Abstract: As we have drawn the year 2008 to a close, we would like to take a moment to sum up the number of technological communications that AMRI scientists have contributed to the scientific community during this year. Please read through this document for a full list of abstracts (as they appear either with the original documents or taken from the SciFinder database) for all of the publications, presentations and patent applications that appeared during the year. We hope to make this bibliographical summary a regular year-end contribution.
2009 AMRI Research Publications

During 2008, twelve research articles have appeared in peer-reviewed scientific journals that described innovations conceived by AMRI scientists. In most of these cases, these manuscripts were written by AMRI lead authors to communicate independent research, or were co-authored with customers to communicate research in collaboration with AMRI. Below are the bibliographies for these publications, including the abstracts, as they appeared with the original documents. The underlined name(s) indicate the lead author(s).

   Matthew E. Voss,\(^1\) Catherine M. Beer,\(^1\) Scott A. Mitchell,\(^2\) Peter A. Blomgren\(^2\) and Paul E. Zhichkin\(^1\).
   \(^1\)Medicinal Chemistry Department, AMRI and \(^2\)CGI Pharmaceuticals, Inc.

   ![Reaction Scheme](image)
   \[\text{1. NaOCH}_3\text{, CH}_3\text{OH, rt} \rightarrow \text{2. (CH}_3\text{O)}_2\text{CHCH}_2\text{NH}_2\text{, HOAc, reflux} \rightarrow \text{3. aq HCl, reflux} \]
   17 examples, yields 49-99%
   \(R =\) heteroaryl, electron-deficient aryl

   Brian T. Gregg, Kathryn C. Golden and John F. Quinn
   Medicinal Chemistry Department, AMRI

   ![Reaction Scheme](image)

   Raymond E. Conrow,\(^1\) Pete Delgado,\(^1\) W. Dennis Dean,\(^1\) Gary R. Callen\(^2\) and Scott V. Plummer\(^2\).
   \(^1\)Alcon Research, Ltd and \(^2\)AMRI Syracuse Research Center

   ![Reaction Scheme](image)
   \[\text{1. Cbz-L-Ala-Osuc, K}_2\text{CO}_3, \text{MeCN} \rightarrow \text{2. BrBr, K}_2\text{CO}_3, 35 ^\circ\text{C} \]
   76% over two steps
   \[\text{1. Red-Al, PhMe, -25 ^\circ\text{C}; Ac}_2\text{O, DMAP, rt} \rightarrow \text{2. Et}_{3}\text{SiH, BF}_3\text{•OEt}_2, \text{CH}_2\text{Cl}_2 \]
   60% over two steps


1Discovery Chemistry Research and Technology, 2Drug Disposition Research, 3Cancer Research, 4Lead Optimization Biology and 5Chemical Product Research and Development Departments, Lilly Research Laboratories, A Division of Eli Lilly and Company and 6Medicinal Chemistry Department, AMRI

6. “Structure–activity relationships of anthranilamide-based factor Xa inhibitors containing piperidinone and pyridinone P4 moieties”, *Bioorganic & Medicinal Chemistry Letters* 2008, 18(9), 2845–2849. James R. Corte,1 Tianan Fang,1 Donald J. P. Pinto,1 Wei Han,a Zilun Hu,1 Xiang-Jun Jiang,1 Yun-Long Li,1 Jolicia F. Gauuan,2 Mark Hadden,2 Darren Orton,2 Alan R. Rendina,1 Joseph M. Luettgen,1 Pancras C. Wong,1 Kan He,1 Paul E. Morin,1 Chong-Hwan Chang,1 Daniel L. Cheney,1 Robert M. Knabb,1 Ruth R. Wexler1 and Patrick Y. S. Lam1

1Bristol-Myers Squibb Research and Development, Princeton, NJ and 2Medicinal Chemistry Department, AMRI
7. “Structure-based design and subsequent optimization of 2-tolyl-(1,2,3-triazol-1-yl-4-carboxamide) inhibitors of p38 MAP kinase”, Bioorganic & Medicinal Chemistry Letters 2008, 18(11), 3251–3255.
Departments of Medicinal Chemistry, Immunology and Inflammation and Biologics and Biomolecular Sciences, Boehringer Ingelheim Pharmaceuticals, Inc., Research and Development Center, 900 Ridgebury Road, Ridgefield, CT 06877 USA and Medicinal Chemistry Department, AMRI

Ian C. Cotterill, Joseph O. Rich, Marc D. Scholten, Lyudmila Mozhaeva and Peter C. Michels
Discovery R&D, Metabolism and Biotransformations Department, AMRI and United States Department of Agriculture, Agricultural Research Service, National Center for Agricultural Utilization Research, Bioproducts and Biocatalysis, 1815 N. University St., Peoria, Illinois

9. “1,4-Cyclohexadiene with Pd/C as a rapid, safe transfer hydrogenation system with microwave heating”, Tetrahedron Letters 2008, 49(42), 6137-6140.
John F. Quinn, Dana A. Razzano, Kathryn C. Golden and Brian T. Gregg
Medicinal Chemistry Department, AMRI
Christer Alstermark,\textsuperscript{1} Kosrat Amin,\textsuperscript{1} Sean R. Dinn,\textsuperscript{2} Thomas Elebring,\textsuperscript{1} Ola Fjellström,\textsuperscript{1} Kevin Fitzpatrick,\textsuperscript{2} William B. Geiss,\textsuperscript{2} Johan Gottfries,\textsuperscript{1} Peter R. Guzzo,\textsuperscript{2} James P. Harding,\textsuperscript{2} Anders Holmèn,\textsuperscript{1} Mohit Kothare,\textsuperscript{2} Anders Lehmann,\textsuperscript{1} Jan P. Mattsson,\textsuperscript{1} Karolina Nilsson,\textsuperscript{1} Gunnel Sundèn,\textsuperscript{1} Marianne Swanson,\textsuperscript{1} Sverker von Unge,\textsuperscript{1} Alex M. Woo,\textsuperscript{2} Michael J. Wyle\textsuperscript{2} and Xiaozhang Zheng\textsuperscript{2}
\textsuperscript{1}AstraZeneca R&D Mölndal, S-431 83 Mölndal, Sweden and \textsuperscript{2}Medicinal Chemistry Department, AMRI

Vadim V. Mozhaev, Lyudmila V. Mozhaeva, Peter C. Michels and Yuri L. Khmelnitsky
Discovery R&D, Metabolism and Biotransformations Department, AMRI

Paul E. Zhichkin, Lisa H. Peterson, Catherine M. Beer and W. Martin Rennells
Medicinal Chemistry Department, AMRI
1. 2 DMF/(COCl)$_2$
2. py, ArNH$_2$
3. ethylenediamine

All three steps in one pot.
31 examples. Yield 34-91%.

D. Craig Hopp, Dennis J. Milanowski, Joshua Rhea, Daniel Jacobsen, John Rabenstein, Chris Smith, Khadidja Romari, Midori Clarke, Linda Francis, Macarena Irigoyen, Michele Luche, Grant J. Carr and Ulla Mocek
Discovery R&D, Bothell Research Center, AMRI
2008 AMRI Review Publications (including Book Chapters)

AMRI scientists were also lead authors on five review publications during 2008, many appearing as chapters in serial book series or in scientific journals, and are abstracted in scientific databases.

   Dmytro O. Tymoshenko, Medicinal Chemistry Department, AMRI

   Dmytro O. Tymoshenko, Medicinal Chemistry Department, AMRI

   Larry Yet, Singapore Research Centre, AMRI

   Larry Yet, Singapore Research Centre, AMRI

   Steven J. Collier, Singapore Research Centre, AMRI
AMRI Research Presented (Oral Papers and Posters)

At least seven presentations were given by AMRI scientists during the year 2008, both as talks given at scientific meetings (two) and as posters presented (four). At this year’s Northeast Regional American Chemical Society Meeting, these two presentations were given by AMRI scientists to audiences of about fifty attendees.

   Matthew E. Voss, Jeffery M. Ralph, Dejian Xie, David D. Manning, Mark A. Wolf, Paolo Pasetto, Matthew D. Surman, Yeyu Cao, Thomas D. Friedrich, Denise Peace and Ian L. Scott
   1Medicinal Chemistry and 2Discovery Research & Development, Chemistry Departments, AMRI and 3Center for Immunology and Microbial Disease, Albany Medical College

   Brian T. Gregg
   Medicinal Chemistry Department, AMRI

   Brian T. Gregg, John F. Quinn, Dmytro O. Tymoshenko, Kathryn C. Golden, Dana A. Razzano
   Medicinal Chemistry Department, AMRI

4. **Oral Presentation:** “Iridium- and Palladium-Catalyzed Syntheses of (S)-(+) and (R)-(-) Conine from Enantiopure Allylic Alcohols”, NERM-123: Abstracts of Papers, 37th Northeast Regional Meeting of the American Chemical Society, Burlington, VT, United States, June 29-July 2, 2008.
   R. Jason Herr, Matthew S. Dowling, Amanda C. Scampini, Tiffany M. Smith
   Medicinal Chemistry Department, AMRI

5. **Poster Presentation:** “2,3-Diaminopyrazines as Inhibitors of Rho Kinase”, NERM-251: Abstracts of Papers, 37th Northeast Regional Meeting of the American Chemical Society, Burlington, VT, United States, June 29-July 2, 2008.
   Discovery Research & Development, Chemistry Department, AMRI
6. **Poster Presentation:** “Discovery of 2-aminobenzoxazole carboxamides as 5-HT3 receptor antagonists”, MEDI 205 (Division of Medicinal Chemistry), 235th ACS National Meeting, New Orleans, LA, April 6-10, 2008. Brian I. Bliss,¹ Kevin L. Christensen,² Marlene L. Cohen,⁵ Russell J. DeOrazio,⁴ Svetlana Dobritsa,² David J. Fairfax,¹ Kevin Fitzpatrick,⁴ Peter R. Guzzo,⁴ James P. Harding,¹ Carla Hassler,⁴ Matthew Isherwood,⁴ John P. Lindsay,³ Jun-Ho Maeng,⁴ David D. Manning,⁴ Liaqat Masih,⁴ Vadim V. Mozhaev,³ Zhicai Yang⁴ and Julianne V. Zaremba³ ¹Medicinal Chemistry, ²Discovery Research & Development, In Vitro Biology, ³Discovery Research & Development, Metabolism and Biotransformation and ⁴Discovery Research & Development, Chemistry Departments, AMRI and ⁵Creative Pharmacology Solutions LLC


Patent Applications Filed and Issued containing AMRI Scientists

The process of obtaining a patent for an invention often takes several years, from the filing of the application through the subsequent review and issuance by various national patent offices. During this year, nine patent applications were filed by AMR Technology, Inc, USA (our corporate holding company for patents assigning all rights to AMRI as the owner of the intellectual property). In addition, three previously filed patent applications were issued as full US patents. In all cases, AMRI scientists were named as co-inventors. Several other patent applications filed by customers and collaborators were also published during the year, in which AMRI scientists were named as co-inventors (four listed below).

Patent applications filed by AMRI covering novel intellectual property (IP) owned by AMR Technology, Inc., USA:

   1Discovery R&D, Chemistry Department, AMRI and 2Bristol-Myers Squibb Company

   Discovery R&D, Chemistry Department, AMRI

   Peter Guzzo, Matthew D. Surman, Alan J. Henderson, Mark Hadden and May Xiaowu Jiang
   Discovery Research R&D, Chemistry Department, AMRI

   Mark W. Wolf,1 Peter R. Guzzo1 and Ian L. Scott2
   1Discovery R&D, Chemistry and 2Discovery R&D, Lead Discovery, AMRI
Mark W. Wolf, Peter R. Guzzo and Ian L. Scott
1Discovery Research R&D, Chemistry and 2Discovery R&D, Lead Discovery, AMRI

David J. Fairfax and Zhicai Yang
1Medicinal Chemistry and 2Discovery R&D, Chemistry, AMRI

David J. Fairfax and Zhicai Yang
1Medicinal Chemistry and 2Discovery R&D, Chemistry, AMRI

Shuang Liu, Yuh-Lin Allen Yang, Aruna Sambandam, Bruce F. Molino and Richard E. Olson
1Discovery R&D, Chemistry, AMRI and 2Bristol-Myers Squibb Company

Peter R. Guzzo, Bruce F. Molino, Wenge Cui, Shuang Liu and Richard E. Olson
1Discovery R&D, Chemistry, AMRI and 2Bristol-Myers Squibb Company

Issued patents previously filed as applications by AMRI:

Bruce F. Molino and Zhicai Yang
Discovery Research R&D, Chemistry, AMRI
Bruce F. Molino and Zhicai Yang
Discovery Research R&D, Chemistry, AMRI

James P. Beck,1 Anthony D. Pechulis2 and Arthur E. Harms2
1DuPont Pharmaceuticals Company and 2Medicinal Chemistry Department, AMRI

Some patents filed by collaborators/customers of AMRI containing AMRI scientists as co-inventors, but for which AMRI is not a co-assignee (NOT a fully inclusive list):

1. “Pyridazinone derivatives useful as glucan synthase inhibitors”, PCT International Application Publication WO 2008/115381 A1 (Schering Corporation, USA and AMRI). Pauline C. Ting,1 Robert G. Aslanian,1 Jianhua Cao,1 David Won-Shik Kim,1 Rongze Kuang,1 Gang Zhou,1 R. Jason Herr,2 Andrew J. Zych,2 Jinhai Yang,2 Heping Wu1 and Nicolas Zorn1
1Medicinal Chemistry Department, Schering-Plough Research Institute and 2Medicinal Chemistry Department, AMRI

Douglas W. Beight,1 Timothy P. Burkholder,1 Todd V. Decollo,1 Alexander G. Godfrey,1 Charles R. Heap,2 Chi-Hsin Richard King,1 Hong-Yu, Li,1 William T. McMillen,1 J. Scott Sawyer,1 Yan Wang,1 Clive G. Diefenbacher,1 Thomas A. Engler,1 Sushant Malhotra1 and Sreenivasa R. Mundla1
1Eli Lilly and Company and 2Medicinal Chemistry Department, AMRI

R. Jason Herr,1 Louis N. Junghem,2 John M. McGill, III,2 Kenneth J. Thrasher2 and Muralikrishna Valluri1
1Medicinal Chemistry Department, AMRI and 2Eli Lilly and Company

Pier F. Cirillo,¹ Donghong A. Gao,¹ Daniel R. Goldberg,¹ Abdelhakim Hammach,¹ Ming-Hong Hao,¹ Victor M. Kamhi,¹ Neil Moss,¹ Matthew R. Netherton,¹ Kevin C. Qian,¹ Mark. S. Ralph,¹ Lifen Wu,¹ Zhaoming Xiong¹ and Ronald A. Aungst, Jr.²

¹Boehringer Ingelheim Pharmaceuticals, Inc. and ²Medicinal Chemistry Department, AMRI