Drugs.”

269. April 20-21, 1993, Garden City, NY; 35th Annual Pharmacy Congress, “Application of Retrometabolic Approaches for Design of Novel Ophthalmic Drugs.”

270. June 5-8, 1993, Washington, D.C.; United States Patent Office, “Novel Anionic Delivery System.”

271. June 20-25, 1993, Edmonton, Alberta CANADA; 13th American Peptide Symposium, "Delivery of Peptides into the Central Nervous System by Sequential Metabolism."

272. July 23-24, 1993, Szeged, HUNGARY; International Workshop on Molecular Mechanism Regulating the Permeability of the Blood-Brain Barrier, "Strategies for Opening the Gateway to the Brain."

273. July 28-29, 1993, Rockville, MD; NIDA Technical Review Meeting on Opiate Pharmacotherapy, "Targeting Drugs to the Brain by Sequential Metabolism."

274. August 6, 1993, Bethesda, MD; NIH Drug Discovery Group Meeting, "Discovery of Novel Drugs for Alzheimer's Disease: Project 3—Neuropeptides."

275. August 8-10, 1993, Novia, MI; Symposium on Ocular Pharmacology, "The Application of Soft Drug Concepts to the Design of Ophthalmic Drugs."

276. August 22-27, 1993, Chicago, IL; 206th Annual Meeting of the American Chemical Society, "Brain Targeting of Peptides via Sequential Metabolism."

277. September 2-4, 1993, Kyoto, JAPAN; International Symposium on Delivery of Protein Drugs – the Next 10 Years, "Peptide Delivery to the Brain by Sequential Metabolism."

278. September 6, 1993, Kobe, JAPAN; Senju Pharmaceuticals.

279. September 7, 1993, Tokyo, JAPAN; Japan Tobacco Company.

280. September 10,1993, Tsukuba, JAPAN; Upjohn Pharmaceuticals, Ltd., "Soft Drugs Concept."

281. September 28-29, 1993, Bethesda, MD; NIDA Technical Review Meeting on Membranes and Barriers: Targeted Drug Delivery, "Retrometabolic Approaches to Drug Targeting."

282. October 22, 25 and 27, 1993, Gainesville, FL; (UF) Frontiers of Human Knowledge (university-wide honors course), "Drug Design and Discovery Based on Retrometabolism Concepts."

283. November 22-24, 1993, London, ENGLAND; IBC Drug Delivery 4, "Site-Specific Drugs by Chemical Transformations."

284. December 2-3, 1993, Washington, D.C.; IBC Meeting on Allergic Disease and Asthma, "Soft Drugs: A Retrometabolic Drug Design Concept."

285. April 23, 1994, Tokyo, JAPAN; Hoshi University Lecture Meeting on Comprehensive Cyclodextrins, "Recent Studies on Cyclodextrins and their Use in Drug Delivery and Targeting."

286. April 25-28, 1994, Tokyo, JAPAN; 7th International Cyclodextrins Symposium, "Optimization of Drug Targeting by Combinations of Chemical Delivery Systems and Cyclodextrins."

287. June 20-25, 1994, Edmonton, Alberta CANADA; 13th American Peptide Symposium, "Delivery of Peptides into the Central Nervous System by Sequential Metabolism."

288. July 28-29, 1994, Rockville, MD; NIDA Technical Review Meeting on Opiate Pharmacotherapy, "Targeting Drugs to the Brain by Sequential Metabolism."

289. August 21-25, 1994, Washington, D.C.; 208th American Chemical Society National Meeting, "Design of Biologically Safer Drug Based on Retrometabolic Concepts."

290. September 2-4, 1994, Kyoto, JAPAN; International Symposium Delivery of Protein Drugs – The Next 10 Years," Peptide Delivery to the Brain by Sequential Metabolism."

291. September 28-29, 1994, Rockville, MD; NIDA Technical Review Meeting on Membranes and Barriers: Targeted Drug Delivery, "Retrometabolic Design Approaches to Drug Targeting."

292. November 14-19, 1994, Buenos Aires, ARGENTINA; XV Pan American Congress of Pharmacy and Biochemistry, "Retrometabolic Drug Design Concepts."

293. December 7, 1994, Budapest, HUNGARY; National Academy of Sciences, "Retrometabolic Drug Design Concepts."

294. December 9, 1994, Budapest, HUNGARY; Technical University of Budapest, "Computer-Assisted Drug Design."

295. December 10, 1994, Budapest, HUNGARY; Gedeon Richter Works, "Soft Steroids."

296. December 12, 1994, Debrecen, HUNGARY; Medical University of Debrecen, "Novel Safe Ophthalmic Drugs."

297. January 26-29, 1995, New Orleans, LA; AOPT Annual Meeting, "Sequential Bioactivation of Methoxime Analogs of β-Adrenergic Antagonists in the Eye."

298. April 2-7, 1995, Anaheim, CA; 209th National Meeting of the American Chemical Society, "Optimization of Drug Targeting by Cyclodextrins."

299. April 10-13, 1995, Amelia Island, FL; 3rd Suncoast Workshop on the Neurobiology of Aging, "The Application of the Molecular Packaging Methods to Brain Targeting of TRH Analogs."

300. April 28-30, 1995, San Diego, CA; Houghten Pharmaceutical Co.

301. May 5, 1995, Birmingham, AL; University of Alabama Vision Research Center Visiting Scholar Program, "Retrometabolic Approaches for the Design of Novel Ophthalmic Drugs."

302. May 19-20, 1995, Thessaloniki, GREECE; 4th Conference in Advanced Medicinal Chemistry, "Retrometabolic Drug Design Concepts in Drug Targeting."

303. July 6-7, 1995, Hiroshima, JAPAN; 11th Annual Meeting of Japan Drug Delivery Systems Society, "Drug Targeting by Chemical and Enzymatic Retrometabolic Approaches to the Brain and Eye."

304. July 17, 1995, Heidelberg, GERMANY; BioResearch, BASF/Pharma Knoll Pharmaceuticals, "Chemical-Enzymatic Targeting of Drugs."

305. September 1-10, 1995, Tokyo, JAPAN; Hoshi University Visiting Professorship, several lectures of drug design.

306. September 3-8, 1995, Tokyo, JAPAN; AFMC International Medicinal Chemistry Symposium, Plenary Session, "Targeted drug Delivery to the Brian Using Chemical Delivery Systems."

307. September 11-13, 1995, Kobe, JAPAN; Academy of Pharmaceutical Science and Technology, Plenary Session, "Computer-Assisted Design of Targeted Drugs Based on Retrometabolic Concepts."

308. September 14, 1995, Osaka, JAPAN; Fujisawa Pharmaceutical Co., Ltd., "Optimal Combination of Chemical-Enzymatic and Physical Drug Targeting Approaches."

309. September 20, 1995, Osaka, JAPAN; ONO Pharmaceutical Co., Ltd., "Retrometabolic Drug Design Approaches and Computer Assisted Design of New Drugs."

310. September 22, 1995, Osaka, JAPAN; Takeda Chemical Industries, Ltd., "Retrometabolic Drug Design Approaches."

311. September 28-October 1, 1995, Geneva, SWITZERLAND; International Symposium on Experimental and Clinical Ocular Pharmacology and Pharmaceutics, Plenary Session, Retrometabolic Design Concepts in Ophthalmic Drug Discovery."

312. October 2, 1995, Milan, ITALY; BioResearch, BASF Pharma/Knoll Pharmaceutical Co., "Brain Targeting of Drugs."

313. October 6, 1995, SINGAPORE; The National University of Singapore, "Design and Development of Soft Drugs."

314. October 12, 1995, Ako, JAPAN; Otsuka Pharmaceutical Co., Ltd., "Design of Safer Ophthalmic Drugs."

315. November 1, 1995, Gainesville, FL; Frontiers of Science, "Designing Targeted Drugs for the Brain and Eye."

316. November 14, 1995, Budapest, HUNGARY; Induction into the Hungarian Academy of Sciences, Plenary Session, "The Chemical and Enzymatic Basis of the Retrometabolic Drug Design Approaches."

317. December 4-5, 1995, Ann Arbor, MI; Parke-Davis, Retrometabolic Drug Design Approaches."

318. February 5, 1996, Budapest, HUNGARY; Gedeon Richter, Ltd., "Brain Targeting Chemical Works of Gedeon Richter."

319. February 9, 1996, Frankfurt, GERMANY; Drug Targeting Symposium, German Chemical Society, "Drug Targeting Based on Retrometabolic Drug Design Approaches."

320. April 1, 1996, Budapest, HUNGARY; 8th International Cyclodextrin Symposium, "Recent Studies on the Use and Structure of Cyclodextrin Complexes."

321. April 19, 1996, Gainesville, FL; University of Florida Department of Neuroscience, "Retrometabolic Approaches to Drug Design and Targeting."

322. July 4, 1996, SINGAPORE; The National University of Singapore, "Recent Advances in Retrometabolic Drug Design."

323. July 9, 1996, Osaka, JAPAN; Senju Pharmaceutical Co., "Novel Antiglaucoma Drugs."

324. August 28, 1996, New York, NY; Forest Laboratories, "Soft Drugs."

325. September 5-12, 1996, Budapest, HUNGARY; Institute for Drug Research, Ltd., "Issues in Drug Development."

326. October 27-31, 1996, Seattle WA; AAPS Annual Meeting & Exposition, "Drug Targeting Based on Retrometabolic Drug Design Approaches."

327. November 18-20, 1996, Gainesville, FL; UF Pharmacy Honors Seminar, "In Search of Magic Bullets, "Retrometabolism-Based Drug Design."

328. January 20-22, 1997, Ispra, ITALY; Data Management in Computer-Aided Drug Design Workshop Joint Research Centre, "Computer-Assisted Design of New Drugs Based on Retrometabolic Concepts."

329. January 23-25, 1997, Brussels, BELGIUM; Janssen Pharmaceutica, "The Application of Chemical Delivery Systems for Brain Targeting of Drugs."

330. March 20, 1997, Gainesville, FL; UF College of Pharmacy National Development Advisory Board, "Issues in Drug Discovery and Targeting."

331. April 3, 1997, Austin, TX; University of Texas at Austin College of Pharmacy, "Design of Safer Drugs Using Retrometabolic Approaches."

332. April 13-17, 1997, San Francisco, CA; National Meeting of the American Chemical Society, "Design of Biologically Safer Chemicals."

333. May 6-9, 1997, Amelia Island, FL; 1st Drug Optimization via Retrometabolism Conference, (Founder and Organizer), "Retrometabolic Drug Design Concepts."

334. May 23-24, 1997, St. Petersburg, FL; Glaxo Dermatology Advisory Board Meeting, "Overview of the Soft Molecule Concept."

335. June 17, 1997, Raleigh, NC; Glaxo Wellcome, Inc.; Retrometabolic Drug Design Approaches."

336. July 9-12, 1997, Gdansk, POLAND; 6th International Symposium on Molecular Aspects of Chemotherapy, "Retrometabolic Approaches for Drug Targeting."

337. September 4, 1997, Budapest, HUNGARY; Chemical Works of Gedeon Richter, "Design of Soft Drugs."

338. September 8, 1997, Frankfurt, GERMANY; ASTA Medica, "Design of Soft Drugs."

339. September 11-14,1997, Munich, GERMANY; 2nd International Symposium on Experimental and Clinical Ocular Pharmacology and Pharmaceutics," Targeted Drug Delivery to Retina via Systemic Routes."

340. September 27-30, 1997, Chicago, IL; Abbott laboratories, Acceptance of Volwiler Research Achievement Award, "Retrometabolic Drug Design and Targeting Concepts."

341. October 22-24, 1997, Bethesda, MD; 3rd Annual Meeting of the Association for Ocular Pharmacology and Therapeutics, "Targeted Drug Delivery to Retina via Systemic Routes."

342. October 27-28, 1997, Arlington, VA; IBC's 7th Annual Conference on Asthma & Allergy, "Design of Soft Corticosteroids."

343. November 11, 1997, Budapest, HUNGARY; Institute for Drug Research, Ltd., 'Drug Development Concepts."

344. November 17 and 19, 1997, Gainesville, FL; UF Honors Seminar in Pharmacy Research, College of Pharmacy, "Retrometabolism-Based Drug Design: Making Magic Bullets Better and Safer."

345. January 14, 1998, Osaka, JAPAN; Santen Pharmaceutical Co., Ltd.; "Design of Safer Ophthalmic Drugs by Retrometabolic Approaches."

346. January 16, 1998, Hiroshima, JAPAN; Hiroshima University School of Medicine, "Design of Safer Ophthalmic Drugs Using Retrometabolic Approaches."

347. January 27,1998, Gainesville, FL; UF Department of Neuroscience, "Brain Targeting of Neuropharmaceuticals by Chemical Delivery Systems."

348. March 2, 1998, Miami, FL; IVAX Corporation, "Retrometabolic Drug Design and Targeting Approaches."

349. March 26-27, 1998, Saskatchewan, CANADA; University of Saskatchewan College of Pharmacy, "Retrometabolic Approaches for Drug Design & Targeting."

350. April 4-11, 1998, Budapest, HUNGARY; Institute for Drug Research, Ltd., "The Past and Future of Drug Discovery Research."

351. May 6, 1998, Budapest, HUNGARY; Institute for Drug Research, Ltd., "Recent Advances in Retrometabolic Drug Design."

352. May 25-28, 1998, Paris, FRANCE; 2nd World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology (Invited Speaker and Session Chair), "Brain Targeting of Basic Amino Acids and their Redox Analogs Containing Peptides."

353. May 31-June 3, 1998, Santiago de Compostela, SPAIN; 9th International Symposium on Cyclodextrins (Invited Speaker and Session Chair), "The Effect of 2-Hydroxypropyl-β Cyclodextrin on the Solubility, Stability and Brain Targeting of Chemical Delivery Systems for Neuropeptides."

354. June 9-11, 1998, Tokyo JAPAN; Challenges for Drug Delivery and Pharmaceutical Technology (Invited Speaker and Session Chair), "Retrometabolic Drug Design Approaches."

355. July 16-20, 1998, Budapest, HUNGARY; Institute for Drug Research, Ltd., "Neuropeptide Targeting to the Brain."

356. July 28-August 3, 1998, Reykjavik, ICELAND; University of Iceland, "Soft Drug Approach in Drug Design."

357. October 19-23, 1998, Debrecen, HUNGARY; Medical University of Debrecen Scientific Symposium to Celebrate its 80th Anniversary, "Retrometabolic Concepts for the Design of Safer Drugs."

358. October 28, 1998, Gainesville, FL; UF Honors Seminar in Pharmacy Research, College of Pharmacy, "Retrometabolism-Based Drug Design: Making Magic Bullets Better and Safer."

359. January 4-31, 1999, Budapest, HUNGARY; Institute for Drug Research, Ltd., and the Hungarian Academy of Sciences, "Computer Drug Design" and "Computer-Assisted Design of Soft Drugs."

360. March 23-April 2, 1999, Budapest, HUNGARY; Institute for Drug Research, Ltd., and the Technical University of Budapest, "Retrometabolism-Based Drug Design" and "Graduate Education at the University of Florida."

361. April 18-20, 1999, Dresden GERMANY; Technical University of Dresden, "Chemical Approaches in the Design of Targeted Drugs."

362. April 25-30, 1999, Jerusalem, ISRAEL; 7th European Congress of Biopharmaceutics & Pharmacokinetics and the 5th Congress of the European Federation of Pharmaceutical Sciences (Invited Speaker and Session Co-Chair), "Drug Targeting Using Retrometabolic Approaches."

363. May 11-14, 1999, Amelia Island, FL; 2nd Retrometabolism-Based Drug Design and Targeting Conference (Founder and Organizer), "Recent Advances in Retrometabolic Drug Design."

364. May 20-21, 1999, Monroe, LA; AAPS-SRDG 2nd Annual Meeting (Keynote Address), "Drug Targeting Using Retrometabolic Approaches."

365. May 24, 1999, Groton, CT; Pfizer Central Research, "Retrometabolic Drug Design and Targeting" and "Computational Approaches to Retrometabolic Drug Design and Targeting."

366. June 2, 1999, New Brunswick NJ; Bristol-Myers Squibb, "Computer-Assisted Design of New Drugs Based on Retrometabolic Concepts" and "Recent Advances in Retrometabolic Design Approaches."

367. September 2-7, 1999, Beerse, BELGIUM; Janssen Pharmaceuticals, "Computational Approaches to Retrometabolic Drug Design and Targeting."

368. September 21, 1999, Tampa, FL; Bausch & Lomb, "Novel Soft Steroids for Ophthalmic Use."

369. September 23-30, 1999, Budapest, HUNGARY; Institute for Drug Research, Ltd., "Computer-Assisted Soft Drug Design."

370. October 25 & 27, 1999, Gainesville, FL; UF Honors Seminar in Pharmacy Research, College of Pharmacy, "Retrometabolic Design."

371. November 14-18, 1999, New Orleans, LA; AAPS Annual Meeting and Exposition, "Retrometabolic Approaches for Drug Design and Targeting."

372. February 18, 2000, Lisbon, PORTUGAL; 3rd International Symposium on Ocular Pharmacology & Therapeutics (ISOPP), "The Creation of a Site Active (Soft) Steroid."

373. July 7, 2000, Paris, FRANCE; 27th International Symposium on Controlled Release of Bioactive Materials, "Cyclodextrins and Brain Delivery."

374. August 29, 2000, Philadelphia, PA; Rohm & Haas Co., "Retrometabolic Drug Design and Targeting."

375. October 23 & 25, 2000, Gainesville, FL; UF Honors Seminar "in Search of Magic Bullets", College of Pharmacy, "Retrometabolic Design."

376. November 1, 2000, Indianapolis, IN; AAPS Annual Meeting and Exposition, "Retrometabolic Approaches to the Design of Ophthalmic Drugs."

377. November 13-16, 2000, Budapest, HUNGARY; Semmelweis University of Medicine, "The Högyes Lecture."

378. November 22, 2000, Osaka, JAPAN; Takeda Chemical Industries, Ltd., "Recent Results in Retrometabolic Drug Design."

379. February 8, 2001, Atlanta, GA; IBC 9th Annual Conference on Alzheimer's Disease, "Brain-Targeting of Drugs and Neuropeptides."

380. March 31, 2001, Tempe, AZ; Muro Asta Medica Investigator Meeting on Loteprednol Etabonate Nasal Spray, "Design of Loteprednol – A Soft Corticosteroid."

381. March 28, 2001, Basel, SWITZERLAND; Roche Pharmaceuticals, Ltd., "Design of Retrometabolism-Based and Specific Receptor-Oriented Drugs."

382. March 28, 2001, Basel, SWITZERLAND; Novartis Pharma, "Design of Retrometabolism-Based and Specific Receptor-Oriented Drugs."

383. April 17, 2001, Hawthorne, NY; Taro Pharmaceuticals USA Inc., "Design of Loteprednol Etabonate, A Novel Soft Steroid."

384. May 13-16, 2001, Amelia Island, FL; 3rd Retrometabolism-Based Drug Design and Targeting Conference (Founder and Organizer), "Design of a New Class of Soft Corticosteroids."

385. May 31, 2001, Stockholm, SWEDEN; Stockholm University, "Recent Advances in Retrometabolic Drug Design and Targeting Approaches."

386. October 25-28, 2001, San Francisco, CA; Foundation Fighting Blindness Meeting on Drug Delivery: Focusing on the Posterior Segment of the Eye, "Design of Novel Ophthalmic Drugs Using Retrometabolic Principles."

387. November 5 & 7, 2001, Gainesville, FL; UF Honors Seminar in Pharmacy Research, College of Pharmacy, "Retrometabolic Design – Magic Bullets."

388. February 13, 2002, Budapest, HUNGARY; Institute for Drug Research, Ltd., Scientific Retreat, "Retrometabolic Drug Design."

389. February 24-March 1, 2002, Ventura, CA; Drug Carriers in Medicine & Biology (Gordon Research Conference), "Brain Drug Delivery via Redox Carriers."

390. March 6-8, 2002, Gainesville, FL; 3rd Annual Heterocyclic Conference, "The Use of Dihydropyridine Pyridinium Salt Redox System for Development of Brain-Specific Drugs."

391. April 4-11, 2002, Taormina, SICILY; 6th Eilat Conference on New Antiepileptic Drugs, "Talampanel."

392. May 5-8, 2002, Reykjavik, ICELAND, 11th International Cyclodextrin Symposium, "Theoretical Insights into the Formation, Structure and Energetics of Some Cyclodextrin Complexes."

393. October 30 & November 1, 2002, Gainesville, FL; UF Honors Seminar in Pharmacy Research, College of Pharmacy, "Retrometabolic Design."

394. February 20, 2003, Budapest, HUNGARY; Institute for Drug Research, Ltd. Annual Scientific Meeting, "Drug Design and Discovery."

395. May 11-14, 2003, Palm Coast, FL; 4th Retrometabolism-Based Drug Design and Targeting Conference (Founder and Organizer), "Soft Corticosteroids: Design Considerations and Recent Advances."

396. February 5-6, 2004, Tokyo, JAPAN; Metabolism & Membrane Transport in Drug Discovery and Development Conference (MMT3D), "Retrometabolic Approaches in Drug Design and Targeting."

397. February 9, 2004, Osaka, JAPAN; Takeda Chemical Industries, Ltd., "Computer-Assisted Drug Design"; "Novel Approaches to Treat Sepsis"; Use of AMPA Antagonists for Treatment of Neurological Diseases" (three lectures).

398. February 18, 2004, Budapest, HUNGARY; Institute for Drug Research, Ltd. Annual Scientific Meeting, "Design of Novel Soft Steroids" and "Recent Advances in Talampanel" (two lectures).

399. May 8-13, 2004, Sardinia, ITALY; Eilat VII Conference on New Antiepileptic Drugs, "Talampanel."

400. May 17-19, 2004, Budapest, HUNGARY; Hungarian Biochemical Society Meeting, "Retrometabolic Drug Design, CDS and Soft Drugs."

401. June 12-17, 2004, Honolulu, HI; Controlled Release Society 31st Annual Meeting, "Drug Targeting to the Brain by Chemical-Enzymatic Approaches."

402. November 7-11, 2004, Baltimore, MD; AAPS Annual Meeting, "Insights for Drug Design Based on Metabolic Activity of the Eye – Soft Drugs and Chemical Delivery Systems."

403. February 17, 2005, Budapest, HUNGARY; 5th Retrometabolism-Based Drug Design and Targeting Conference (Founder and Organizer), "Overview of and Recent Advances in Retrometabolic Drug Delivery."

404. June 21-23, 2005, Budapest, HUNGARY; Institute for Drug Research Talampanel Investigator's Meeting, "History of Talampanel – Pre-Clinical & Toxicology."

405. September 26-28, 2005, Siófok, HUNGARY; 1st BBB Conference on Pharmaceutical Sciences, "Etiprednol Dicloacetate: Design and Development of a New Soft Steroid."

406. October 23-26, 2005, Sarasota, FL; 37th Annual Meeting of the Hungarian Medical Association of America, "Anti-inflammatory Soft Glucocorticoids. The Design and Development of Two Generations of New, Safer Drugs."

407. November 5-10, 2005, Nashville, TN; 2005 AAPS Annual Meeting and Exposition, "Can Peptides Ever Become Drugs? – Targeted Delivery of Peptides."

408. May 2, 2006, Biberach, GERMANY; Boehringer Ingelheim Research Institute, "Soft Steroids in Asthma and COPD."

409. September 5, 2006, Reykjavik, ICELAND; University of Iceland; "Design and Activity of Two Classes of Soft Steroids."

410. October 29-November 3, 2006, San Antonio, TX; AAPS Annual Meeting and Exposition, "Targeted Drug Delivery by Sequential Metabolism."

411. June 4, 2007, Göd, HUNGARY; 6th Retrometabolism-Based Drug Design and Targeting Conference (Founder and Organizer), "Transporter Enhanced Soft Corticosteroid Activity."

412. June 9, 2007, Munich, GERMANY; 6th Global Gator Meeting (University of Florida), "Safe Targeted Drugs by Retrometabolic Design: Soft Drugs and Chemical Delivery Systems."

413. August 5-10, 2007, Torino, ITALY; 41st IUPAC Congress, "Recent Developments in Retrometabolic Drug Design and Targeting Strategies."

414. November 10-15, 2007, San Diego, CA; AAPS Annual Meeting and Exposition – Special Lecture as Recipient of Distinguished Pharmaceutical Scientist Award, "Retrometabolic Drug Design and Targeting Strategies: Chemical Delivery Systems (CDS)."

415. April 24-26, 2008, Orlando, FL; Bausch & Lomb, Keynote Lecture and Symposium Honoring the 10th Anniversary of Loteprednol Etabonate, "Retrometabolic Drug Design" and "Discovery and Development of LE" (two lectures).

416. April 22, 2009, Nutley, NJ; Hoffman-La Roche, Inc., "Retrometabolic Drug Design."

417. May 10-13, 2009, Villas of Grand Cypress (Orlando), FL; 7th Retrometabolism-Based Drug Design and Targeting Conference (Founder and Organizer), "Recent Advances in Retrometabolic Drug Design (RMDD) and Development."

418. September 8-11, 2010, Primosten, CROATIA; 5th Central European Conference "Chemistry Towards Biology," "Retrometabolic Design: Soft Drugs and Chemical Delivery Systems."

419. March 8, 2011, Cambridge, MA; Novartis Institutes for Biomedical Research, "Drug Targeting by Chemical-Enzymatic Delivery Systems."

420. May 22-25, 2011, Sopron, HUNGARY; Hungarian Chemical Society National Conference Plenary Lecture as Recipient of Fabinyi Prize, "From Remote Substituent Effects to Retrometabolic Drug Design – 50 Years of Research in Chemistry."

421. June 2, 2011, Graz, AUSTRIA; 8th Retrometabolism-Based Drug Design and Targeting Conference (Founder and Organizer), "Recent Advances in Retrometabolic Design Concepts."

422. January 16-18, 2012, Tokyo, JAPAN; International Symposium on Past, Present and Future of Molecular Pharmacokinetics, "Transporters in Retrometabolic Drug Design."

423. May 12-15, 2013, Villas of Grand Cypress (Orlando), FL; 9th Retrometabolism-Based Drug Design and Targeting Conference (Founder and Organizer), "Recent Advances in Retrometabolic Drug Design (RMDD) and Targeting."

424. October 17-21, 2015, Orlando, FL; 10th Retrometabolism-Based Drug Design and Targeting Conference (Founder and Organizer); in conjunction with 20th North American ISSX Meeting, "Second Generation of Soft Steroids."

425. January 29, 2016, Newport Beach, CA; Association of Hungarian-American Academicians Scientific Meeting, "Retrometabolic Drug Design."

426. July 6-7, 2016, Tokyo, JAPAN; 30th Anniversary Symposium of the Nagai Foundation Tokyo – Link to the Past and Bridge to the Future, "The Role of the Nagai Foundation Tokyo in the Advancement of Drug Discovery Research and Retrometabolic Drug Design."

427. July 12, 2016, Tokyo, JAPAN; KAKEN Pharmaceutical Co., Ltd. (lecture in Tokyo offices, with live feed to satellite facilities), "Soft Anticholinergics."

428. October 27, 2016, Gainesville, FL; University of Florida College of Pharmacy Seminar Series, "Recent Advances in Soft Drug Design."

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5. N. Bodor and O. Mantsch, " Synthesis of 5β-Androstan-3α, 6α-diol-17-one from 16,20-Oxido-3α,6α,20-triacetoy-pregnane," Romanian Patent 65,038; November 20, 1970.

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10. N. Bodor and J. Kaminski, "1,4-Dichloro-2,2,5,5-Tetrasubstituted-3,6-Piperazinediones," U.S. Patent 3,891,649; June 24, 1975.

11. N. Bodor, K. Sloan and A. Hussain, "Novel, Transient Pro-Drug Forms of L-DOPA," U.S. Patent 3,891,696; July 29, 1975.

12. N. Bodor and J. Kaminski, "3-Chloro-Tetrahydro-1,3-Oxazines or Oxazolidines," U.S. Patent 3,897,425; July 29, 1975.

13. T. Higuchi, N. Bodor and E. Shek, "Novel Pro-Drug Derivatives of Pyridinium Aldoxime Type Cholinesterase Reactivators and Process for Preparing Same," U.S. Patent 3,929,813; December 30, 1975.

14. N. Bodor and J. Kaminski, "3-Chloro-2-Oxazolidinones," U.S. Patent 3,931,213; January 6, 1976.

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18. N. Bodor and J. Kaminski, "Method for Inhibiting Bacterial Growth with Certain Selected 3-Chloro-Tetrahydro-1,3-Oxazines or Oxazolidines," U.S. Patent 3,954,985; May 4, 1976.

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21. N. Bodor and S. Yuan, "Novel Synthesis of Optically Active M-Acyloxy-α-[(Methylamino)Methyl]Benzyl Alcohols, the Pharmaceutically Acceptable Acid Addition Salts Thereof and Intermediate Useful in the Preparation Thereof," U.S. Patent 3,966,749; June 29, 1976.

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23. N. Bodor, "Soft Quaternary Surface Active Agents Exhibiting Antibacterial Activity," U.S. Patent 3,989,711; November 2, 1976.

24. N. Bodor, "1-Hydrocarbonoyloxymethyl-3-carbamoyl or 3-Carboethoxy-Pyridinium Salts," U.S. Patent 3,998,815; December 21, 1976.

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Approximately 25 patent applications are pending as of December 2017.

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About this Book

Innovative approach to drug design that's more likely to result in an approvable drug product

Retrometabolic drug design incorporates two distinct drug design approaches to obtain soft drugs and chemical delivery systems, respectively. Combining fundamentals with practical step-by-step examples, *Retrometabolic Drug Design and Targeting* gives readers the tools they need to take full advantage of retrometabolic approaches in order to develop safe and effective targeted drug therapies. The authors, both pioneers in the fields of soft drugs and retrometabolic drug design, offer valuable ideas, approaches, and solutions to a broad range of challenges in drug design, optimization, stability, side effects, and toxicity.

Retrometabolic Drug Design and Targeting begins with an introductory chapter that explores new drugs and medical progress as well as the challenges of today's drug discovery. Next, it discusses:

- Basic concepts of the mechanisms of drug action
- Drug discovery and development processes
- Retrometabolic drug design
- Soft drugs
- Chemical delivery systems

Inside the book, readers will find examples from different pharmacological areas detailing the rationale for each drug design. These examples set forth the relevant pharmacokinetic and pharmacodynamic properties of the new therapeutic agents, comparing these properties to those of other compounds used for the same therapeutic purpose. In addition, the authors review dedicated computer programs that are available to support and streamline retrometabolic drug design efforts.

Retrometabolic Drug Design and Targeting is recommended for all drug researchers interested in employing this newly tested and proven approach to developing safe and effective drugs.

Nicholas Bodor. A Chemist from Transylvania in the American Chemical Society's Hall of Fame

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Most contributions of chemists to Medicinal Chemistry consist in discovering or inventing one or several new medicinal drugs. Very few chemists open up new methods for finding many medicinal drugs; Professor Nicholas Bodor (Nick to his friends) is such a chemist.

He was born in Satu Mare on February 1, 1939 in a family of Hungarian ethnicity. On the paternal side one can trace the roots of his Transylvanian family to the 14th century, and to the 16th century on the maternal side. From early childhood he showed exceptional qualities. He started school when he was 5 years old, two years ahead of all his classmates, and graduated first in his class at the age of 15. Based on a tough competition (180 candidates for 20 places), he was accepted in 1954 as a 15-year-old student to a five-year program as a Research Chemist at the Chemistry Faculty of the Bolyai University. All his studies had been in the Hungarian language, but in 1959 when he graduated as an organic chemist with an exceptional *red diploma*, Ceausescu's chauvinistic dictatorship closed the Bolyai University, unifying it with the Romanian counterpart (Babes Bolyai University) and discontinued courses in Hungarian.

As a result, Nick lost the promised academic position at the Bolyai University and started to work at a factory producing enameled products (dishes, stoves, etc.) in Satu Mare. He went through hard training to be an industrial engineer. In 1961, however, he was accepted at the Chemical Pharmaceutical Research Institute in Cluj (CPRI-Cluj), a subsidiary of the main Institute in Bucuresti. Because he wanted to continue his studies, he had to be accepted to the Russian-modeled doctorate (*aspirantura*). At that time, there were only two professors with the right to train aspirantura students in organic chemistry — professors Costin Nenitzescu and Eugen Angelescu, both in Bucuresti (nobody had this right in Cluj). Nick was accepted by Professor Angelescu at the end of 1961 (mainly due to the rare *red diplom*a and a personal interview), while he was still working full time at the CPRI-Cluj. Soon afterwards Professor Alexandru Silberg, who taught organic chemistry at the Babes Bolyai University in Cluj, received the right to supervise doctoral students and he became the new supervisor for Nick's doctoral research. After having finished with the mandatory oral examinations in a year, he started working on the research project, a subject he himself had selected (Isonitrosation of Substituted Nitrobenzenes, Application of the Hammett-Taft Equation) and approved by the new supervisor. Soon afterwards, quite fortunately, the Soviet-style aspirantura was converted into an Academy doctorate. At the research institute Nick had a very heavy workload. He was supposed to work only seven hours a day because of *dangerous work*. — and it was indeed, as they did not even have fume hoods. Thus, he would check out at 2:00 p.m. and immediately checked-in to start his thesis work. He worked alone every day until about 10:00 p.m. The research progressed smoothly and by 1964 he had typed (in the Romanian language) the Doctoral Thesis and the 50-page summary. The summary was sent out to some 100 selected chemists in the country. The rule was to have three Committee Members/Reviewers; two of the three had to be members of the Romanian Academy; all three had to be from different institutes in different cities.

Thus, as one of the three referees, I met Nick for the first time and this is how our friendship started. He defended his thesis (in Romanian) in January 1965, and the title *Doctor in Chimie* was approved in unanimity. The process continued with further review at the Romanian Academy of Science, and then by the Supreme Committee of Scientific Titles (such tight controls existed because at that time in Romania a significant monthly stipend was paid in addition to the salary for those who heldthe degree).

At the CPRI-Cluj Nick was responsible for many, mostly synthetic, projects. He published his first paper in 1964 in *Rev. Roumaine Chim.* in English [1] demonstrating a novel mechanism (opposite to the published work by the Syntex group) of direct iodination of 20-oxopregnanes, followed by four papers based on his thesis. However, in addition to the multiple synthetic chemical work, he was also interested in the theoretical and mechanistic aspects of organic chemistry. He was fascinated by Derek Barton's *Conformational Analysis* (Nobel Prize work) and the six brilliant papers published by M. J. S. Dewar in *J. Am. Chem. Soc.* on *The electronic basis of organic chemistry.* Nick wrote a few papers on the *Remote Effects* that had been discussed by Dewar in one of his papers. Nick did not like the demonstration of separation of substituent effects and provided an alternate proof. He sent the manuscript to Michael Dewar, who subsequently invited Nick to work at University of Texas in Austin, offering to him an R. A. Welch postdoctoral fellowship. When he asked for permission to leave, the authorities in Romania did not reply. However, due to the 1968 uprising in Czechoslovakia, he was provided an opportunity through some influential friends to be allowed to go to the University of Texas. However, he had to promise though to return in one year, which he did. Working with Michael Dewar was very rewarding and successful. Nick arrived in Austin in November 1968 and by February 1969 a joint paper was submitted to be published in *Tetrahedron* [2]. After his return to Romania, Michael Dewar invited Nick again, and he joined him in Austin in 1970. This time he did not return to Romania, and was thus sentenced *in absentia* according to the standard procedure for *defectors from the socialist regime*. Michael Dewar's semiempirical computational methods for organic substances based on molecular orbital

quantum-chemical parameters determined from empirical data were in full development [3]. In two years, Nicholas Bodor and Michael J. S. Dewar published eleven joint papers, mostly in the *Journal of the American Chemical Society*. Nick also published several papers without Dewar but with other post-doctoral students of Dewar such as Nenad Trinajstiæ from Croatia, or with Emil Pop from CPRI-Cluj, in Romania.

During this period Nick met and married Sheryl, his wife for 45 years. In order to take care of his family, Nick had to move to a different position. He accepted an offer from Professor Higuchi (University of Kansas at Lawrence, Kansas), who had started a research company, INTERx. This main job was to invent new *prodrugs* (a misnomer – predrug would be a better name for a molecule that after administration changes to an improved structure by a chemical reaction, possibly due to enzymes at the desired site). After one year he was promoted to Director of Research. In this position he authored some 70 patents and numerous publications (about 50), including his first *Science* paper [4].

In 1978 Nick was approached by the new Dean of the College of Pharmacy at the University of Florida and offered a position there as a Full Professor (a rare occurrence for a young researcher) and subsequently in half a year was named Chair of the Department of Medicinal Chemistry. He is now a Graduate Research Professor Emeritus (active) at the College of Pharmacy, University of Florida (UF) in Gainesville. In 1979 Nick received the first of a long line of NIH Grants. He built a group of coworkers that at some point consisted of up to 75 members of vastly different backgrounds. More than 50 doctoral students and more than 100 postdoctoral fellows were trained by him. He is also Executive Director of the College's Center for Drug Discovery that he founded in 1986.

Here one needs a brief digression for describing the concepts of *synthon*, and *retrosynthetic (or disconnection) approach*. At present, about 100 million chemical structures are known and recorded in the *Chemical Abstracts Service* (CAS) of the American Chemical Society, the vast majority of these are organic compounds obtained in the search for new medicinal drugs. Up until the 1970s, in order to find whether a chemical structure was new, one had to spend days in the library leafing through *Chemical Abstracts Indexes* and looking at possible IUPAC names for the particular isomer with the analytically found molecular structure. Nowadays, this only takes minutes thanks to chemical applications of graph theory that deal with molecular graphs (hydrogen-depleted graphs with vertices for atoms and edges for covalent bonds). The graphs have to be assembled directly on the computer screen with the CAS SciFinder Program. Thus, without words or names, the structure is directly found and chemistry is thus the best documented science. Of course, when using words, chemistry is not different from other sciences. Molecular graphs can be cut in various ways, and computer programs first introduced by E. J. Corey (1990 Nobel Prize for Chemistry) show all possibilities for the assembly of smaller units (*synthons*) into a target molecule – this is the r*etrosynthetic (or disconnection) approach*.

In the late 1970s Nicholas Bodor applied a similar concept that includes enzyme-catalyzed reactions occurring in living cells, and invented the retrometabolic drug design system [5]. It is based on the mechanism of drug action in various tissues and it aims at improving the therapeutic index and diminish unwanted side effects. It combines two complementary concepts, namely (i) *chemical delivery systems* (CDS) with (ii) *soft drugs* (SD). In general*, a CDS is inactive* by design and is enzymatically *activated* stepwise to produce the active drug *only* (or preferentially) at the target site/organ. At the other end of the retrometabolic design loop are the soft drugs. A *SD is an active drug,* designed in such a way to be *deactivated* in a predictable and controllable way after it achieves its therapeutic role. One method of the soft drug principles of Dr. Bodor is to apply the *inactive metabolite approach.* According to this, the design starts with an inactive metabolite of a known drug which is then chemically modified (activated) to produce an isosteric/isoelectronic analogue of the active drug which then, when applied at the site of need, will perform the desired function. However, when it is absorbed or reaches the systemic circulation, it will be deactivated to the very inactive metabolite the design started from. By design this deactivation takes place by hydrolytic enzymes and avoids the usual oxidative metabolic processes. On the other side of the retrometabolic drug design loop are the CDSs. A striking example for a CDS introduced by Bodor is the *brain targeting of drugs* based on a redox targetor system, such as 1,4-dihydrotrigonelline↔trigonelline salt. The structurally similar, ubiquitous $NAD^+ \leftrightarrow NADH$ redox coenzyme system assures oxidation of the initial lipophilic drug targetor conjugate to the hydrophilic, inactive quaternary form, which is due to the unique architecture of the blood-brain barrier (BBB), is *locked-in* the brain, but is eliminated fast from the whole body. Thus, further enzymatic liberation of the drug takes place essentially only in the brain, in a sustained manner. The first successful brain delivery-targeting of neuropeptides was accomplished by Bodor by combining the above redox targetor system with strategically selected amino acid *spacers* and large lipophilic modifiers, called *molecular packaging* undergoing *sequential metabolism*, a general method applied now to a variety of neuropeptides, which was highlighted by the *Harvard Health Letters* as one of the top ten discoveries of 1992. Other types of CDSs invented by Dr. Bodor target drugs to the eye, to the lungs and to specific receptors.

Among hundreds of drugs found worldwide through Nick's methodology and his computerized expert system, one should mention the soft drug Loteprenol Etabonate, an ophthalmic corticosteroid invented by Nick that is used in suspensions against eye inflammation (for instance, after cataract surgery) and allergic diseases. It was approved in 1998 and is sold in five different products. It is one of the most important and safest eye drugs. Another eye-specific drug invented by Nick is betaxoxime, which is inactive when administered but becomes active in eyes after converting, by design, an oxime into a ketone function, followed by its stereospecific reduction.

Nick organizes the biennial Retrometabolism Based Drug Design and Targeting Conference. In addition to Florida, meetings in this international series have also taken place in Japan, Hungary and Austria. He has authored or co-authored 520+ papers and over 200 patents. More than half of these patents were assigned to the University of Florida.

The first two companies that he founded were Pharmatec (which went public in1985) and Xenon Vision in1986, both with participation of the University of Florida. In 1999 he accepted a position at IVAX Corp., a world-wide pharmaceutical company (some 12,500 employees) as its Chief Scientific Officer. He was for several years President of the IVAX Research Institute, Inc. and Managing Director of the IVAX Drug Research Institute in Budapest, Hungary (formerly the Central

Pharmaceutical Research Institute of Hungary) with a leave of absence from the University of Florida. After IVAX merged with Teva in 2006, he returned to UF and additionally started Bodor Laboratories Inc. where he works today with both his son Erik and daughter Nicole to continue development of his new technologies. One current project focuses on Sofpironium Bromide, a soft anticholinergic invented by Nick with unique structure and properties which has recently shown success in a Phase IIb study for the treatment of hyperhidrosis, a medical condition with significant unmet needs.

Nicholas Bodor has been honored by numerous awards, among which are:

- Member of the Hungarian Academy of Sciences (1995)
- Fellow of the American Academy of Pharmaceutical Sciences (1983)
- Fellow of the American Association of Pharmaceutical Scientists (1986)
- Fellow of the American Association for the Advancement of Science (1989)
- Fellow of the American College of Clinical Pharmacology (1991)
- Honorary Member of the Panhellenic Society of Pharmacists (1989)
- Fellow of the International Nagai Foundation Tokyo (1995)
- AACP Volwiler Research Achievement Award (1997)
- AAPS Distinguished Pharmaceutical Scientist Award (2007)
- Florida Scientist of the Year (1984)
- Doctor Honoris Causa, University of Florida (2005)
- Doctor Honoris Causa, Technical University of Budapest (1989)
- Doctor Honoris Causa, Medical University of Debrecen (1990)
- Fabinyi Prize of the Hungarian Chemical Society, given to eminent scientists living outside Hungary (2010)
- Gold Cross of Merit of the Hungarian Republic (2004)
- Commander's Cross of the Order of Merit of the Hungarian Republic (2010)
- Hall of Fame of the American Chemical Society (2012)

In addition, a Distinguished Professorship named the *Nicholas Bodor Professor in Drug Discovery*, was established at the University of Florida in 2007. Furthermore, a Nicholas Bodor Distinguished Lectureship was introduced in 2014.

Dr. Emil Pop, who had been his fellow researcher at CPRI-Cluj, was invited by Nick to Gainesville, Florida, to work first at the University of Florida and then at Pharmatec/Pharmos as Director of Chemistry. Later, Nick helped Dr. Pop to established his successful synthesis company, Alchem Corp. (Dr. Pop passed away recently). For about the last 15 years, Professor Bodor has also supported two scholarships at two high schools in Romania, his alma mater in Satu Mare and at the Bolyai College in Tirgu Mures, awarding annually a diploma and significant monetary support to the best student in chemistry.

I believe that Professor Nicholas Bodor's remarkable activity deserves to be better known and appreciated by Romanian chemists.

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