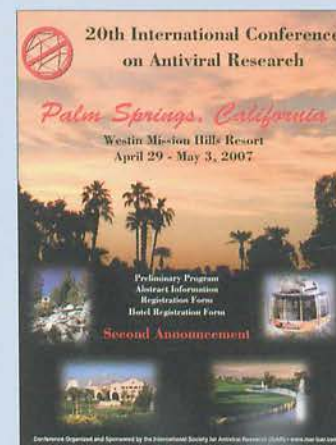
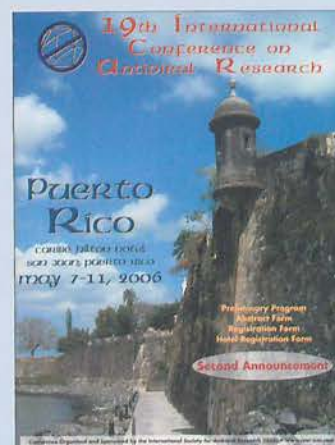
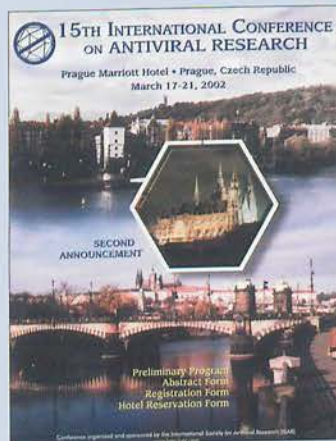
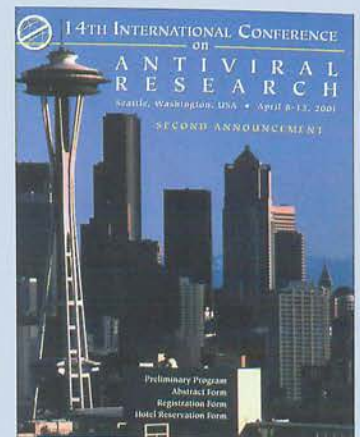
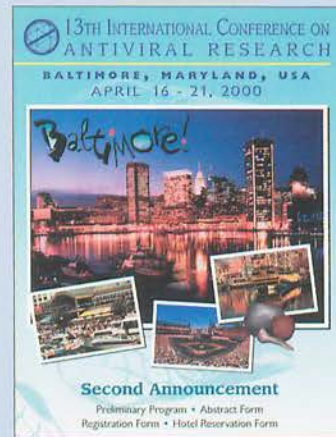
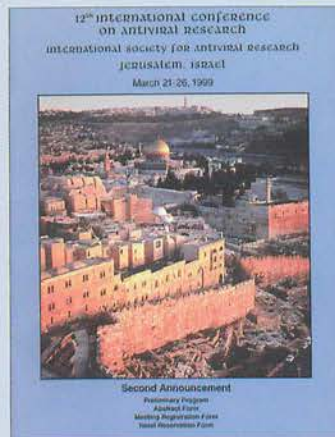
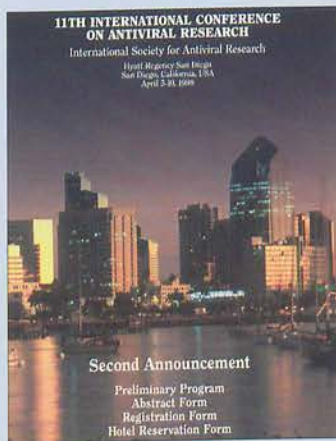


The International Society for Antiviral Research:

1998 – 2007

The Second Decade





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Antiviral Research:

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On behalf of the Society, thanks are extended to all the members who assisted in the production of this document. Your contributions are much appreciated. Special thanks to William M. Shannon, Ph.D., the principal author, who did yeoman work in writing the text. We believe you will find it informative and easy reading due to his considerable efforts, for which we are grateful. Special thanks also to George J. Galasso, Ph.D., who provided valuable input, helpful advice, and the logistical coordination that facilitated the production of this publication.

The International Society for Antiviral Research: The Second Decade (1998-2007)

Section One - The Continued Growth and Importance of Antiviral Research as a Major Scientific Discipline

As we reflect on the second 10 years of the International Society for Antiviral Research (ISAR) and of its sponsorship of the annual International Conference on Antiviral Research (ICAR), we are struck by the fact that there has been a steady growth in the global perception of the real importance of antiviral research as a scientific discipline, a specialized field of medicine that is clearly producing positive results for the benefit of mankind. During this period, we have become much more aware of the very significant impact that our Society and its membership has had on biomedical science in the area of developing effective and selective treatments for important viral diseases. As the late Frank M. Schabel, Jr. (Southern Research Institute), one of the early pioneers in antiviral research, used to like to say: "There's no success like success." During the past decade, there has been intense, worldwide media attention and publicity devoted to the stepwise advances and many real successes that have occurred in our collective antiviral research and development efforts worldwide. Consequently, there has been a widespread expansion of public awareness and interest in the use of antiviral drugs. Along with this new awareness and interest, there has also been a concomitant increase in public expectations as to our future ability to combat important viral diseases with drugs. Frank would have been amazed at the success and broad acceptance of antiviral research as a new scientific discipline. This relatively rapid growth in general interest and attention to what is happening in our very specialized field of endeavor initially resulted from the large amount of work that resulted in the successful development of new antiviral drugs with which to treat genital herpesvirus infections and, subsequently, to treat deadly HIV-1 infections. Much attention has been focused on the progress made in the continuing efforts to stem the disastrous worldwide AIDS pandemic. Then, there has been a new public awareness of expanded antiviral drug research in response to the increased incidence of hepatitis virus infec-

tions in the population, with new treatments for patients infected with hepatitis B or hepatitis C viruses. In addition, there have been discussions concerning the possibility of treating other potentially important viral diseases of public health importance such as those caused by the SARS coronavirus, West Nile encephalitis virus, and monkeypox, i.e., viral diseases that have appeared to dominate the news in recent times.

High visibility has also been given to attempts to provide protection and biodefense against other emerging virus infections and potential bioterrorist threats, especially after the events following the historic 9/11 terrorist attacks on the United States. More recently, there has been broad media coverage of the successful efforts to develop newer and more effective antiviral drugs for the treatment and prevention of influenza virus infections and of their potential use for the control of pandemic influenza. The identification of new H5N1 avian flu strains causing deaths in Asia and the Middle East has raised the specter of another possible pandemic similar to the deadly 1918 Spanish flu pandemic and media attention has turned to the potential use of antiviral drugs in such a future epidemic on an almost even footing with its coverage of the efforts to develop a vaccine. It is obvious that the age of antiviral chemotherapy and chemoprevention has arrived. The general public is now fully aware of the potential usefulness and value of antiviral research and development. The drugs Relenza and Tamiflu have become well known household names in the United States because of the frequency with which they have been mentioned during evening newscasts on national television, both on network and cable TV shows. Anti-herpesvirus drugs currently provide approximately \$1 billion per year in pharmaceutical sales revenues because of direct consumer marketing. People around the world are well aware of the life-saving potential of antiviral drugs. They have seen the human immunodeficiency

ciency virus (HIV) successfully targeted by newer and more effective combinations of antiviral drugs that have put infected AIDS patients in remission from their disease for longer and longer periods of time. The combination antiviral chemotherapy approach has been widely observed and documented to significantly extend the life expectancies of infected patients. We have also seen incremental improvements in the effectiveness and selectivity of these new drug combinations for the treatment of AIDS. Meanwhile, there is still no effective and approved HIV-1 vaccine available to date for the prevention of this insidious infectious disease.

When one examines the growing list of antiviral drugs that have now received approval by the U. S. Food and Drug Administration (FDA) for marketing and clinical use (See Table 1), it is immediately apparent that 28 of the 62 currently approved antiviral drugs and antiviral drug combinations (i.e., 45% or almost half) are directed toward the treatment of HIV/AIDS infections. Of these anti-HIV drugs, 19 (68%) were approved between 1997 and 2006. Robert T. (“Chip”) Schooley (University of California-San Diego) reviewed the status of anti-retroviral drug research and development at the 19th ICAR in San Juan, Puerto Rico with a plenary lecture entitled “AIDS Therapeutics 20 Years After AZT: Are We There Yet?” In his lecture, he listed chronologically the steady advances in our understanding of HIV replication, HIV disease pathogenesis, and anti-HIV drug research and development - from AZT, approved in 1987, to the latest approved combinations of anti-HIV agents such as GlaxoSmithKlines’s Trizivir (AZT + 3TC + abacavir) and Gilead’s Atripla (tenofovir + emtricitabine + Efavirenz). As with the approved anti-herpesvirus drugs, nucleoside analogs as a chemical class have provided us with some of our most potent and effective anti-HIV agents as well. The anti-HIV drug abacavir (Ziagen), approved in 1998, was developed by Glaxo Wellcome based on the earlier identification of Carbovir as a potent and selective anti-HIV agent, the first public report of which was made at the 2nd ICAR held in Williamsburg, VA in 1988 by Robert Vince (University of Minnesota) and Bill Shannon (Southern Research Institute) and their many collaborators at the NCI. Carbovir and its derivatives, including their potential use in combina-

tions with other anti-HIV drugs, were eventually licensed to the Burroughs Wellcome Company by the University of Minnesota. Abacavir, a 6-substituted cyclopropylamino analog of Carbovir that was subsequently identified by scientists at BW, served as an intracellular monophosphate prodrug of Carbovir monophosphate to which it was metabolized within the cell and then further converted to Carbovir triphosphate, the active form of the drug. Following the development of abacavir and its approval for marketing and clinical use, substantial royalties were paid by Glaxo Wellcome to the University of Minnesota. These funds have recently been used to develop a new Center for Drug Design on the University of Minnesota Medical Center campus in Minneapolis, MN. This successful outcome represents a clear example of the benefits of scientific interchanges and collaborations between universities, research institutes, government, and industry, an idea that has been fomented, encouraged and ardently supported through the establishment of the ISAR and its associated ICAR. Abacavir was combined with AZT and 3TC to produce GSK’s three-drug synergistic anti-HIV nucleoside analog combination Trizivir, approved in 2000. Gilead’s Tenofovir, approved in 2001, and Emtricitabine, approved in 2003, have been combined to produce Truvada, approved in 2004. When formulated with Efavirenz, a non-nucleoside RT inhibitor, Truvada becomes Gilead’s three-drug anti-HIV combination Atripla, a product developed through a joint venture between Bristol-Myers Squibb and Gilead Sciences and approved by the FDA in 2006. John C. Martin, CEO of Gilead Sciences and Past President of ISAR, remarked that “when we acquired Triangle Pharmaceuticals and FTC, we never thought that we would make so much progress so rapidly.” He credits the multidisciplinary nature of ISAR, which allows active interactions and collaborations to occur between chemists, biologists, and clinicians for these advances and he gives major credit to the government scientists at the NIH and the FDA for assisting and implementing processes that accelerate access to antiviral drugs. The recently implemented “New Guidance for Combination Products” issued by the FDA has allowed for the rapid review of new combination drug applications and for the fast tracking of antiviral drug combinations like Truvada (approved after 4½ months) and Atripla (approved

after only 2½ months). According to Chip Schooley, these fixed-dose combinations “have been quite effective in helping to reduce the problems of drug resistance and have also resulted in simplification by co-formulation.” He remarked that “in 20 years, we have gone from no drugs for HIV/AIDS, to proof of concept, to highly-active antiretroviral therapy (HAART), to one pill once a day” and that “this has to be considered good progress!” But he also remarked that “this is not the time to cut back on antiviral therapeutic research” and that “we need more drugs, better drugs, and better toxicity management.”

From the mid 1990’s on, several other classes of anti-HIV drugs have been identified, notably the protease inhibitors (PIs) and the non-nucleoside reverse transcriptase inhibitors (NNRTIs). Effective and approved anti-HIV drugs have come from both of these antiviral categories. Of the 11 approved protease inhibitors, 8 (73%) have been approved since 1997. These anti-HIV drugs, approved for use during the past decade of the Society, include Nelfinavir (1997), Amprenavir (1999), Lopinavir (2000), Kaletra (the combination of Lopinavir + Ritonavir; 2000), Lexiva (2003), Reyataz (2003),

Tiprinavir (2005), and Darunavir (2006). Approval was given to three NNRTIs: Nevirapine (1996), Delavirdine (1997), and Efavirenz (1998). When these drugs, which inhibit HIV by different mechanisms of action, were combined with anti-HIV nucleoside analogs, synergistic clinical efficacy was achieved and we witnessed the most important advances in the treatment of AIDS since the beginning of the epidemic. During the past 10 years, we have also been encouraged to hear reports of steady advances in the development of HIV entry inhibitors, a new class of antivirals, and of studies with combinations of these agents with which to block virus replication at the point of virus entry into the T-lymphocyte. T-20 (Fuseon) was the first fusion inhibitor to be approved by the FDA and second-generation fusion inhibitors such as T-1249 are being developed. New HIV entry inhibitors, CCR5 antagonists, are advancing in clinical development by Pfizer and by Schering-Plough, while GSK and ONO have earlier pipeline candidates under evaluation. Another molecular target for antiviral attack has been the HIV integrase and new antiviral drugs that inhibit this critical enzyme are currently being developed by Merck, by Gilead, and by GSK in partnership with Shionogi.

TABLE 1
CURRENT U. S. FDA-APPROVED ANTIVIRAL DRUGS *

Drug	Year Approved
Anti-HIV Drugs	
Nucleoside RT Inhibitors and Combinations:	
Zidovudine (AZT; Retrovir)	1987
Didanosine (ddI; Videx)	1991
Zalcitabine (ddC; Hivid)	1992
Stavudine (d4T; Zerit)	1994
Lamivudine (3TC; Epivir)	1995
Combivir (AZT + 3TC)	1997
Abacavir (ABC; Ziagen)	1998
Trizivir (AZT + 3TC + ABC)	2000
Tenofovir disoproxil fumarate (Viread)	2001
Emtricitabine (Emtriva; FTC)	2003
Truvada (Tenofovir + Emtricitabine)	2004
Epzicom (3TC + ABC)	2004
Atripla (Tenofovir + Emtricitabine + Efavirenz)	2006

Protease Inhibitors:

Saquinavir (Invirase; Fortovase)	1995
Indinivir (Crixivan)	1996
Ritonavir (Norvir)	1996
Nelfinavir (Viracept)	1997
Amprenavir (Agenerase)	1999
Lopinavir (Aluviran)	2000
Kaletra (Lopinavir + Ritonavir)	2000
Lexiva (Fosamprenavir Calcium)	2003
Reyataz (Atazanavir; Zrivada; Latazanavir)	2003
Tipranavir (Aptivus)	2005
Darunavir (Prezista)	2006

Non-Nucleoside RT Inhibitors:

Nevirapine (Viramune)	1996
Delavirdine (Rescriptor)	1997
Efavirenz (Sustiva)	1998

Viral Fusion Inhibitors:

T-20 (Fuzeon; Enfuvirtide; Pentafuside)	2003
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Anti-HBV Drugs

Intron A (Interferon alpha-2b)	1983
Roferon A (Interferon alpha 2a)	1984
Epivir-HBV (3TC; Lamivudine)	1998
Pegasys (Pegylated interferon alpha-2a)	2002
Hepsera (Adefovir dipivoxil)	2002
Baraclude (Entecavir)	2005

Anti-HCV Drugs

Intron A (Interferon alfa 2b)	1983
Roferon A (Interferon alfa 2a)	1984
Infergen (Interferon alfacon-1; Intermune)	1997
Rebetol (Ribavirin)	1998
Rebetron (Intron A + Rebetol)	1998
Peg-Intron (Pegylated Interferon alfa 2b)	2001
Pegasys (Pegylated Interferon alfa 2a)	2002
Copegus (Ribavirin)	2002
Peginterferon (Pegasys + Copegus)	2002
Ribavirin, generic, stand alone	2004

Anti-Herpesvirus Drugs

Idoxuridine (IDU; Stoxil; Herplex; Dendrid)	1963
Vidarabine (Ara-A; Vira-A)	1976
Trifluridine (Viroptic)	1980
Acyclovir (ACV; Zovirax)	1982
Ganciclovir (DHPG; Cytovene)	1989
Foscavir (PFA; Foscarnet)	1991
Famciclovir (Famvir)	1994
Valacyclovir (Valtrex)	1995
Cidofovir (HPMPC; Vistide)	1996

Penciclovir (Denavir)	1996
Fomivirsen (Vitravene)	1998
Abreva (n-docosanol), OTC	2000
Valganciclovir (Valcyte)	2001

Anti-RSV Drugs

Ribavirin (Virazole)	1984
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Anti-Influenza Drugs

Symmetrel (Amantadine HCl)	1966
Flumadine (Rimantadine HCl)	1993
Relenza (Zanamivir)	1999
Tamiflu (Oseltamivir)	1999

Treatments for Genital Warts

Alferon N (Interferon alfa n3)	1989
Imiquimod (Aldara)	1997

*As of August, 2006

Treatment for chronic hepatitis B virus (HBV) infections, which is a serious disease afflicting an estimated 1.25 million people in the United States and causing more than 5,000 deaths each year, has improved significantly during this past decade. A number of anti-HBV drugs have now been identified and used in the clinical management of this disease. These include Eпивir-HBV (3TC; Lamivudine), Pegasys (pegylated interferon alpha-2a), Hepsera (adefovir dipivoxil), and Baraclude (entecavir) and all of these drugs have been approved by the U. S. FDA for general use against chronic HBV infections during the last ten years. Entecavir has also been approved recently (June, 2006) by the European Union Commission for the clinical treatment of chronic hepatitis B infections in Europe. The estimated numbers of chronic HBV infections in other countries around the world is staggering, with China clearly leading the list with an approximate 125 million cases. Brazil has an estimated 3.7 million infected people, Korea has 2.6 million cases, and Japan has 1.7 million cases. Chronic HBV disease, which can lead to cirrhosis, hepatocellular carcinoma, and death, is a global problem. In large-scale multinational studies, pegylated interferon alfa-2a treatment was observed to produce a sustained antiviral response in both

HBeAg-positive and HBeAg-negative patients at 24 weeks following a defined 48 week period of therapy. Hepsera (adefovir dipivoxil), an acyclic nucleotide analog of adenosine monophosphate (AMP) first synthesized by Antonin Holy and his associates in Prague and studied extensively by Erik De Clercq and his group in Leuven, was developed by Gilead Sciences for use against human HBV infections. It is metabolized to the active form adefovir diphosphate by cellular kinases and inhibits HBV DNA polymerase (a reverse transcriptase) by competing with the natural substrate deoxyadenosine triphosphate (dATP) and also by acting as a DNA chain terminator after its incorporation into viral DNA. The combination appears to have an additive effect against HBV. Baraclude (entecavir), a guanosine nucleotide analog that has been found to have potent and selective activity against HBV, also targets the viral DNA polymerase. This drug, developed by Bristol-Myers Squibb, is phosphorylated to the active triphosphate derivative which then competes with the natural substrate dGTP to inhibit all three activities of the HBV DNA polymerase: (1) base priming, (2) reverse transcription of the negative strand from the pregenomic messenger RNA, and (3) synthesis of the positive strand of HBV DNA. Baraclude has been observed to be clinically

effective in a randomized, double-blind, multinational trial in reducing viral loads to undetectable levels in 67% of HBeAg-positive naïve patients with chronic HBV infection after 48 weeks of therapy. It is clear that step-wise progress is being made in our ability to combat this chronic disease with selective antiviral chemotherapy.

Approximately 2.7 million Americans are chronically infected with hepatitis C virus. With the development of Rebetron (Intron A + ribavirin) combination therapy for the treatment of HCV infections by Schering Plough and its approved use by the FDA in 1998, a major advance was made in the clinical management of chronic HCV disease. More recent advances have been made with the development of the pegylated interferons by both Schering Plough (Peg-Intron; pegylated interferon alfa-2b) and by Roche (Pegasys; pegylated interferon alfa-2a). Combination therapy with Pegasys + Copegus (ribavirin) was approved by the FDA in 2002 for the treatment of adults with chronic HCV infections who have compensated liver disease and who have not been previously treated with alpha interferon. This combination has allowed the physician to tailor the dose and duration of a patient's antiviral therapy to the genotype of the virus and therefore, more effectively treat the disease and achieve a sustained virological response with a lower dose and more limited side effects. The combination has been approved in over 50 countries around the world, including countries in the European Union. In 2005, the U. S. FDA approved the Pegasys + Copegus combination for the treatment of chronic HCV in patients co-infected with HIV. In pivotal clinical studies, this antiviral combination therapy resulted in 40 % of patients co-infected with HCV and HIV/AIDS achieving a sustained virological response, i.e., the patients had continued undetectable HCV levels in the blood at 24 weeks after therapy. This result represents good progress in the ability to treat this disease in the most refractory of patients.

Improvements in the available therapies for herpesvirus infections have also been made during the last decade, with the development and approval of cidofovir (HPMPC; Vistide) for the treatment of CMV retinitis in AIDS patients, penciclovir cream

(Denavir) for the topical treatment of recurrent oral herpesvirus infections, and valganciclovir (Valcyte) for the treatment of CMV retinitis in AIDS patients and also for the prevention of CMV disease in certain organ transplant patients. Gilead Sciences received U. S. FDA approval for Vistide in 1996 and final approval from the European regulatory commission in 1997 to market the drug in all of the European Union countries. Outside the United States, the drug is marketed by its partner Pfizer. In pivotal clinical studies, the drug was found to significantly delay the progression of CMV retinitis in infected AIDS patients. Penciclovir (Denavir), approved by the U. S. FDA in 1996, became the first topically effective antiviral drug for use in the treatment of herpes labialis, a disease that affects approximately 40 million individuals in the United States alone. More recently, Roche received U. S. FDA approval for valganciclovir (Valcyte), an L-valyl ester (prodrug) of ganciclovir, for use in the prevention and treatment of CMV disease. Valganciclovir exists as a mixture of two diastereomers, both of which are converted rapidly to ganciclovir by cellular esterases. Ganciclovir, an analog of 2'-deoxyguanosine is then preferentially phosphorylated to ganciclovir triphosphate in virus-infected cells and inhibits CMV DNA synthesis by competing with 2'-deoxyGTP, the natural substrate for the viral DNA polymerase. From the discovery perspective, a more promising class of anti-CMV agents, the benzimidazole ribosides, also progressed in their development during this timeframe. The original drug leads in this series emerged from the pioneering work of Leroy Townsend and John Drach at the University of Michigan, who subsequently partnered with Karen Biron and other scientists at Burroughs Wellcome (which later became GlaxoWellcome and eventually GlaxoSmithKline), to identify and develop clinical drug candidates. This development effort matrixed across the expertise resident within the ISAR scientific community, and the resulting chemistry and biology studies were presented at annual ICARs throughout the first and second decades of the ISAR. This fruitful academic, industrial and government collaboration ultimately yielded two clinical candidates with distinct and novel modes of action that both entered clinical trials. Maribavir (5,6-dichloro-2-(isopropylamino)-1- β -L-ribofuranosyl-1H-benzimidazole), a first-in-

class viral protein kinase inhibitor, is now entering Phase 3 clinical development under the stewardship of ViroPharma, Inc. for prophylaxis of CMV in solid organ and stem cell transplant patients. In another focus area, imiquimod (Aldara), an immunomodulator, was approved by the FDA in 1997 for use in the treatment of genital warts.

Significant advances have been made recently in the development of new drugs for the prophylaxis and treatment of influenza A and B virus infections. These include GSK's Relenza (zanamivir) and Roche's Tamiflu (oseltamivir), both drugs approved by the U. S. FDA in 1999. Another potentially useful new anti-influenza drug, peramivir, is currently in clinical trials and is being developed by BioCryst Pharmaceuticals (Birmingham, AL). Both zanamivir and oseltamivir inhibit influenza virus replication via inhibition of the influenza virus neuraminidase with the possibility of alteration of virus particle aggregation and release. Peramivir, which also inhibits the influenza virus neuraminidase, has been shown in preclinical studies to be more potent than zanamivir and oseltamivir against both influenza A and B strains *in vitro* and it has been reported to be highly effective in preventing acute respiratory disease in mice and ferrets. Because of poor bioavailability when administered by the oral route in humans, the drug has been re-formulated for parenteral (intravenous or intramuscular) delivery and

these formulations have shown good efficacy in pre-clinical animal model evaluations. Preliminary studies, published in the ISAR's official journal *Antiviral Research*, have indicated that a single intramuscular injection of peramivir is comparable to five days of oral treatment with oseltamivir. In addition, peramivir inhibits the replication of avian influenza (H5N1) strains and it is effective against influenza virus strains that have become resistant to zanamivir and oseltamivir. Clinical trials are now in progress to evaluate this promising new anti-influenza drug in humans.

The progress made in antiviral research and development during the past ten years has truly been remarkable, but there are still many unmet medical needs. According to Richard J. Whitley of the University of Alabama at Birmingham (UAB) Medical Center, the ISAR's first President, there is a need for better and less toxic drugs for the effective treatment of viral infections that are increasingly observed in organ and stem cell transplant patients. There is also a need for new antivirals to replace the mutagenic drug ribavirin for the treatment of respiratory syncytial (RS) virus infections in neonates. Finally, there is the obvious need to develop selective antiviral agents for effective use against the many important viral diseases for which there is currently no available therapy at all.

Section Two – The Success of ISAR/ICAR as the Leading Professional Scientific Organization and Forum for Antiviral Research: Contributions to the Field

Following a successful first decade of operation, the leadership of the International Society for Antiviral Research (ISAR) looked forward to the future with an earned optimism and a continued desire to provide the membership with a mature, robust, and financially stable Society and a valuable and exciting international conference that would represent the leading professional scientific organization and forum, respectively, for all aspects of antiviral research and development from antiviral drug design, synthesis, and discovery to preclinical and clinical antiviral drug research, development, and approved clinical use. While other, more specialized, antiviral meetings had been organized over the past decade for individual viral diseases such as AIDS, hepatitis, or influenza, only the ISAR's multidisciplinary International Conference on Antiviral Research (ICAR) has covered the entire field of viral diseases and all aspects of antiviral research and development. It remains the primary international forum for all active investigators in the field of antiviral research and the ISAR remains their home base.

By 1998, The ISAR membership had grown back to approximately 750, up from 664 in 1997. Koen Andries and Jack Secrist were re-elected for additional three-year terms as ISAR Secretary and Treasurer, respectively. The annual International Conference on Antiviral Research (ICAR) continued to be organized by Earl Kern (Conference Committee Chair) and Rich Whitley (Program Committee Chair). Together, Earl and Rich did an outstanding job in these two very important leadership roles for much of the Society's second decade. The 11th ICAR was successfully held in San Diego, California, assisted by The Conference Table, Ltd, and hosted by Karl Hostetler and Doug Richman (UCSD). The conference was attended by 464 members from 24 countries. John C. Martin became the first ISAR President of its second decade and Karen K. Biron became President-Elect. At the San Diego meeting, during the annual banquet, the ISAR Award of Excellence, a very prestigious award which has

been given only four times by the Society, was presented to each of two very deserving awardees: Erik De Clercq of the Rega Institute for Medical Research in Leuven, Belgium and Richard J. Whitley of the University of Alabama at Birmingham (UAB) Medical Center in Birmingham, Alabama. Both Erik and Rich were past Presidents of the ISAR and received this rare honor for their numerous scientific achievements and for their many contributions to the Society during its first decade. Erik and Rich have remained very active members of the Society to this day and they have contributed greatly to its continued success over the past ten years as well, giving of their time and energy in many different capacities, playing a number of very important roles within the Society during this very active period in its history. Both Erik and Rich recently indicated that they were deeply honored to have received this award from the Society and that they remain committed to the future success of the ISAR. Elected to the ISAR Board of Directors during the San Diego conference were Erik De Clercq, Hugh Field, Catherine Laughlin, and Rich Whitley. The historical booklet entitled "The International Society for Antiviral Research: The First Decade", produced by George J. Galasso, a Past President and a co-founder of the Society, was distributed to the conference attendees and subsequently mailed to the membership. This document was well done and provided us with an excellent look-back at the founding of the Society and its early years of operation. The present booklet picks up where the history of the first 10 years of the Society leaves off and it represents the recollections, contributions, and reflections of many of the Society's past officers and committee members who, through their dedicated efforts and hard work, have played such an important role in the continuing success of the ISAR.

The 12th ICAR was held in Jerusalem, Israel, hosted by Ehud Katz of the Hebrew University – Hadassah Medical School. The meeting and the scientific program was again of excellent quality and was organized with the local assistance of Dr. Katz

and the professional staff of Kenes, Ltd. As with previous meetings outside of the United States and Europe, attendance by the ISAR membership was greatly reduced. Only 250 attendees were present for about 150 presentations. In addition to the expense involved, political instabilities and tension in the region may have somewhat dampened the attendance at the 1999 conference, although the situation was closely monitored. At that time of relative peace in the Middle East, many attendees ventured out on their own to tour the near-by Old City or did so on organized tours. Participants reported that all of the conference tours were spectacular, especially the post-conference tour of Jordan and the ruins at Petra. Cathy Laughlin remembered an incident at the border between Israel and Jordan however, that caused some initial concern. Then ISAR President-Elect Karen Biron was in line along with the rest of the ICAR tourists to cross the border from Jordan back into Israel. Karen waited and waited for the return of her passport as all of the other tourists crossed the line back into Israel. Ultimately, she was detained by the Israeli border guards for nearly a half-hour because of some unstated problem with her passport, while the rest of the group waited. When they finally released her without adequate explanation, Cathy and the rest of the group who were unable to go back to help Karen, breathed a big sigh of relief upon her belated return to the group. Karen thinks that she drew the lucky number for the border guards-in-training to try out their new computerized search tools.

During the Jerusalem conference, the ISAR Board voted to establish the Gertrude B. Elion Memorial Lecture Award with the generous support promised from the Glaxo Wellcome Company and it was planned that the first lecture would be held during the 13th ICAR (See details in Section Three below). Also during this meeting, George Galasso convinced the ISAR leadership that a professional conference organizer was needed as a contractor to handle all of the logistics of the annual meetings, to maintain the ISAR Membership Directory, and to provide the continuity of a longer-term working relationship with the ISAR Officers and the Conference and Program Committees that only a multi-year contract could provide. Proposals were solicited from a number of companies using the NIH-style "Request

for Proposal (RFP)" mechanism and a panel was assembled to review all submitted proposals. Courtesy Associates of Washington, D.C. provided the best proposal in terms of what they could offer for the available money. A contract was awarded to Courtesy Associates for 3 years with an option to renew for an additional 2 years.

The Inner Harbor of Baltimore, MD was the site for the 13th ICAR held in 2000, hosted by George Galasso (Local Committee Chair), this time assisted by Courtesy Associates which had won the ISAR contract to be its professional conference organizer and secretariat. The scientific meeting was excellent and Courtesy Associates did a great job to provide an efficiently run conference and memorable special events, such as the Opening Reception which was held at the National Aquarium and was capped off with outgoing ISAR President John Martin feeding the dolphins. Karen Biron became the new President of ISAR, John Drach became President-Elect and Brent Korba was elected the new ISAR Secretary to replace Koen Andries who had done a fine job as Secretary of the Society and who had been instrumental in developing and maintaining the ISAR Membership Directory. Jack Secrist was re-elected Treasurer for a third term. Michael Rossman became the first recipient of the Gertrude B. Elion Memorial Lecture Award for his pioneering research on the molecular architecture of the capsid of the human rhinovirus and the binding of the antiviral agent pleconoril into a deep pocket within the capsid. The Baltimore conference counted 401 members in attendance from 21 countries and there were 180 presentations. The total ISAR membership, however, had dropped to 647 by the beginning of 2000 and it thus became apparent that greater efforts were again needed to recruit new members to the Society and to retain its existing members. In December, 2000, George Galasso coordinated a task force of ISAR members to discuss the suggestions and proposals that had been solicited from the membership in an attempt to improve the Society. This effort resulted in several changes: The annual Conference was shortened by one day, the ISAR-ICAR web page was improved and expanded, the Membership Committee more actively recruited new members to the Society, a brochure describing the ISAR was developed and made available, the

William H. Prusoff Young Investigator Lecture Award and ICAR Poster Awards were instituted (See Section Three below). The Society also decided to have a trial Press Conference in conjunction with the ICAR. Press releases were invited from selected researchers making presentations at the Conference.

Membership in the ISAR increased slightly in 2001 to 689 with 57% of the members coming from the United States, 30 % from Europe (including the UK), 5% from Japan, 4% from Canada, and 4% from the rest of the world. For the first time, seats on the ISAR Board of Directors were organized by region and candidates were elected for these numbered seats. This was done in order to assure sufficient international representation in the Society's decision making processes. Elected to the Board in 2001 were: David Bernstein (USA) for Seat 1, Jan Balzarini (Belgium) for Seat 2, Joe Martin (UK) for Seat 3, and Catherine Laughlin (USA) for Seat 4.

The 14th ICAR was held in Seattle, WA in 2001 with Larry Corey as the Local Host. Again, the ICAR organizers had the able assistance of Courtesy Associates as the Conference Secretariat. The annual satellite symposium entitled "Clinical Update on Antiviral Drugs" was held preceding the Conference and the program again contained excellent presentations of cutting-edge clinical research results with a number of antiviral drugs. This pre-Conference clinical symposium, initiated at the 7th ICAR in Charleston, SC, had always been very well attended and extremely well received by the ISAR membership and this year was no different. Over 430 members attended the Seattle Conference during which the first ICAR Poster Awards were presented since their establishment for each of three candidate categories: Category 1 -Graduate Students, Category 2 - Post-Graduates, and Category 3 - Young Investigators. John Drach and Kirk Field had worked diligently to establish the Poster Award presentation event for the annual ICAR and it had been a resounding success. The second Gertrude B. Elion Memorial Lecture Award was presented to Leroy Townsend of the University of Michigan and the first William H. Prusoff Young Investigator Lecture Award was presented to Chris McGuigan, Cardiff University in Wales (the current ISAR President).

The American Herpes Foundation, a non-profit organization, sponsored an award for research excellence in herpesvirus research to be presented at the Seattle ICAR. This award, intended to raise awareness about control of herpesvirus infections is given to physicians-in-training and consists of a plaque and a \$10,000 stipend, half of which is to be presented to the award recipient and half to the recipient's department. Awards presented at the 2001 ICAR were given to Jennifer Moffat of the Upstate Medical University of the State University of New York (SUNY) and to William Nichols of the Fred Hutchinson Cancer Center at the University of Washington Medical Center in Seattle, WA.

The Society's website was expanded to include an advance copy of the next ICAR Program, a summary of the previous ICAR, and the criteria for the ISAR awards. The website also included membership and meeting application forms, job listings, information on future ICARs, listing of other meetings of interest to the membership, and links to other websites, including the Society's three sponsored journals. Brent Korba initiated many of these improvements and these changes were seen to provide a better service to the membership and a much greater visibility for the ISAR outside of the organization.

The events of September 11th, 2001 and its aftermath shook the world and changed it forever. The bioterrorist attacks which followed, in which anthrax spores were mailed to members of the U. S. Senate and U. S. House of Representatives and to others around the country resulting in a number of inhalation anthrax infections and deaths, brought home to the civilized world the importance of public health preparedness and measures to combat the potential threats of bioterrorism. It clearly underscored the importance of developing effective antiviral drugs that could be stockpiled for possible use against infectious viruses considered to be threat agents by the National Centers for Disease Control (NCDC), the National Institute of Allergy and Infectious Diseases (NIAID), and by the U. S. Army Medical Research Institute for Infectious Diseases (USAMRIID). On November 1, 2001, ISAR President Karen K. Biron sent an official letter to U. S. President George W. Bush expressing the full sup-

port of the Society for his planned initiatives to mobilize the scientific, medical, and pharmaceutical communities to meet these biological threats and she offered our immediate assistance in any way that was needed. She urged the President to consider increasing the funding to the National Institutes of Health (NIH) for antiviral research and development and to the establishment of a new partnership between academia, government agencies, and pharmaceutical companies which would more efficiently utilize their chemists, virologists, and clinicians to identify new antiviral drugs to combat the potentially deadly viruses that could be used in future bioterrorist attacks. The ISAR was ready to take a leadership role in helping to organize such a Task Force. This was an important and timely letter for the Society's President to have written and to have sent to the U. S. Commander-in-Chief. The ISAR leadership had the full support of the membership and many offered their services to the appropriate government agencies to assist them in designing biodefense initiatives for the United States and its allies. The full text of the ISAR letter to President Bush was published in the *ISAR News*, Vol. 11, No. 2 (December, 2001). Since those events of 2001, ISAR scientists have joined scientists worldwide to increase international preparedness against acts of bioterrorism and the annual ICAR has provided a forum for data presentation and discussion.

Antiviral research has had a number of advocates within the U. S. government, starting with George Galasso who, in 1969, established the Antiviral Substances Program at the National Institutes of Health. George was heavily involved in directing the funding for a large number of antiviral research programs in the early days and his efforts were critically important in the establishment of antiviral research as a new scientific discipline. His advocacy and support was essential for the clinical development of the first systemically effective antiviral drug, vidarabine (ara-A), an anti-herpes drug which had resulted from an early collaborative research program that involved Parke, Davis & Co. (Francis Miller, Barney Sloan and Bob Buchanan), Southern Research Institute (Frank Schabel, Bob Sidwell, and Bill Shannon), UAB (Charles Alford, Larry Chien, and Rich Whitley), the NIAID, and a clinical evaluation group that included 21 medical

centers across the country. Rich Whitley recently indicated that "when he thinks of the key people in the ISAR who have clearly made benchmark contributions to the field, he thinks of Bill Prusoff, Trudy Elion, and George Galasso". As a scientific administrator at the NIAID, George provided strong advocacy for the American antiviral research community and guided the research efforts of many to help establish a vibrant and successful national program that would expand in size, scope, and acceptance. George has continued to provide his advocacy and organizational skills to assist the ISAR very effectively in so many ways, even after his retirement from the NIH and up to the present time. When George became the Chief of the Infectious Diseases Branch at the NIAID, the Antiviral Substances Program was then led by Maureen Meyers and, subsequently, by Catherine Laughlin who maintained and continued the expansion of antiviral research funding throughout a period of rapid growth for the field worldwide. Under their leadership, a number of important programs were put into place including the establishment of the Collaborative Antiviral Testing Group, the use of the National Cooperative Drug Discovery Group (NCDDG) grant mechanism for antiviral research initiatives, and contracts for extramural funding of antiviral drug discovery projects. These mechanisms were instrumental in assisting the development of several antivirals including the origination and preclinical development of maribavir through a collaboration between Leroy Townsend and John Drach at the University of Michigan and Karen Biron and her colleagues at the Burroughs Wellcome Company (now GlaxoSmithKline) as described in more detail earlier in Section One above. Other scientists who have been instrumental in championing antiviral research from within U. S. government agencies were Michael A. Ussery, Steve Turk, and Christopher Tseng, all currently at the NIAID, and these loyal ISAR members have played major roles in assisting many investigators in the field build strong and productive antiviral research programs. These government scientists have also continued to contribute much toward promoting important interactions among ISAR members at the annual ICAR. After 9/11, the NIAID's budgets were increased for biodefense and infectious disease research and Cathy Laughlin's attention turned to her additional respon-

sibilities which now included helping in the nation's efforts to provide a solid defense program against bioterrorist threats. Stockpiling of antiviral drugs, coordination of research efforts, not only for countermeasures against the designated threat agents, but also for emerging virus infections, became the order of the day. Significant momentum was achieved in the search for agents with antiviral activities against the poxviruses and these efforts were coordinated with John Huggins and others at the U. S. Army Medical Research Institute for Infectious Diseases (USAMRIID) in Frederick, MD and at the NCDC in Atlanta, GA. New antiviral therapeutics were developed and tested in animal models for potential use in combating various poxvirus infections, including smallpox.

The 15th ICAR was held in March 2002 in the historic city of Prague in the Czech Republic. This very successful conference was hosted by Antonin (Tony) Holy. The conference was attended by 325 registrants representing 29 countries. It was appropriate that the Gertrude B. Elion Memorial Lecture Award was presented to Tony Holy during this conference, held in his home country, for his outstanding contributions in antiviral research. He has been responsible for the design and chemical synthesis of many novel nucleosides and nucleotides leading to the development of a new class of antiviral agents, the acyclic nucleoside phosphonates. His synthetic work, in active collaboration with Erik De Clercq's group in Belgium and Gilead Sciences in the United States, has subsequently led to the development of the approved antiviral drugs *cidofovir*, *adefovir*, and *tenofovir* for the treatment of HCMV, HBV, and HIV/AIDS, respectively. Like Trudy, Tony has been a mentor to many young investigators and a dear friend to his many colleagues and collaborators. He has been a loyal and active member of the ISAR since its founding. Ralf Bartenschlager of the University of Mainz received the Prusoff Award for 2002 for his research on hepatitis viruses and notably for his development of a replicon system that provided the first reliable cell culture system for HCV replication. A press release program was initiated to provide more publicity for the ICAR, but there were only a few participants in this program at the Prague meeting; others who were invited, declined to participate. The response to the few press

releases that did go out electronically, however, was indeed encouraging and the Board decided to consider whether or not to continue with this service that utilized NewsWise, an online resource. The ISAR later contracted with NewsWise to send out press releases, on topics to be presented at the next ICAR, to over 15,000 science writers by e-mail and this organization would also send out information about the Society and the ICAR to selected journalists prior to and during the conference in the form of traditional press releases. The membership did not seem to favor this program, so it was terminated.

John C. Drach of the University of Michigan became the new ISAR President and Jack Secrist of Southern Research Institute became the President-Elect. In his first letter to the membership, John Drach called for a greater involvement of members in the activities of the Society and asked for interested members to serve on the various ISAR committees. By December of 2002, several individuals had heeded his call and had volunteered to serve the Society more actively. The Society had always had a hard time getting volunteers and the new President and President-Elect were committed to making a real effort to increase the number of new faces in the Society's various activities. A number of members rotated off standing ISAR committees in 2002 and new leadership took the reins. Upon his retirement from NIH in 1996, George Galasso took over the task of obtaining major funding sources for the annual ICAR, as well as designing the annual Posters and Announcements, and other logistical services for the Society. Kirk Field headed the Finance Committee and expanded the efforts to raise separate Corporate Funding to support the Society. Amy Patick took over the responsibility of chairing the Travel Grants Committee, a job held previously by John Drach, the new ISAR President. A number of members rotated off the Program Committee, including Hugh Field, Paul Lietman, and Rich Whitley who not only chaired that committee but also was the organizer and convener of the Clinical Symposium that precedes the ICAR every year. Rich Whitley had done a magnificent job of organizing these clinically-oriented symposia on antiviral drugs over the years and these pre-Conference sessions had been observed to significantly grow in importance and popularity under his careful leadership and

guidance. The Clinical Symposium had, by this time, become an essential and expected event preceding the annual ICAR and it was apparent that someone would need to take over the important responsibility of organizing this very valuable scientific session in the future. During the Prague meeting, the Board voted to combine the Program and Conference Committees. Earl Kern was appointed Chairman of the newly expanded Conference Committee and Paul Griffiths agreed to join this Committee and to take direct responsibility for organizing the Clinical Symposium. At the Prague meeting, Joseph Colacino with the support of George Galasso had suggested to ISAR President John Drach that the Society should consider initiating an ISAR Placement Service. After a subsequent discussion with the Board, the Society established the Placement Service and charged a new committee under the chairmanship of Joe Colacino to guide its operation. The Placement Service was designed to provide a forum for prospective employers, such as pharmaceutical and biotech companies, research institutes and universities to advertise their position openings and the ads would be posted on the ISAR web page at no charge. Plans were made for on-site space to be provided at the next ICAR for prospective employers to meet and interview interested candidates. Plans were also made to advertise the new ISAR Placement Service in the two official journals of the Society published by Elsevier: *Antiviral Research* and *Antiviral Chemistry and Chemotherapy*.

A very successful 16th ICAR was held in Savannah, GA in 2003 with an extensive and diverse scientific program. There were 407 registrants counted from 22 countries and over 160 abstracts of papers submitted for presentation at this conference. Travel funds were awarded to 24 applicants from 13 countries to attend the Savannah ICAR. A Biodefense Mini-Symposium was included in the program to cover the timely subjects of bioterrorism and biopreparedness. The 2003 Gertrude B. Elion Memorial Lecture Award was presented to John C. Martin (Gilead Sciences) who, because of illness was not able to attend the conference in Savannah, but presented his lecture "A Brief History of Nucleotide Antivirals" at the 17th ICAR in Tucson

the following year. The William H. Prusoff Young Investigator Lecture Award for 2003 was personally presented by Bill Prusoff himself to Johan Neyts (Rega Institute for Medical Research; Leuven, Belgium). George Galasso conducted a survey of the participants at the Savannah ICAR and the respondents overwhelmingly expressed their general satisfaction with the conference and its format and saw no need for change. Newly elected were: Amy Patick (Pfizer) as the new ISAR Secretary and John Morrey (Utah State University) as the new ISAR Treasurer.

The planned retirement of Earl Kern as Chairman of the ISAR Conference Committee, following the 17th ICAR to be held in Tucson, AZ, loomed as a huge vacancy to be filled for a key leadership position having responsibility for one of the primary functions of the Society. This posed the particularly serious question of who would be willing and able to become the successor to Earl as the Conference Committee Chair because the Program Committee had been combined with the Conference Committee. Earl Kern had taken the major responsibility for the conferences since the very early days of the Society and, as chair of the Conference Committee, he had a very large role to play in site selection, abstract collection and handling, contacting speakers, working closely with the Program Committee and its subcommittees to provide the best program that could be assembled, and generally making sure that the ICAR ran smoothly in every respect, every year, for so many years. These shoes would indeed be huge ones to fill! Earl Kern had performed an enormous job for the Society and he did it extremely well, helping to make the ICAR the leading international forum for antiviral research and helping the ISAR achieve its stated goals and objectives in a manner *par excellence*. Since a substitute could not be found, ISAR President John Drach suggested that the outgoing President chair the Committee for two years following his tenure. Fortunately, John Drach's tenure ended in time for him to assume the role following the Tucson ICAR and his involvement would provide a smooth transition in leadership for this very important position. This was certainly a welcome suggestion and Jack Secrist, who became ISAR President during the Tucson ICAR made it official.

Approaching the end of the first five years of the Courtesy Associates contract with ISAR for assistance in the conduct of the ICAR and for maintenance of the ISAR Membership Directory, George Galasso was asked to re-advertise the RFP for the contract and assemble a review panel to select the winning proposal. Serving on this panel were: Bob Buckheit, Kirk Field, Brent Korba, Jack Secrist, and George Galasso as the Executive Secretary of the committee. A number of proposals were received, the applications were carefully reviewed, and Courtesy Associates was again selected as the best organization to assist the ISAR. It was awarded a five-year contract to continue its services for the Society. That business behind it, the ISAR leadership again, aware of the need for more participation by the younger members of the Society and the need for them to assume a more active role in its operations, called for a greater participation of the ISAR membership in the Society's committees and conducted another survey to determine if any changes should be made in the format or frequency of the ICAR. Respondents again affirmed their commitment to the ISAR sponsoring yearly conferences and to the ICAR maintaining its existing format. The Board was satisfied that the annual conference was achieving its desired end results: to maintain a focus on antiviral research in all scientific disciplines, to cover all viruses of current interest, and to encompass all aspects of antiviral research from rational drug design, chemical synthesis, *in vitro* testing, animal model development and preclinical studies, all the way to clinical trials and approved clinical use. Although the Board began to be concerned about its goal of financial growth and stability, the ICAR has become the premier venue for keeping up with what is happening in antiviral research and development worldwide and the Board therefore decided that no changes should be made in the ICAR's obviously well-received and successful current format. Nevertheless, it was determined that as priorities shift and funding becomes tighter in the pharmaceutical industry, the role of the ISAR and its ICAR will continue to be assessed by the leadership in future years to ensure that it continues to serve its membership in the best possible way.

The 17th ICAR in Tucson, AZ was a very successful meeting in a beautiful resort location. All

who were there will remember the stunning setting as a full moon rose over the surrounding mountains during the outdoor opening reception. The scientific program clearly reflected many of the changes that had occurred in international antiviral research priorities, emphasis, and focus. The conference included a mini-symposium on emerging viral infections and attendees were rewarded with a current status update on existing world outbreaks of SARS, West Nile, monkeypox, and influenza, with an assessment of the public health responses to each of these infectious diseases. The oral and poster sessions were of the highest quality with over 150 abstracts submitted for presentation at the conference and there was not enough time on the program to schedule all of the excellent, highly-rated papers for oral presentation. All of the committee members agreed that the quality of the science submitted for presentation was clearly improving over the years. Richard J. Whitley was presented the Gertrude B. Elion Memorial Lecture Award for 2004 and Fabien Zoulim was presented the William H. Prusoff Young Investigator Lecture Award for 2004. A new ISAR award was instituted at the 17th ICAR for Outstanding Contributions to the Society. The award, which will be given only rarely, is intended for individuals who have significantly contributed to the success of the Society. The inaugural award was very appropriately presented to Earl R. Kern on the occasion of his resignation as Chairman of the ICAR Organizing Committee, based on his long and outstanding service to the Society since its inception and based on his signal efforts to make the Society and its annual conference a continuing success. The award was presented by outgoing ISAR President John Drach, who with the collusion of Earl's wife Aloma, devised a PowerPoint 'roast' of Earl going back to his high school days in Wyoming. In a more serious vein, John remarked that the award was truly deserved and that Earl had clearly left his indelible, positive mark on the Society for all time. Earlier that day, during the ISAR Business Meeting, John also gave a very brief 'roast' of incoming President Jack Secrist and then announced the latest election results: Chris McGuigan (University of Cardiff, Wales) was selected as the President-Elect of the Society and new members of the ISAR Board of Directors included Masanori Baba (Japan), Jan Balzarini (Belgium), Joe Colacino (U.S.A.), and

continued on page 21



ISAR Presidents: Erik De Clercq, George J. Galasso, Hugh J. Field, Earl R. Kern, John A. Secrist III, Christopher McGuigan, and Amy K. Patick (Vice-President). Not shown: Richard J. Whitley, John C. Martin, Karen K. Biron, and John C. Drach



ISAR Awards of Excellence: Richard J. Whitley, Gertrude B. Elion, Erik De Clercq, 1998



Questioning the speaker
ICAR 2004



ISAR Leadership 1998: Catherine Laughlin, Koen Andries, Richard Whitley, John Martin, Karen Biron, Jack Secrist, Earl Kern, Erik De Clercq 11th ICAR, San Diego



John Martin passing on the Presidency to Karen Biron , 13th ICAR Baltimore, 2000



Questioning the speaker 13th ICAR Baltimore, 2000



Coffee Break



Opening Reception, 19th ICAR, San Juan, 2006



Opening Reception, 19th ICAR, San Juan, 2006



Session Participants, 19th ICAR, San Juan, 2006



Poster Session, 19th ICAR, San Juan, 2006



Poster Session, 19th ICAR, San Juan, 2006



Session Speaker Arnold Monto



Coffee Break



Mini-Symposium panelists listen intently to a question from the audience, 19th ICAR



John Drach presenting the 2004 Elion Award to Richard Whitley, 17th ICAR, Tucson, 2004



George Galasso, Kirk Field and Bill Shannon discussing this publication, 19th ICAR, San Juan, 2006



Session Participants



Lunch in Tucson ICAR 2004



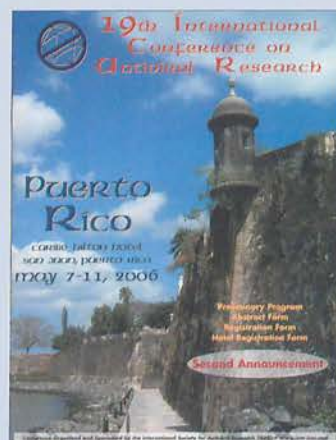
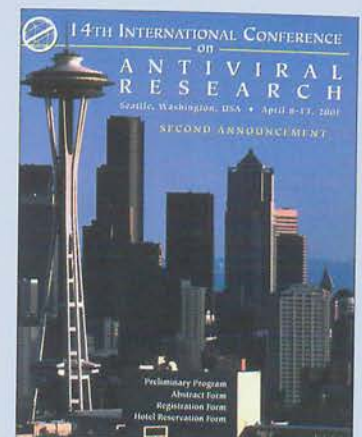
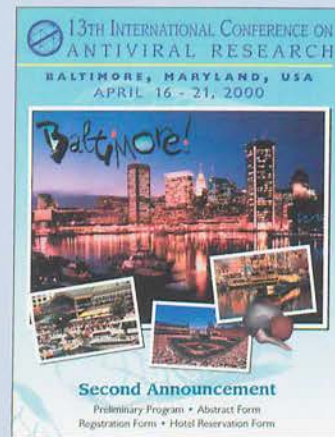
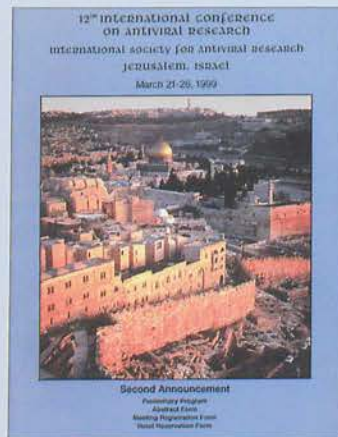
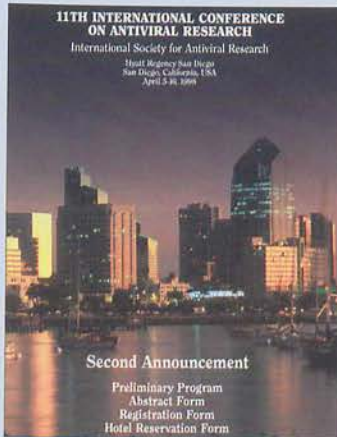
George Galasso, local 13th ICAR Chair, getting advice from Ehud Katz, local 12th ICAR Chair, in Jerusalem 1999.



The International Society for Antiviral Research:

1998 – 2007

The Second Decade





The International
Society for
Antiviral Research:

The Second Decade
1998–2007

On behalf of the Society, thanks are extended to all the members who assisted in the production of this document. Your contributions are much appreciated. Special thanks to William M. Shannon, Ph.D., the principal author, who did yeoman work in writing the text. We believe you will find it informative and easy reading due to his considerable efforts, for which we are grateful. Special thanks also to George J. Galasso, Ph.D., who provided valuable input, helpful advice, and the logistical coordination that facilitated the production of this publication.

The International Society for Antiviral Research: The Second Decade (1998-2007)

Section One - The Continued Growth and Importance of Antiviral Research as a Major Scientific Discipline

As we reflect on the second 10 years of the International Society for Antiviral Research (ISAR) and of its sponsorship of the annual International Conference on Antiviral Research (ICAR), we are struck by the fact that there has been a steady growth in the global perception of the real importance of antiviral research as a scientific discipline, a specialized field of medicine that is clearly producing positive results for the benefit of mankind. During this period, we have become much more aware of the very significant impact that our Society and its membership has had on biomedical science in the area of developing effective and selective treatments for important viral diseases. As the late Frank M. Schabel, Jr. (Southern Research Institute), one of the early pioneers in antiviral research, used to like to say: "There's no success like success." During the past decade, there has been intense, worldwide media attention and publicity devoted to the stepwise advances and many real successes that have occurred in our collective antiviral research and development efforts worldwide. Consequently, there has been a widespread expansion of public awareness and interest in the use of antiviral drugs. Along with this new awareness and interest, there has also been a concomitant increase in public expectations as to our future ability to combat important viral diseases with drugs. Frank would have been amazed at the success and broad acceptance of antiviral research as a new scientific discipline. This relatively rapid growth in general interest and attention to what is happening in our very specialized field of endeavor initially resulted from the large amount of work that resulted in the successful development of new antiviral drugs with which to treat genital herpesvirus infections and, subsequently, to treat deadly HIV-1 infections. Much attention has been focused on the progress made in the continuing efforts to stem the disastrous worldwide AIDS pandemic. Then, there has been a new public awareness of expanded antiviral drug research in response to the increased incidence of hepatitis virus infec-

tions in the population, with new treatments for patients infected with hepatitis B or hepatitis C viruses. In addition, there have been discussions concerning the possibility of treating other potentially important viral diseases of public health importance such as those caused by the SARS coronavirus, West Nile encephalitis virus, and monkeypox, i.e., viral diseases that have appeared to dominate the news in recent times.

High visibility has also been given to attempts to provide protection and biodefense against other emerging virus infections and potential bioterrorist threats, especially after the events following the historic 9/11 terrorist attacks on the United States. More recently, there has been broad media coverage of the successful efforts to develop newer and more effective antiviral drugs for the treatment and prevention of influenza virus infections and of their potential use for the control of pandemic influenza. The identification of new H5N1 avian flu strains causing deaths in Asia and the Middle East has raised the specter of another possible pandemic similar to the deadly 1918 Spanish flu pandemic and media attention has turned to the potential use of antiviral drugs in such a future epidemic on an almost even footing with its coverage of the efforts to develop a vaccine. It is obvious that the age of antiviral chemotherapy and chemoprevention has arrived. The general public is now fully aware of the potential usefulness and value of antiviral research and development. The drugs Relenza and Tamiflu have become well known household names in the United States because of the frequency with which they have been mentioned during evening newscasts on national television, both on network and cable TV shows. Anti-herpesvirus drugs currently provide approximately \$1 billion per year in pharmaceutical sales revenues because of direct consumer marketing. People around the world are well aware of the life-saving potential of antiviral drugs. They have seen the human immunodeficiency

ciency virus (HIV) successfully targeted by newer and more effective combinations of antiviral drugs that have put infected AIDS patients in remission from their disease for longer and longer periods of time. The combination antiviral chemotherapy approach has been widely observed and documented to significantly extend the life expectancies of infected patients. We have also seen incremental improvements in the effectiveness and selectivity of these new drug combinations for the treatment of AIDS. Meanwhile, there is still no effective and approved HIV-1 vaccine available to date for the prevention of this insidious infectious disease.

When one examines the growing list of antiviral drugs that have now received approval by the U. S. Food and Drug Administration (FDA) for marketing and clinical use (See Table 1), it is immediately apparent that 28 of the 62 currently approved antiviral drugs and antiviral drug combinations (i.e., 45% or almost half) are directed toward the treatment of HIV/AIDS infections. Of these anti-HIV drugs, 19 (68%) were approved between 1997 and 2006. Robert T. ("Chip") Schooley (University of California-San Diego) reviewed the status of anti-retroviral drug research and development at the 19th ICAR in San Juan, Puerto Rico with a plenary lecture entitled "AIDS Therapeutics 20 Years After AZT: Are We There Yet?" In his lecture, he listed chronologically the steady advances in our understanding of HIV replication, HIV disease pathogenesis, and anti-HIV drug research and development - from AZT, approved in 1987, to the latest approved combinations of anti-HIV agents such as GlaxoSmithKlines's Trizivir (AZT + 3TC + abacavir) and Gilead's Atripla (tenofovir + emtricitabine + Efavirenz). As with the approved anti-herpesvirus drugs, nucleoside analogs as a chemical class have provided us with some of our most potent and effective anti-HIV agents as well. The anti-HIV drug abacavir (Ziagen), approved in 1998, was developed by Glaxo Wellcome based on the earlier identification of Carbovir as a potent and selective anti-HIV agent, the first public report of which was made at the 2nd ICAR held in Williamsburg, VA in 1988 by Robert Vince (University of Minnesota) and Bill Shannon (Southern Research Institute) and their many collaborators at the NCI. Carbovir and its derivatives, including their potential use in combina-

tions with other anti-HIV drugs, were eventually licensed to the Burroughs Wellcome Company by the University of Minnesota. Abacavir, a 6-substituted cyclopropylamino analog of Carbovir that was subsequently identified by scientists at BW, served as an intracellular monophosphate prodrug of Carbovir monophosphate to which it was metabolized within the cell and then further converted to Carbovir triphosphate, the active form of the drug. Following the development of abacavir and its approval for marketing and clinical use, substantial royalties were paid by Glaxo Wellcome to the University of Minnesota. These funds have recently been used to develop a new Center for Drug Design on the University of Minnesota Medical Center campus in Minneapolis, MN. This successful outcome represents a clear example of the benefits of scientific interchanges and collaborations between universities, research institutes, government, and industry, an idea that has been fomented, encouraged and ardently supported through the establishment of the ISAR and its associated ICAR. Abacavir was combined with AZT and 3TC to produce GSK's three-drug synergistic anti-HIV nucleoside analog combination Trizivir, approved in 2000. Gilead's Tenofovir, approved in 2001, and Emtricitabine, approved in 2003, have been combined to produce Truvada, approved in 2004. When formulated with Efavirenz, a non-nucleoside RT inhibitor, Truvada becomes Gilead's three-drug anti-HIV combination Atripla, a product developed through a joint venture between Bristol-Myers Squibb and Gilead Sciences and approved by the FDA in 2006. John C. Martin, CEO of Gilead Sciences and Past President of ISAR, remarked that "when we acquired Triangle Pharmaceuticals and FTC, we never thought that we would make so much progress so rapidly." He credits the multidisciplinary nature of ISAR, which allows active interactions and collaborations to occur between chemists, biologists, and clinicians for these advances and he gives major credit to the government scientists at the NIH and the FDA for assisting and implementing processes that accelerate access to antiviral drugs. The recently implemented "New Guidance for Combination Products" issued by the FDA has allowed for the rapid review of new combination drug applications and for the fast tracking of antiviral drug combinations like Truvada (approved after 4½ months) and Atripla (approved

after only 2½ months). According to Chip Schooley, these fixed-dose combinations “have been quite effective in helping to reduce the problems of drug resistance and have also resulted in simplification by co-formulation.” He remarked that “in 20 years, we have gone from no drugs for HIV/AIDS, to proof of concept, to highly-active antiretroviral therapy (HAART), to one pill once a day” and that “this has to be considered good progress!” But he also remarked that “this is not the time to cut back on antiviral therapeutic research” and that “we need more drugs, better drugs, and better toxicity management.”

From the mid 1990’s on, several other classes of anti-HIV drugs have been identified, notably the protease inhibitors (PIs) and the non-nucleoside reverse transcriptase inhibitors (NNRTIs). Effective and approved anti-HIV drugs have come from both of these antiviral categories. Of the 11 approved protease inhibitors, 8 (73%) have been approved since 1997. These anti-HIV drugs, approved for use during the past decade of the Society, include Nelfinavir (1997), Amprenavir (1999), Lopinavir (2000), Kaletra (the combination of Lopinavir + Ritonavir; 2000), Lexiva (2003), Reyataz (2003),

Tipranavir (2005), and Darunavir (2006). Approval was given to three NNRTIs: Nevirapine (1996), Delavirdine (1997), and Efavirenz (1998). When these drugs, which inhibit HIV by different mechanisms of action, were combined with anti-HIV nucleoside analogs, synergistic clinical efficacy was achieved and we witnessed the most important advances in the treatment of AIDS since the beginning of the epidemic. During the past 10 years, we have also been encouraged to hear reports of steady advances in the development of HIV entry inhibitors, a new class of antivirals, and of studies with combinations of these agents with which to block virus replication at the point of virus entry into the T-lymphocyte. T-20 (Fuseon) was the first fusion inhibitor to be approved by the FDA and second-generation fusion inhibitors such as T-1249 are being developed. New HIV entry inhibitors, CCR5 antagonists, are advancing in clinical development by Pfizer and by Schering-Plough, while GSK and ONO have earlier pipeline candidates under evaluation. Another molecular target for antiviral attack has been the HIV integrase and new antiviral drugs that inhibit this critical enzyme are currently being developed by Merck, by Gilead, and by GSK in partnership with Shionogi.

TABLE 1
CURRENT U. S. FDA-APPROVED ANTIVIRAL DRUGS *

Drug	Year Approved
Anti-HIV Drugs	
Nucleoside RT Inhibitors and Combinations:	
Zidovudine (AZT; Retrovir)	1987
Didanosine (ddI; Videx)	1991
Zalcitabine (ddC; Hivid)	1992
Stavudine (d4T; Zerit)	1994
Lamivudine (3TC; Epivir)	1995
Combivir (AZT + 3TC)	1997
Abacavir (ABC; Ziagen)	1998
Trizivir (AZT + 3TC + ABC)	2000
Tenofovir disoproxil fumarate (Viread)	2001
Emtricitabine (Emtriva; FTC)	2003
Truvada (Tenofovir + Emtricitabine)	2004
Epzicom (3TC + ABC)	2004
Atripla (Tenofovir + Emtricitabine + Efavirenz)	2006

Protease Inhibitors:

Saquinavir (Invirase; Fortovase)	1995
Indinivir (Crixivan)	1996
Ritonavir (Norvir)	1996
Nelfinavir (Viracept)	1997
Amprenavir (Agenerase)	1999
Lopinavir (Aluviran)	2000
Kaletra (Lopinavir + Ritonavir)	2000
Lexiva (Fosamprenavir Calcium)	2003
Reyataz (Atazanavir; Zrivada; Latazanavir)	2003
Tipranavir (Aptivus)	2005
Darunavir (Prezista)	2006

Non-Nucleoside RT Inhibitors:

Nevirapine (Viramune)	1996
Delavirdine (Rescriptor)	1997
Efavirenz (Sustiva)	1998

Viral Fusion Inhibitors:

T-20 (Fuzeon; Enfuvirtide; Pentafuside)	2003
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Anti-HBV Drugs

Intron A (Interferon alpha-2b)	1983
Roferon A (Interferon alpha 2a)	1984
Epivir-HBV (3TC; Lamivudine)	1998
Pegasys (Pegylated interferon alpha-2a)	2002
Hepsera (Adefovir dipivoxil)	2002
Baraclude (Entecavir)	2005

Anti-HCV Drugs

Intron A (Interferon alfa 2b)	1983
Roferon A (Interferon alfa 2a)	1984
Infergen (Interferon alfacon-1; Intermune)	1997
Rebetol (Ribavirin)	1998
Rebetron (Intron A + Rebetol)	1998
Peg-Intron (Pegylated Interferon alfa 2b)	2001
Pegasys (Pegylated Interferon alfa 2a)	2002
Copegus (Ribavirin)	2002
Peginterferon (Pegasys + Copegus)	2002
Ribavirin, generic, stand alone	2004

Anti-Herpesvirus Drugs

Idoxuridine (IDU; Stoxil; Herplex; Dendrid)	1963
Vidarabine (Ara-A; Vira-A)	1976
Trifluridine (Viroptic)	1980
Acyclovir (ACV; Zovirax)	1982
Ganciclovir (DHPG; Cytovene)	1989
Foscavir (PFA; Foscarnet)	1991
Famciclovir (Famvir)	1994
Valacyclovir (Valtrex)	1995
Cidofovir (HPMPC; Vistide)	1996

Penciclovir (Denavir)	1996
Fomivirsen (Vitravene)	1998
Abreva (n-docosanol), OTC	2000
Valganciclovir (Valcyte)	2001

Anti-RSV Drugs

Ribavirin (Virazole)	1984
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Anti-Influenza Drugs

Symmetrel (Amantadine HCl)	1966
Flumadine (Rimantadine HCl)	1993
Relenza (Zanamivir)	1999
Tamiflu (Oseltamivir)	1999

Treatments for Genital Warts

Alferon N (Interferon alfa n3)	1989
Imiquimod (Aldara)	1997

*As of August, 2006

Treatment for chronic hepatitis B virus (HBV) infections, which is a serious disease afflicting an estimated 1.25 million people in the United States and causing more than 5,000 deaths each year, has improved significantly during this past decade. A number of anti-HBV drugs have now been identified and used in the clinical management of this disease. These include Epivir-HBV (3TC; Lamivudine), Pegasys (pegylated interferon alpha-2a), Hepsera (adefovir dipivoxil), and Baraclude (entecavir) and all of these drugs have been approved by the U. S. FDA for general use against chronic HBV infections during the last ten years. Entecavir has also been approved recently (June, 2006) by the European Union Commission for the clinical treatment of chronic hepatitis B infections in Europe. The estimated numbers of chronic HBV infections in other countries around the world is staggering, with China clearly leading the list with an approximate 125 million cases. Brazil has an estimated 3.7 million infected people, Korea has 2.6 million cases, and Japan has 1.7 million cases. Chronic HBV disease, which can lead to cirrhosis, hepatocellular carcinoma, and death, is a global problem. In large-scale multinational studies, pegylated interferon alfa-2a treatment was observed to produce a sustained antiviral response in both

HBeAg-positive and HBeAg-negative patients at 24 weeks following a defined 48 week period of therapy. Hepsera (adefovir dipivoxil), an acyclic nucleotide analog of adenosine monophosphate (AMP) first synthesized by Antonin Holy and his associates in Prague and studied extensively by Erik De Clercq and his group in Leuven, was developed by Gilead Sciences for use against human HBV infections. It is metabolized to the active form adefovir diphosphate by cellular kinases and inhibits HBV DNA polymerase (a reverse transcriptase) by competing with the natural substrate deoxyadenosine triphosphate (dATP) and also by acting as a DNA chain terminator after its incorporation into viral DNA. The combination appears to have an additive effect against HBV. Baraclude (entecavir), a guanosine nucleotide analog that has been found to have potent and selective activity against HBV, also targets the viral DNA polymerase. This drug, developed by Bristol-Myers Squibb, is phosphorylated to the active triphosphate derivative which then competes with the natural substrate dGTP to inhibit all three activities of the HBV DNA polymerase: (1) base priming, (2) reverse transcription of the negative strand from the pregenomic messenger RNA, and (3) synthesis of the positive strand of HBV DNA. Baraclude has been observed to be clinically

effective in a randomized, double-blind, multinational trial in reducing viral loads to undetectable levels in 67% of HBeAg-positive naïve patients with chronic HBV infection after 48 weeks of therapy. It is clear that step-wise progress is being made in our ability to combat this chronic disease with selective antiviral chemotherapy.

Approximately 2.7 million Americans are chronically infected with hepatitis C virus. With the development of Rebetron (Intron A + ribavirin) combination therapy for the treatment of HCV infections by Schering Plough and its approved use by the FDA in 1998, a major advance was made in the clinical management of chronic HCV disease. More recent advances have been made with the development of the pegylated interferons by both Schering Plough (Peg-Intron; pegylated interferon alfa-2b) and by Roche (Pegasys; pegylated interferon alfa-2a). Combination therapy with Pegasys + Copegus (ribavirin) was approved by the FDA in 2002 for the treatment of adults with chronic HCV infections who have compensated liver disease and who have not been previously treated with alpha interferon. This combination has allowed the physician to tailor the dose and duration of a patient's antiviral therapy to the genotype of the virus and therefore, more effectively treat the disease and achieve a sustained virological response with a lower dose and more limited side effects. The combination has been approved in over 50 countries around the world, including countries in the European Union. In 2005, the U. S. FDA approved the Pegasys + Copegus combination for the treatment of chronic HCV in patients co-infected with HIV. In pivotal clinical studies, this antiviral combination therapy resulted in 40 % of patients co-infected with HCV and HIV/AIDS achieving a sustained virological response, i.e., the patients had continued undetectable HCV levels in the blood at 24 weeks after therapy. This result represents good progress in the ability to treat this disease in the most refractory of patients.

Improvements in the available therapies for herpesvirus infections have also been made during the last decade, with the development and approval of cidofovir (HPMPC; Vistide) for the treatment of CMV retinitis in AIDS patients, penciclovir cream

(Denavir) for the topical treatment of recurrent oral herpesvirus infections, and valganciclovir (Valcyte) for the treatment of CMV retinitis in AIDS patients and also for the prevention of CMV disease in certain organ transplant patients. Gilead Sciences received U. S. FDA approval for Vistide in 1996 and final approval from the European regulatory commission in 1997 to market the drug in all of the European Union countries. Outside the United States, the drug is marketed by its partner Pfizer. In pivotal clinical studies, the drug was found to significantly delay the progression of CMV retinitis in infected AIDS patients. Penciclovir (Denavir), approved by the U. S. FDA in 1996, became the first topically effective antiviral drug for use in the treatment of herpes labialis, a disease that affects approximately 40 million individuals in the United States alone. More recently, Roche received U. S. FDA approval for valganciclovir (Valcyte), an L-valyl ester (prodrug) of ganciclovir, for use in the prevention and treatment of CMV disease. Valganciclovir exists as a mixture of two diastereomers, both of which are converted rapidly to ganciclovir by cellular esterases. Ganciclovir, an analog of 2'-deoxyguanosine is then preferentially phosphorylated to ganciclovir triphosphate in virus-infected cells and inhibits CMV DNA synthesis by competing with 2'-deoxyGTP, the natural substrate for the viral DNA polymerase. From the discovery perspective, a more promising class of anti-CMV agents, the benzimidazole ribosides, also progressed in their development during this timeframe. The original drug leads in this series emerged from the pioneering work of Leroy Townsend and John Drach at the University of Michigan, who subsequently partnered with Karen Biron and other scientists at Burroughs Wellcome (which later became GlaxoWellcome and eventually GlaxoSmithKline), to identify and develop clinical drug candidates. This development effort matrixed across the expertise resident within the ISAR scientific community, and the resulting chemistry and biology studies were presented at annual ICARs throughout the first and second decades of the ISAR. This fruitful academic, industrial and government collaboration ultimately yielded two clinical candidates with distinct and novel modes of action that both entered clinical trials. Maribavir (5,6-dichloro-2-(isopropylamino)-1-β-L-ribofuranosyl-1H-benzimidazole), a first-in-

class viral protein kinase inhibitor, is now entering Phase 3 clinical development under the stewardship of ViroPharma, Inc. for prophylaxis of CMV in solid organ and stem cell transplant patients. In another focus area, imiquimod (Aldara), an immunomodulator, was approved by the FDA in 1997 for use in the treatment of genital warts.

Significant advances have been made recently in the development of new drugs for the prophylaxis and treatment of influenza A and B virus infections. These include GSK's Relenza (zanamivir) and Roche's Tamiflu (oseltamivir), both drugs approved by the U. S. FDA in 1999. Another potentially useful new anti-influenza drug, peramivir, is currently in clinical trials and is being developed by BioCryst Pharmaceuticals (Birmingham, AL). Both zanamivir and oseltamivir inhibit influenza virus replication via inhibition of the influenza virus neuraminidase with the possibility of alteration of virus particle aggregation and release. Peramivir, which also inhibits the influenza virus neuraminidase, has been shown in preclinical studies to be more potent than zanamivir and oseltamivir against both influenza A and B strains *in vitro* and it has been reported to be highly effective in preventing acute respiratory disease in mice and ferrets. Because of poor bioavailability when administered by the oral route in humans, the drug has been re-formulated for parenteral (intravenous or intramuscular) delivery and

these formulations have shown good efficacy in pre-clinical animal model evaluations. Preliminary studies, published in the ISAR's official journal *Antiviral Research*, have indicated that a single intramuscular injection of peramivir is comparable to five days of oral treatment with oseltamivir. In addition, peramivir inhibits the replication of avian influenza (H5N1) strains and it is effective against influenza virus strains that have become resistant to zanamivir and oseltamivir. Clinical trials are now in progress to evaluate this promising new anti-influenza drug in humans.

The progress made in antiviral research and development during the past ten years has truly been remarkable, but there are still many unmet medical needs. According to Richard J. Whitley of the University of Alabama at Birmingham (UAB) Medical Center, the ISAR's first President, there is a need for better and less toxic drugs for the effective treatment of viral infections that are increasingly observed in organ and stem cell transplant patients. There is also a need for new antivirals to replace the mutagenic drug ribavirin for the treatment of respiratory syncytial (RS) virus infections in neonates. Finally, there is the obvious need to develop selective antiviral agents for effective use against the many important viral diseases for which there is currently no available therapy at all.

Section Two – The Success of ISAR/ICAR as the Leading Professional Scientific Organization and Forum for Antiviral Research: Contributions to the Field

Following a successful first decade of operation, the leadership of the International Society for Antiviral Research (ISAR) looked forward to the future with an earned optimism and a continued desire to provide the membership with a mature, robust, and financially stable Society and a valuable and exciting international conference that would represent the leading professional scientific organization and forum, respectively, for all aspects of antiviral research and development from antiviral drug design, synthesis, and discovery to preclinical and clinical antiviral drug research, development, and approved clinical use. While other, more specialized, antiviral meetings had been organized over the past decade for individual viral diseases such as AIDS, hepatitis, or influenza, only the ISAR's multidisciplinary International Conference on Antiviral Research (ICAR) has covered the entire field of viral diseases and all aspects of antiviral research and development. It remains the primary international forum for all active investigators in the field of antiviral research and the ISAR remains their home base.

By 1998, The ISAR membership had grown back to approximately 750, up from 664 in 1997. Koen Andries and Jack Secrist were re-elected for additional three-year terms as ISAR Secretary and Treasurer, respectively. The annual International Conference on Antiviral Research (ICAR) continued to be organized by Earl Kern (Conference Committee Chair) and Rich Whitley (Program Committee Chair). Together, Earl and Rich did an outstanding job in these two very important leadership roles for much of the Society's second decade. The 11th ICAR was successfully held in San Diego, California, assisted by The Conference Table, Ltd, and hosted by Karl Hostetler and Doug Richman (UCSD). The conference was attended by 464 members from 24 countries. John C. Martin became the first ISAR President of its second decade and Karen K. Biron became President-Elect. At the San Diego meeting, during the annual banquet, the ISAR Award of Excellence, a very prestigious award which has

been given only four times by the Society, was presented to each of two very deserving awardees: Erik De Clercq of the Rega Institute for Medical Research in Leuven, Belgium and Richard J. Whitley of the University of Alabama at Birmingham (UAB) Medical Center in Birmingham, Alabama. Both Erik and Rich were past Presidents of the ISAR and received this rare honor for their numerous scientific achievements and for their many contributions to the Society during its first decade. Erik and Rich have remained very active members of the Society to this day and they have contributed greatly to its continued success over the past ten years as well, giving of their time and energy in many different capacities, playing a number of very important roles within the Society during this very active period in its history. Both Erik and Rich recently indicated that they were deeply honored to have received this award from the Society and that they remain committed to the future success of the ISAR. Elected to the ISAR Board of Directors during the San Diego conference were Erik De Clercq, Hugh Field, Catherine Laughlin, and Rich Whitley. The historical booklet entitled "The International Society for Antiviral Research: The First Decade", produced by George J. Galasso, a Past President and a co-founder of the Society, was distributed to the conference attendees and subsequently mailed to the membership. This document was well done and provided us with an excellent look-back at the founding of the Society and its early years of operation. The present booklet picks up where the history of the first 10 years of the Society leaves off and it represents the recollections, contributions, and reflections of many of the Society's past officers and committee members who, through their dedicated efforts and hard work, have played such an important role in the continuing success of the ISAR.

The 12th ICAR was held in Jerusalem, Israel, hosted by Ehud Katz of the Hebrew University – Hadassah Medical School. The meeting and the scientific program was again of excellent quality and was organized with the local assistance of Dr. Katz

and the professional staff of Kenes, Ltd. As with previous meetings outside of the United States and Europe, attendance by the ISAR membership was greatly reduced. Only 250 attendees were present for about 150 presentations. In addition to the expense involved, political instabilities and tension in the region may have somewhat dampened the attendance at the 1999 conference, although the situation was closely monitored. At that time of relative peace in the Middle East, many attendees ventured out on their own to tour the near-by Old City or did so on organized tours. Participants reported that all of the conference tours were spectacular, especially the post-conference tour of Jordan and the ruins at Petra. Cathy Laughlin remembered an incident at the border between Israel and Jordan however, that caused some initial concern. Then ISAR President-Elect Karen Biron was in line along with the rest of the ICAR tourists to cross the border from Jordan back into Israel. Karen waited and waited for the return of her passport as all of the other tourists crossed the line back into Israel. Ultimately, she was detained by the Israeli border guards for nearly a half-hour because of some unstated problem with her passport, while the rest of the group waited. When they finally released her without adequate explanation, Cathy and the rest of the group who were unable to go back to help Karen, breathed a big sigh of relief upon her belated return to the group. Karen thinks that she drew the lucky number for the border guards-in-training to try out their new computerized search tools.

During the Jerusalem conference, the ISAR Board voted to establish the Gertrude B. Elion Memorial Lecture Award with the generous support promised from the Glaxo Wellcome Company and it was planned that the first lecture would be held during the 13th ICAR (See details in Section Three below). Also during this meeting, George Galasso convinced the ISAR leadership that a professional conference organizer was needed as a contractor to handle all of the logistics of the annual meetings, to maintain the ISAR Membership Directory, and to provide the continuity of a longer-term working relationship with the ISAR Officers and the Conference and Program Committees that only a multi-year contract could provide. Proposals were solicited from a number of companies using the NIH-style "Request

for Proposal (RFP)" mechanism and a panel was assembled to review all submitted proposals. Courtesy Associates of Washington, D.C. provided the best proposal in terms of what they could offer for the available money. A contract was awarded to Courtesy Associates for 3 years with an option to renew for an additional 2 years.

The Inner Harbor of Baltimore, MD was the site for the 13th ICAR held in 2000, hosted by George Galasso (Local Committee Chair), this time assisted by Courtesy Associates which had won the ISAR contract to be its professional conference organizer and secretariat. The scientific meeting was excellent and Courtesy Associates did a great job to provide an efficiently run conference and memorable special events, such as the Opening Reception which was held at the National Aquarium and was capped off with outgoing ISAR President John Martin feeding the dolphins. Karen Biron became the new President of ISAR, John Drach became President-Elect and Brent Korba was elected the new ISAR Secretary to replace Koen Andries who had done a fine job as Secretary of the Society and who had been instrumental in developing and maintaining the ISAR Membership Directory. Jack Secrist was re-elected Treasurer for a third term. Michael Rossman became the first recipient of the Gertrude B. Elion Memorial Lecture Award for his pioneering research on the molecular architecture of the capsid of the human rhinovirus and the binding of the antiviral agent pleconoril into a deep pocket within the capsid. The Baltimore conference counted 401 members in attendance from 21 countries and there were 180 presentations. The total ISAR membership, however, had dropped to 647 by the beginning of 2000 and it thus became apparent that greater efforts were again needed to recruit new members to the Society and to retain its existing members. In December, 2000, George Galasso coordinated a task force of ISAR members to discuss the suggestions and proposals that had been solicited from the membership in an attempt to improve the Society. This effort resulted in several changes: The annual Conference was shortened by one day, the ISAR-ICAR web page was improved and expanded, the Membership Committee more actively recruited new members to the Society, a brochure describing the ISAR was developed and made available, the

William H. Prusoff Young Investigator Lecture Award and ICAR Poster Awards were instituted (See Section Three below). The Society also decided to have a trial Press Conference in conjunction with the ICAR. Press releases were invited from selected researchers making presentations at the Conference.

Membership in the ISAR increased slightly in 2001 to 689 with 57% of the members coming from the United States, 30 % from Europe (including the UK), 5% from Japan, 4% from Canada, and 4% from the rest of the world. For the first time, seats on the ISAR Board of Directors were organized by region and candidates were elected for these numbered seats. This was done in order to assure sufficient international representation in the Society's decision making processes. Elected to the Board in 2001 were: David Bernstein (USA) for Seat 1, Jan Balzarini (Belgium) for Seat 2, Joe Martin (UK) for Seat 3, and Catherine Laughlin (USA) for Seat 4.

The 14th ICAR was held in Seattle, WA in 2001 with Larry Corey as the Local Host. Again, the ICAR organizers had the able assistance of Courtesy Associates as the Conference Secretariat. The annual satellite symposium entitled "Clinical Update on Antiviral Drugs" was held preceding the Conference and the program again contained excellent presentations of cutting-edge clinical research results with a number of antiviral drugs. This pre-Conference clinical symposium, initiated at the 7th ICAR in Charleston, SC, had always been very well attended and extremely well received by the ISAR membership and this year was no different. Over 430 members attended the Seattle Conference during which the first ICAR Poster Awards were presented since their establishment for each of three candidate categories: Category 1 -Graduate Students, Category 2 - Post-Graduates, and Category 3 - Young Investigators. John Drach and Kirk Field had worked diligently to establish the Poster Award presentation event for the annual ICAR and it had been a resounding success. The second Gertrude B. Elion Memorial Lecture Award was presented to Leroy Townsend of the University of Michigan and the first William H. Prusoff Young Investigator Lecture Award was presented to Chris McGuigan, Cardiff University in Wales (the current ISAR President).

The American Herpes Foundation, a non-profit organization, sponsored an award for research excellence in herpesvirus research to be presented at the Seattle ICAR. This award, intended to raise awareness about control of herpesvirus infections is given to physicians-in-training and consists of a plaque and a \$10,000 stipend, half of which is to be presented to the award recipient and half to the recipient's department. Awards presented at the 2001 ICAR were given to Jennifer Moffat of the Upstate Medical University of the State University of New York (SUNY) and to William Nichols of the Fred Hutchinson Cancer Center at the University of Washington Medical Center in Seattle, WA.

The Society's website was expanded to include an advance copy of the next ICAR Program, a summary of the previous ICAR, and the criteria for the ISAR awards. The website also included membership and meeting application forms, job listings, information on future ICARs, listing of other meetings of interest to the membership, and links to other websites, including the Society's three sponsored journals. Brent Korba initiated many of these improvements and these changes were seen to provide a better service to the membership and a much greater visibility for the ISAR outside of the organization.

The events of September 11th, 2001 and its aftermath shook the world and changed it forever. The bioterrorist attacks which followed, in which anthrax spores were mailed to members of the U. S. Senate and U. S. House of Representatives and to others around the country resulting in a number of inhalation anthrax infections and deaths, brought home to the civilized world the importance of public health preparedness and measures to combat the potential threats of bioterrorism. It clearly underscored the importance of developing effective antiviral drugs that could be stockpiled for possible use against infectious viruses considered to be threat agents by the National Centers for Disease Control (NCDC), the National Institute of Allergy and Infectious Diseases (NIAID), and by the U. S. Army Medical Research Institute for Infectious Diseases (USAMRIID). On November 1, 2001, ISAR President Karen K. Biron sent an official letter to U. S. President George W. Bush expressing the full sup-

port of the Society for his planned initiatives to mobilize the scientific, medical, and pharmaceutical communities to meet these biological threats and she offered our immediate assistance in any way that was needed. She urged the President to consider increasing the funding to the National Institutes of Health (NIH) for antiviral research and development and to the establishment of a new partnership between academia, government agencies, and pharmaceutical companies which would more efficiently utilize their chemists, virologists, and clinicians to identify new antiviral drugs to combat the potentially deadly viruses that could be used in future bioterrorist attacks. The ISAR was ready to take a leadership role in helping to organize such a Task Force. This was an important and timely letter for the Society's President to have written and to have sent to the U. S. Commander-in-Chief. The ISAR leadership had the full support of the membership and many offered their services to the appropriate government agencies to assist them in designing biodefense initiatives for the United States and its allies. The full text of the ISAR letter to President Bush was published in the *ISAR News*, Vol. 11, No. 2 (December, 2001). Since those events of 2001, ISAR scientists have joined scientists worldwide to increase international preparedness against acts of bioterrorism and the annual ICAR has provided a forum for data presentation and discussion.

Antiviral research has had a number of advocates within the U. S. government, starting with George Galasso who, in 1969, established the Antiviral Substances Program at the National Institutes of Health. George was heavily involved in directing the funding for a large number of antiviral research programs in the early days and his efforts were critically important in the establishment of antiviral research as a new scientific discipline. His advocacy and support was essential for the clinical development of the first systemically effective antiviral drug, vidarabine (ara-A), an anti-herpes drug which had resulted from an early collaborative research program that involved Parke, Davis & Co. (Francis Miller, Barney Sloan and Bob Buchanan), Southern Research Institute (Frank Schabel, Bob Sidwell, and Bill Shannon), UAB (Charles Alford, Larry Chien, and Rich Whitley), the NIAID, and a clinical evaluation group that included 21 medical

centers across the country. Rich Whitley recently indicated that "when he thinks of the key people in the ISAR who have clearly made benchmark contributions to the field, he thinks of Bill Prusoff, Trudy Elion, and George Galasso". As a scientific administrator at the NIAID, George provided strong advocacy for the American antiviral research community and guided the research efforts of many to help establish a vibrant and successful national program that would expand in size, scope, and acceptance. George has continued to provide his advocacy and organizational skills to assist the ISAR very effectively in so many ways, even after his retirement from the NIH and up to the present time. When George became the Chief of the Infectious Diseases Branch at the NIAID, the Antiviral Substances Program was then led by Maureen Meyers and, subsequently, by Catherine Laughlin who maintained and continued the expansion of antiviral research funding throughout a period of rapid growth for the field worldwide. Under their leadership, a number of important programs were put into place including the establishment of the Collaborative Antiviral Testing Group, the use of the National Cooperative Drug Discovery Group (NCDDG) grant mechanism for antiviral research initiatives, and contracts for extramural funding of antiviral drug discovery projects. These mechanisms were instrumental in assisting the development of several antivirals including the origination and preclinical development of maribavir through a collaboration between Leroy Townsend and John Drach at the University of Michigan and Karen Biron and her colleagues at the Burroughs Wellcome Company (now GlaxoSmithKline) as described in more detail earlier in Section One above. Other scientists who have been instrumental in championing antiviral research from within U. S. government agencies were Michael A. Ussery, Steve Turk, and Christopher Tseng, all currently at the NIAID, and these loyal ISAR members have played major roles in assisting many investigators in the field build strong and productive antiviral research programs. These government scientists have also continued to contribute much toward promoting important interactions among ISAR members at the annual ICAR. After 9/11, the NIAID's budgets were increased for biodefense and infectious disease research and Cathy Laughlin's attention turned to her additional respon-

sibilities which now included helping in the nation's efforts to provide a solid defense program against bioterrorist threats. Stockpiling of antiviral drugs, coordination of research efforts, not only for countermeasures against the designated threat agents, but also for emerging virus infections, became the order of the day. Significant momentum was achieved in the search for agents with antiviral activities against the poxviruses and these efforts were coordinated with John Huggins and others at the U. S. Army Medical Research Institute for Infectious Diseases (USAMRIID) in Frederick, MD and at the NCDC in Atlanta, GA. New antiviral therapeutics were developed and tested in animal models for potential use in combating various poxvirus infections, including smallpox.

The 15th ICAR was held in March 2002 in the historic city of Prague in the Czech Republic. This very successful conference was hosted by Antonin (Tony) Holy. The conference was attended by 325 registrants representing 29 countries. It was appropriate that the Gertrude B. Elion Memorial Lecture Award was presented to Tony Holy during this conference, held in his home country, for his outstanding contributions in antiviral research. He has been responsible for the design and chemical synthesis of many novel nucleosides and nucleotides leading to the development of a new class of antiviral agents, the acyclic nucleoside phosphonates. His synthetic work, in active collaboration with Erik De Clercq's group in Belgium and Gilead Sciences in the United States, has subsequently led to the development of the approved antiviral drugs cidofovir, adefovir, and tenofovir for the treatment of HCMV, HBV, and HIV/AIDS, respectively. Like Trudy, Tony has been a mentor to many young investigators and a dear friend to his many colleagues and collaborators. He has been a loyal and active member of the ISAR since its founding. Ralf Bartenschlager of the University of Mainz received the Prusoff Award for 2002 for his research on hepatitis viruses and notably for his development of a replicon system that provided the first reliable cell culture system for HCV replication. A press release program was initiated to provide more publicity for the ICAR, but there were only a few participants in this program at the Prague meeting; others who were invited, declined to participate. The response to the few press

releases that did go out electronically, however, was indeed encouraging and the Board decided to consider whether or not to continue with this service that utilized NewsWise, an online resource. The ISAR later contracted with NewsWise to send out press releases, on topics to be presented at the next ICAR, to over 15,000 science writers by e-mail and this organization would also send out information about the Society and the ICAR to selected journalists prior to and during the conference in the form of traditional press releases. The membership did not seem to favor this program, so it was terminated.

John C. Drach of the University of Michigan became the new ISAR President and Jack Secrist of Southern Research Institute became the President-Elect. In his first letter to the membership, John Drach called for a greater involvement of members in the activities of the Society and asked for interested members to serve on the various ISAR committees. By December of 2002, several individuals had heeded his call and had volunteered to serve the Society more actively. The Society had always had a hard time getting volunteers and the new President and President-Elect were committed to making a real effort to increase the number of new faces in the Society's various activities. A number of members rotated off standing ISAR committees in 2002 and new leadership took the reins. Upon his retirement from NIH in 1996, George Galasso took over the task of obtaining major funding sources for the annual ICAR, as well as designing the annual Posters and Announcements, and other logistical services for the Society. Kirk Field headed the Finance Committee and expanded the efforts to raise separate Corporate Funding to support the Society. Amy Patick took over the responsibility of chairing the Travel Grants Committee, a job held previously by John Drach, the new ISAR President. A number of members rotated off the Program Committee, including Hugh Field, Paul Lietman, and Rich Whitley who not only chaired that committee but also was the organizer and convener of the Clinical Symposium that precedes the ICAR every year. Rich Whitley had done a magnificent job of organizing these clinically-oriented symposia on antiviral drugs over the years and these pre-Conference sessions had been observed to significantly grow in importance and popularity under his careful leadership and

guidance. The Clinical Symposium had, by this time, become an essential and expected event preceding the annual ICAR and it was apparent that someone would need to take over the important responsibility of organizing this very valuable scientific session in the future. During the Prague meeting, the Board voted to combine the Program and Conference Committees. Earl Kern was appointed Chairman of the newly expanded Conference Committee and Paul Griffiths agreed to join this Committee and to take direct responsibility for organizing the Clinical Symposium. At the Prague meeting, Joseph Colacino with the support of George Galasso had suggested to ISAR President John Drach that the Society should consider initiating an ISAR Placement Service. After a subsequent discussion with the Board, the Society established the Placement Service and charged a new committee under the chairmanship of Joe Colacino to guide its operation. The Placement Service was designed to provide a forum for prospective employers, such as pharmaceutical and biotech companies, research institutes and universities to advertise their position openings and the ads would be posted on the ISAR web page at no charge. Plans were made for on-site space to be provided at the next ICAR for prospective employers to meet and interview interested candidates. Plans were also made to advertise the new ISAR Placement Service in the two official journals of the Society published by Elsevier: *Antiviral Research* and *Antiviral Chemistry and Chemotherapy*.

A very successful 16th ICAR was held in Savannah, GA in 2003 with an extensive and diverse scientific program. There were 407 registrants counted from 22 countries and over 160 abstracts of papers submitted for presentation at this conference. Travel funds were awarded to 24 applicants from 13 countries to attend the Savannah ICAR. A Biodefense Mini-Symposium was included in the program to cover the timely subjects of bioterrorism and biopreparedness. The 2003 Gertrude B. Elion Memorial Lecture Award was presented to John C. Martin (Gilead Sciences) who, because of illness was not able to attend the conference in Savannah, but presented his lecture "A Brief History of Nucleotide Antivirals" at the 17th ICAR in Tucson

the following year. The William H. Prusoff Young Investigator Lecture Award for 2003 was personally presented by Bill Prusoff himself to Johan Neyts (Rega Institute for Medical Research; Leuven, Belgium). George Galasso conducted a survey of the participants at the Savannah ICAR and the respondents overwhelmingly expressed their general satisfaction with the conference and its format and saw no need for change. Newly elected were: Amy Patick (Pfizer) as the new ISAR Secretary and John Morrey (Utah State University) as the new ISAR Treasurer.

The planned retirement of Earl Kern as Chairman of the ISAR Conference Committee, following the 17th ICAR to be held in Tucson, AZ, loomed as a huge vacancy to be filled for a key leadership position having responsibility for one of the primary functions of the Society. This posed the particularly serious question of who would be willing and able to become the successor to Earl as the Conference Committee Chair because the Program Committee had been combined with the Conference Committee. Earl Kern had taken the major responsibility for the conferences since the very early days of the Society and, as chair of the Conference Committee, he had a very large role to play in site selection, abstract collection and handling, contacting speakers, working closely with the Program Committee and its subcommittees to provide the best program that could be assembled, and generally making sure that the ICAR ran smoothly in every respect, every year, for so many years. These shoes would indeed be huge ones to fill! Earl Kern had performed an enormous job for the Society and he did it extremely well, helping to make the ICAR the leading international forum for antiviral research and helping the ISAR achieve its stated goals and objectives in a manner *par excellence*. Since a substitute could not be found, ISAR President John Drach suggested that the outgoing President chair the Committee for two years following his tenure. Fortunately, John Drach's tenure ended in time for him to assume the role following the Tucson ICAR and his involvement would provide a smooth transition in leadership for this very important position. This was certainly a welcome suggestion and Jack Secrist, who became ISAR President during the Tucson ICAR made it official.

Approaching the end of the first five years of the Courtesy Associates contract with ISAR for assistance in the conduct of the ICAR and for maintenance of the ISAR Membership Directory, George Galasso was asked to re-advertise the RFP for the contract and assemble a review panel to select the winning proposal. Serving on this panel were: Bob Buckheit, Kirk Field, Brent Korba, Jack Secrist, and George Galasso as the Executive Secretary of the committee. A number of proposals were received, the applications were carefully reviewed, and Courtesy Associates was again selected as the best organization to assist the ISAR. It was awarded a five-year contract to continue its services for the Society. That business behind it, the ISAR leadership again, aware of the need for more participation by the younger members of the Society and the need for them to assume a more active role in its operations, called for a greater participation of the ISAR membership in the Society's committees and conducted another survey to determine if any changes should be made in the format or frequency of the ICAR. Respondents again affirmed their commitment to the ISAR sponsoring yearly conferences and to the ICAR maintaining its existing format. The Board was satisfied that the annual conference was achieving its desired end results: to maintain a focus on antiviral research in all scientific disciplines, to cover all viruses of current interest, and to encompass all aspects of antiviral research from rational drug design, chemical synthesis, *in vitro* testing, animal model development and preclinical studies, all the way to clinical trials and approved clinical use. Although the Board began to be concerned about its goal of financial growth and stability, the ICAR has become the premier venue for keeping up with what is happening in antiviral research and development worldwide and the Board therefore decided that no changes should be made in the ICAR's obviously well-received and successful current format. Nevertheless, it was determined that as priorities shift and funding becomes tighter in the pharmaceutical industry, the role of the ISAR and its ICAR will continue to be assessed by the leadership in future years to ensure that it continues to serve its membership in the best possible way.

The 17th ICAR in Tucson, AZ was a very successful meeting in a beautiful resort location. All

who were there will remember the stunning setting as a full moon rose over the surrounding mountains during the outdoor opening reception. The scientific program clearly reflected many of the changes that had occurred in international antiviral research priorities, emphasis, and focus. The conference included a mini-symposium on emerging viral infections and attendees were rewarded with a current status update on existing world outbreaks of SARS, West Nile, monkeypox, and influenza, with an assessment of the public health responses to each of these infectious diseases. The oral and poster sessions were of the highest quality with over 150 abstracts submitted for presentation at the conference and there was not enough time on the program to schedule all of the excellent, highly-rated papers for oral presentation. All of the committee members agreed that the quality of the science submitted for presentation was clearly improving over the years. Richard J. Whitley was presented the Gertrude B. Elion Memorial Lecture Award for 2004 and Fabien Zoulim was presented the William H. Prusoff Young Investigator Lecture Award for 2004. A new ISAR award was instituted at the 17th ICAR for Outstanding Contributions to the Society. The award, which will be given only rarely, is intended for individuals who have significantly contributed to the success of the Society. The inaugural award was very appropriately presented to Earl R. Kern on the occasion of his resignation as Chairman of the ICAR Organizing Committee, based on his long and outstanding service to the Society since its inception and based on his signal efforts to make the Society and its annual conference a continuing success. The award was presented by outgoing ISAR President John Drach, who with the collusion of Earl's wife Aloma, devised a PowerPoint 'roast' of Earl going back to his high school days in Wyoming. In a more serious vein, John remarked that the award was truly deserved and that Earl had clearly left his indelible, positive mark on the Society for all time. Earlier that day, during the ISAR Business Meeting, John also gave a very brief 'roast' of incoming President Jack Secrist and then announced the latest election results: Chris McGuigan (University of Cardiff, Wales) was selected as the President-Elect of the Society and new members of the ISAR Board of Directors included Masanori Baba (Japan), Jan Balzarini (Belgium), Joe Colacino (U.S.A.), and

continued on page 21



ISAR Presidents: Erik De Clercq, George J. Galasso, Hugh J. Field, Earl R. Kern, John A. Secrist III, Christopher McGuigan, and Amy K. Patick (Vice-President). Not shown: Richard J. Whitley, John C. Martin, Karen K. Biron, and John C. Drach



ISAR Awards of Excellence: Richard J. Whitley, Gertrude B. Elion, Erik De Clercq, 1998



Questioning the speaker
ICAR 2004



ISAR Leadership 1998: Catherine Laughlin, Koen Andries, Richard Whitley, John Martin, Karen Biron, Jack Secrist, Earl Kern, Erik De Clercq 11th ICAR, San Diego



John Martin passing on the Presidency to Karen Biron , 13th ICAR Baltimore, 2000



Questioning the speaker 13th ICAR Baltimore, 2000



Coffee Break



Opening Reception, 19th ICAR, San Juan, 2006



Opening Reception, 19th ICAR, San Juan, 2006



Session Participants, 19th ICAR, San Juan, 2006



Poster Session, 19th ICAR, San Juan, 2006



Poster Session, 19th ICAR, San Juan, 2006



Session Speaker Arnold Monto



Coffee Break



Mini-Symposium panelists listen intently to a question from the audience, 19th ICAR



John Drach presenting the 2004 Elion Award to Richard Whitley, 17th ICAR, Tucson, 2004



George Galasso, Kirk Field and Bill Shannon discussing this publication, 19th ICAR, San Juan, 2006



Session Participants



Lunch in Tucson ICAR 2004



George Galasso, local 13th ICAR Chair, getting advice from Ehud Katz, local 12th ICAR Chair, in Jerusalem 1999.



16th ICAR Poster Awardees, John Drach, ISAR President (L) and Kirk Field, Chair of the Judging Committee (R), with winners of poster awards: Christopher Jarvis, You-Hoon Chong, Gloria Komazin, Xin Wang, Jeongmin Kim. Absent: Kurt Vermeire. Savannah, 2003



John Drach presenting the 2004 Prusoff Award to Fabien Zoulim, 17th ICAR, Savannah, 2003



The 2002 Elion Awardee Antonin Holy and Bill Prusoff at the 15th ICAR, Prague, 2002



Publication Committee: Anthony Vere Hodge, Hugh J. Field, Erik De Clercq, Robert W. Sidwell (Chair) A. Kirk Field, and Donald F. Smees., 19th ICAR, San Juan, 2006



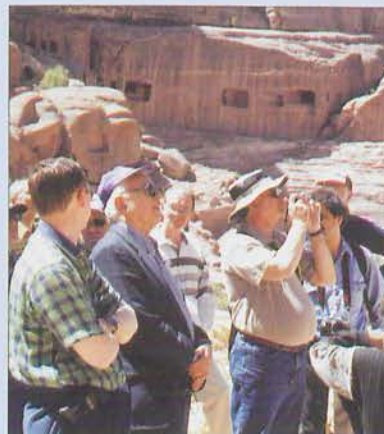
Opening Reception, 16th ICAR, Savannah, 2003



Bill Shannon, Hugh Field, and Anthony Vere Hodge



Session participants with Bill Prusoff as usual front and center at 27th ICAR with Vasu Nair to his right



12th ICAR Attendees on Post-Conference in Petra, 1999.

Susan Daluge (U.S.A.). Jack Secrist became the new ISAR President and took over the reins of leadership. The ISAR Treasurer, John Morrey, presented the Financial Report to the membership and indicated that the Society's finances in 2004 were less solid than the year before because of rising expenses and fewer contributions from ICAR Sponsors. This was somewhat alarming since the 18th ICAR was scheduled to be held in Barcelona, Spain and was anticipated to be an expensive conference for the Society to conduct. George Galasso, who was responsible for raising funds for the ICAR, urgently asked the membership to assist in identifying new sources of financial support for the annual conference, noting that two major conference contributors had been lost in the year 2004.

The 18th ICAR was held in Barcelona in April, 2005. This was the first ICAR where abstract submission and meeting registration were handled electronically via a website hosted by an outside provider, SPLTrak. As the new Conference Committee Chair, John Drach traveled up a long learning curve working with SPLTrak to get the site customized for ISAR and up and running. At one point, John marveled at the fact that abstracts from all over the world were on his computer and that, along with the Program itself, he would send them from his computer to Belgium for electronic type setting. Then they would go to Ireland for printing and finally to Barcelona as a regular hard copy edition of *Antiviral Research* in time for the ICAR. The program, as always, provided non-concurrent oral and poster presentations with emphasis given to particular disease categories or virus families. A timely plenary lecture provided the introduction to each oral presentation session. The program also included a mini-symposium on "Biodefense and Emerging Infections", a highlight of the conference. As usual the conference was preceded by a Clinical Symposium entitled "Update on Antiviral Drugs" and this symposium, sponsored by pharmaceutical companies, provided attendees with an excellent overview of ongoing research efforts involving the promising antiviral drugs that were currently under development at the time. Erik De Clercq was presented the 2005 Gertrude B. Elion Memorial Lecture Award and his lecture entitled "Antiviral Drug Development: Where Chemistry Meets Biology and

Medicine" traced the successful path of antiviral drug discovery and development, emphasizing the importance of close collaborations between chemists, biologists, and physicians. The 2005 William H. Prusoff Young Investigator Lecture Award was given to Arianna Loregian (Univ. of Padova). The ISAR Poster Award competition was intense in the Graduate Student award category with two first prize winners and two second prize winners selected. Fewer contenders competed in the Postdoctorate and Young Investigator award categories, so only a single award winner was selected for each of these categories. José Esté, the local host for the conference, provided an excellent and hospitable venue and he ensured that all of the arrangements in Barcelona were handled very well. The Conference participants were given a free afternoon for tours of the city. John Drach, the new Conference Committee Chair, did an outstanding job of organizing the meeting. Karen Biron and Courtesy Associates also provided much assistance in helping to organize the scientific and logistical aspects of the ICAR, respectively. John's introduction of the on-line abstract system was well accepted by the membership. John also demonstrated his brilliant talent as a flamenco dancer during the evening post-banquet entertainment event.

The financial condition of the Society became a topic of concern once again. Much of the financial challenge in 2005 had been due to the change in the exchange rate of the euro versus the U. S. dollar between the time that the conference arrangements were finalized and the actual date of the meeting. In addition, there had always been a financial challenge to the Society for conferences held in European hotels because of their requirements for additional payments for meeting space and other conference-related activities. This is not the case in North America where the hotels provide the conference room space as part of the package if the meeting is booked in their hotels and a block of guest rooms is reserved and guaranteed. President Jack Secrist indicated that this fact would have to be taken into consideration in the future when sites for the annual ICAR are selected. The Financial Report for 2005 indicated that expenses had exceeded income, that the ending balance in the Operating Account was over \$100,000 less than the opening

balance, and that the Investment (reserve) Account had fallen from \$264,852 to \$190,490. In addition, major contributions to the ISAR and pharmaceutical company support for ICAR was seen to be much reduced. While cost-cutting measures were put into effect and while John Drach and the ISAR Treasurer John Morrey minimized expenses wherever possible, the Barcelona conference still ran at a significant deficit. Due to the increasing concern about the diminishing financial reserves, the Society initiated some cost cutting measures. The Conference had previously supported two ICAR Receptions, one following the Clinical Symposium on Sundays and a second on the official opening of the Conference on Monday. This was the first year that the Society decided to hold only the Clinical Symposium Reception. Philip A. Furman was appointed Chair of the Finance Committee and was given the important task of raising funds for the ISAR. He replaced A. Kirk Field who had served as Chair of the Finance Committee for the previous three years and who had done an outstanding job in setting an effective framework for the committee's work. George Galasso continued to take on the important responsibility of raising funds for the ICAR and also for obtaining some of the ISAR funding. Under Phil Furman, the Finance Committee took on a more international flavor with Eddie Littler helping with fund-raising in Europe and Masonori Baba assisting with fund-raising in Japan. The Committee, which also included Roger Ptak, Jim McSharry, and the ISAR Treasurer John Morrey, sent out a fund-raising letter to 187 companies. They received a response from only 14 (<10%) and none came from Europe or Japan. Interest in antiviral research and development had clearly been waning within the large pharmaceutical companies for several years and many of these companies had terminated their internal programs in favor of targeting larger markets where the turn-around time to profits was shorter and the profits were quantitatively larger. The Committee observed that these priority shifts within the larger pharmaceutical companies were severely impacting the Society and that its traditional funding sources had changed. More and more of the stable base funding for the ISAR and the ICAR was now coming from the smaller biotech companies that targeted the smaller niche markets and, while less financially able to fund the Society's activities than the big com-

panies, they were highly involved in current antiviral drug research and they did what they could to help the Society. Phil Furman recently indicated that there is a real need for the younger investigators in the antiviral research community to take on the challenge to find innovative ways to keep the Society and antiviral research going financially in the future. One very welcome source of revenue in 2005 was the transfer of half of the remaining funds of the disbanded Inter-American Society for Chemotherapy (IASC) to the ISAR. This amounted to a gain of \$23,038 for the ISAR treasury. While not a huge amount, it came at a time when ISAR funding had significantly declined and the gift was much appreciated.

During the Barcelona conference, it was decided that the expanded Conference Committee should again be split back into two separate committees, the Conference Committee and the Program Committee, as originally called for by the Society's By-Laws. The work of the consolidated committee was really too much for one individual to coordinate, although John Drach did a yeoman's job of pulling it all off successfully. It was decided that, following the 19th ICAR in San Juan, P.R. (for which John Drach would again serve as the Chair of the expanded Conference Committee) the immediate Past President would then become the Chairman of the Conference Committee and the President-Elect would then become the Chairman of the Program Committee. This would not only satisfy the mandate of the ISAR By-Laws, but it would also provide for the automatic rotation of the leadership of these important committees in the future. This arrangement appeared to be a much more workable solution to enable a smooth succession of leadership for these two committees and would obviously involve the efforts of many new faces and younger individuals in the activities of the Society and its ICAR. This has been considered by many members to be a very positive change for the future. The planning for the 20th ICAR in Palm Springs, CA will therefore be done by Jack Secrist (Past President) as Chair of the Conference Committee, by Amy Patick (President-Elect) as Chair of the Program Committee, with the continued assistance of John Drach and Courtesy Associates. Thus, Chris McGuigan, the new ISAR President will have much well-seasoned and experi-

enced help with the next ICAR in Palm Springs. The obvious downside of rotating chairs for the Program and Conference Committees in the future is the loss of past experience. Each new chairperson needs to undergo a learning period and as soon as he/she gains this useful information, he/she rotates off. This again emphasizes the need for an experienced contractor such as Courtesy Associates, Inc. which would provide the multi-year past experience role in assisting with the planning and coordination of the ICAR. If the Society is financially able to afford the continuation of this professional conference organizing service in the future, it would certainly be money well spent. Todd Parsley (Imquest) has taken over the chair of the Membership Committee from Bob Buckheit. In 2005, the total ISAR membership stood at 856, a number that indicated that the Society was in fact growing again. It is hoped that the ISAR will continue to expand its membership and will continue to be able to raise the funds necessary to organize its excellent annual conferences well into the future.

The 19th ICAR in San Juan was extremely well organized and planned, although Past President John Drach, who was responsible for much of the planning as Chair of the Conference Committee, was not able to attend because of his wife Jean's illness at the time of the meeting. The venue was wonderful and the scientific program was outstanding, starting with the annual pre-conference Satellite Symposium "Clinical Update on Antiviral Drugs". The conference format remained the same as in previous years with a plenary lecture preceding each oral presentation session, two comprehensive poster sessions, and a mini-symposium on emerging virus diseases. The 2006 Gertrude B. Elion Memorial Lecture Award was presented to Robert W. Sidwell (Utah State University). His lecture, entitled "Influenza: Search for a Cure", was one of the highlights of the conference as he discussed the recent development of several new antiviral drugs for the prophylaxis and treatment of influenza. Tomas Cihlar (Gilead Sciences) was awarded the 2006 William H. Prusoff Young Investigator Lecture Award and presented a lecture entitled "Understanding the Biological Attributes of Nucleoside Phosphonates from the First (Cidofovir) to the Newest (GS-9131)". This very excellent presentation, dedicated to his mentor Antonin Holy, traced the development of HPMPC

(Cidofovir) for the treatment of CMV infections, PMEA (Adefovir) for HIV-1 and HBV infections, and PMPA (Tenofovir) for HIV-1 and HBV infections. He also provided new information on the latest anti-HIV drug in the series, GS-9131, an amidate prodrug that enhances the intracellular delivery of its metabolic product GS-9148 (a nucleotide analog). GS-9148 is a potent inhibitor of the HIV-1 reverse transcriptase, but does not display cross-resistance with the other NRTIs. He indicated that much of the credit for the development of these nucleoside phosphonates as useful new antiviral drugs should be given to Erik De Clercq (Rega Institute; Leuven, Belgium) and John Martin (Gilead Sciences; Foster City, CA) who worked tirelessly in close collaboration to make these antiviral R & D accomplishments finally happen. These were clearly major contributions to the field by long-time ISAR members who have played major roles in the Society through the years.

Joe Colacino, Chairman of the Placement Committee hosted a Placement Breakfast during the San Juan conference that was an outstanding success and, as a result, this event will be held again at future conferences of the Society to enable additional interactions between potential employers attending the conference and scientists seeking new positions. Joe will also serve as the interim Secretary of the ISAR following the election of Amy Patick as the new President-Elect of the Society. Changes in ISAR Committee leadership positions and in other Society responsibilities were made with Bob Buckheit taking over the Chair of the ICAR Poster Awards Subcommittee from Vasu Nair and Erik De Clercq agreeing to take over the heavy responsibility of fund-raising for the ICAR from George Galasso who has indicated that he will resign the position following the 20th ICAR. George has done an outstanding job for the Society. Brent Korba, who has served as the ISAR-ICAR internet site webmaster, has done a wonderful job of improving the Society's website over the years. The website has recently been moved from Georgetown University to Cardiff University in Wales and Andrea Brancale there is currently doing a major upgrade. A new Online Directory has been added which will allow any ISAR member to search for other members by name, by location, or—in due course—by area of interest.

Robert W. Sidwell has continued to chair the Publications Committee since its inception and he has worked ardently to provide the Society membership with an excellent newsletter, the *ISAR News*. Bob has done an outstanding job as the Editor of the *ISAR News* and he has played a key role in making the ISAR a successful and respected organization. Bob has used the newsletter to communicate information about the annual ICAR to the membership extremely well. Jack Secrist, the Past President of ISAR, recently noted that Bob's dedicated and very effective efforts through the years have provided "a great benefit to the Society". With the impending retirement of Bob Sidwell, there will be another big pair of shoes to fill. Kirk Field, a member of the Publications Committee who for 8 years had written up the excellent ICAR scientific meeting summaries for the *ISAR News*, has also recently retired and has turned over this important task to Anthony Vere Hodge. Other Publication Committee members have included Erik De Clercq, Donald F. Smee, Hugh Field, and George Holan. All of these long-term members have worked extremely well together as an effective team to provide the Society with the first-class *ISAR News*. It is hoped that one or more corporate sponsors will soon be found to provide the financial means for the Society to continue the publication and distribution of the *ISAR News* in hard copy format.

All of the goals of the Society have been met except for the development of a "robust and financially stable" Treasury. A number of cost cutting procedures have been initiated, we no longer produce Posters for the upcoming ICAR, the hardcopy of the Membership Directory has given way to an

electronic version on the web page, the ISAR Newsletter may meet a similar fate. An ICAR Abstract Selection Committee used to meet in January to review and select abstracts and formalize the program for the annual conference; the Committee will henceforth conduct its function by electronic means and by telephone conference call. Other cost cutting measures need to be considered if the downward trend in funding continues. The Society established Travel Grants and Poster Awards in its solvent days, however if the Society coffers continue to diminish, these too may cease. Although the Society is still financially sound, it cannot continue to erode away at its reserves.

Overall, the second ten years of the ISAR have been a continuing success story, made possible by the dedicated efforts of the Society's excellent leadership and by the many members who have generously contributed their time and energy working on the various ISAR Committees. The chronology of the development of new antiviral drugs now approved for the treatment of important virus infections has closely paralleled the maturation and growth of the ISAR and closely reflects the many important scientific contributions of its membership. The ISAR has truly become the leading professional scientific society for those working in the field of antiviral research and the annual ICAR has clearly become the premier forum for the interchange of ideas; for the promotion of collaborative interactions between chemists, biologists, and clinicians; and for the presentation of critical findings that herald the latest advances in the development of new drugs for viral diseases of public health importance.

Section Three – Presentation of the ISAR Award of Excellence and Establishment of the Gertrude B. Elion Memorial Lecture Award, the William H. Prusoff Young Investigator Lecture Award, the ISAR Award for Outstanding Contributions to the Society, and the ICAR Poster Awards: A History and Talks with the Awardees

The International Society for Antiviral Research (ISAR) has sponsored and presented five meritorious awards: The ISAR Award of Excellence, The Gertrude B. Elion Memorial Lecture Award, the William H. Prusoff Young Investigator Lecture Award, the ISAR Award for Outstanding Contributions to the Society, and the ICAR Poster Awards. The Board of Directors, in conjunction with the Awards Committee, chaired by George J. Galasso, has been responsible for the selection of appropriate candidates for the first of these awards listed above. The Awards Committee has been responsible for selecting the candidates for the next three awards listed. The ICAR Poster Award Subcommittee, currently chaired by Robert W. Buckheit, Jr., has reviewed the competing posters at the Society's annual conference, has selected the award recipients, and has presented the ICAR Poster Awards at the conference banquet.

ISAR Award of Excellence

In 1988, the Society decided to establish a special award for scientists who had made truly significant scientific contributions to the field of antiviral research. This prestigious ISAR Award of Excellence, which would be awarded from time to time, was the very first achievement award to be established by the Society. The Board of Directors in conjunction with the Awards Committee makes the selection. The first recipients of the ISAR Award of Excellence were William H. (Bill) Prusoff (the father of antiviral chemotherapy) in 1988 and the late Gertrude B. (Trudy) Elion (the developer of acyclovir and other important antiviral and anticancer agents) in 1991. Both of these individuals truly embodied the spirit and aspirations of the ISAR and, in 1999 and 2000, new ISAR awards were established in their honor (See below). In this past decade, there have been only two additional recipients of the ISAR Award of Excellence, namely Erik De Clercq and Richard J. Whitley, two of our

Society's most preeminent and well-known scientists, and these two individuals were honored together in 1998. Much of the success of antiviral research as a scientific discipline has been due to the efforts of the four pioneer research scientists who have received this highest award of the Society.

Gertrude B. Elion Memorial Lecture Award

Following the passing in 1999 of Nobel Laureate Gertrude B. ("Trudy") Elion, a Charter member of the ISAR and one of the world's pioneer women scientists who actively conducted research and development in the area of the pharmaceutical sciences, Richard J. Whitley approached Lynn Smiley and David Barry of the Glaxo Wellcome Company and solicited funds for the establishment of an annual ISAR memorial lecture award to honor Trudy, who was one of our most loyal and active participants. The Board voted later in 1999 to establish this new award with the initial funding promised from Glaxo Wellcome and proposed that the first lecture be presented at the 13th ICAR in Baltimore, MD in April, 2000. The initial funding from Glaxo Wellcome for the Gertrude B. Elion Memorial Lecture Award was for \$10,000 per year for three years. Karen Biron has been able to successfully obtain the continued generous support of GlaxoSmithKline for this award over subsequent years and up to the present time, with a commitment of \$10,000 annual funding to the ISAR. The Elion award has been conferred at the time of the lecture at the annual conference of the Society. The funds have been used for the monetary award itself, for minimal administrative fees, and for travel and per diem for the awardee. The actual award was established in the amount of \$7,500 (the award being a constant dollar amount), whereas expenses for travel and per diem have varied from year to year. Any remaining funds left over have been kept in escrow for future Elion

awards. The Board decided that the Awards Committee of the ISAR would select the recipient of the Elion award each year and that the award would be given to an outstanding scientist, not necessarily in the field of antiviral research, but certainly to one who has made considerable contributions to the antiviral field, either directly or indirectly.

The criteria were established that the recipient should be a senior scientist (basic or clinical researcher) of international stature. If the nominee had some ties to Trudy, this would be considered in a favorable light. The primary selection criterion, however, was the scientific prominence of the candidate. In addition to scientific reputation, it was established that the candidate recipient should have some of the characteristics typical of Trudy, i.e., have a genuine love of science; be not only admired, but also respected by the scientific community; have a reputation for scientific integrity; and be approachable, especially to young scientists. Since this honor was established as a lecture award, the awardees were asked to give a 45-minute lecture on their research at the annual conference. It was decided that the membership would be asked to submit nominations to the Award Committee for the following year's Elion award. The Committee members would then consider the submitted nominations and could also submit nominations themselves. The list would be narrowed down by the Committee to two or three finalists and then the Committee would select the recipient from the remaining candidates. The name of the awardee is then submitted to the President of the ISAR for his/her letter notifying the recipient of the Award and also notifying GlaxoSmithKline of the selection. The awardee then submits the title of his/her talk to the Chair of the Program Committee in time for the inclusion in the Annual Program in a prominent position. There have been eight recipients of the Elion Award since its establishment: Michael Rossmann in 2000, Leroy B. Townsend in 2001, Antonin Holy in 2002, John C. Martin in 2003, Richard J. Whitley in 2004, Erik De Clercq in 2005, Robert W. Sidwell in 2006 and Frederick G. Hayden in 2007.

The Society now seeks to establish this award in perpetuity and it has recently requested additional funding for an endowment, similar to the

Prusoff Award (see below) to enable the Elion Award to continue into the future and to become more financially protected, especially as travel and accommodation costs for recipients continue to rise significantly and corporate contributions have shrunk in recent years. Leroy B. Townsend, the second recipient of this award, is one of the individuals working hard to make an endowment fund for this lecture award a reality. Leroy was a great admirer and friend of Trudy Elion and he recalled his close interactions with her while serving on many NIH Review Committee panels. Leroy remembered that Trudy had decided that she wouldn't fly again on a small plane to a particular Committee meeting site following a previous unpleasant flying incident on the same aircraft. Leroy drove her to the site and from then on and they became good friends and professional colleagues. "When Trudy needed an expert chemist on a Review Committee, she always asked for Leroy Townsend." At the recent ICAR in San Juan, Leroy recalled how honored he felt to have received the Elion Award and how he would very much like to see this important ISAR award continued in Trudy's name as a lasting memorial to her.

Rich Whitley, the 2004 Elion Award recipient, indicated that "the Gertrude B. Elion Memorial Lecture Award represents the heart of the ISAR and is only awarded for individual contributions that unequivocally establish the excellence of contributions to antiviral therapy." He noted that "Trudy Elion was the ideal role model for all investigators in the field of antiviral research" and that "her wisdom, gentility, humor, and warmth set a standard for all scientists in the field." Rich indicated that it was especially meaningful for him to have received this award because "this award came from the heart of ISAR."

Erik De Clercq, the 2005 Elion Awardee said that he has "kept the fondest memories of his encounters with Trudy", whom he considers the "Grande Dame" of antiviral research. He said that he continuously cites her work in his courses for the students when referring to acyclovir as the "gold standard" for the treatment of herpesvirus infections.

Bob Sidwell, the 2006 Elion Award recipient remembered clearly the time that his group had nominated Trudy for an honorary degree at Utah State

University in 1994. She was invited, accepted the invitation, and came to Logan, Utah. She told Bob that she "had never really visited the Mountain West and, besides, she wanted to see the Institute for Antiviral Research Program close-up." Since Bob was Trudy's host while in Utah, he said that he spent quite a bit of time with her. He recalled that "she really did not want to talk much about her Nobel Prize and the work she did to receive it; instead, she wanted to know about our research program and about life in the West." She toured Logan Canyon (which is on the National Registry of Scenic Byways) and took many pictures. Later, after receiving the honorary degree (her 18th honorary degree up to that time), she remarked how touched she was that a number of the students had shaken her hand and congratulated her as they passed by her on the receiving line of academic officials and honorees. Since the College of Agriculture at Utah State had its own graduation ceremony and since this College was the host for Trudy, the Dean asked her if she would like to speak to the students for a few minutes. She agreed. Her speech essentially was: "Students, if you want to get ahead in this world, you have got to work hard. That's what I did." End of speech. "Sure easy to remember though!" noted Bob. Instead of taking her out to some fancy place to eat after the graduation ceremonies, Bob said that they "took her up the canyon and cooked her a Dutch oven dinner over the coals and we had a little group entertain us with cowboy music and stories." Bob recalled that Trudy seemed to really enjoy herself and that, every time he saw her after that at the ICAR, she went out of her way to thank him for a good time. He said that Trudy "was a real down-to-earth lady" and that he remembers that at every ICAR, "she always sat on the front row of every session." Bob said that, particularly because of his personal experiences with Trudy, he was "extremely honored to be invited to give the Gertrude B. Elion Memorial Award Lecture. It was a most satisfying culmination of a career that, for me, started nearly 50 years ago." Bob plans to retire at the end of 2006, "so my wife and I can do a few things together while we still have our health."

William H. Prusoff Young Investigator Lecture Award

Bristol-Myers Squibb (BMS) endowed the William H. Prusoff Young Investigator Lecture Award, which has been awarded annually by the ISAR to promising new investigators at the time of the lecture at the annual conference of the Society. The initial endowment was for \$100,000 and this money was set aside and invested to enable the award to continue well into the future. The dollar amount of the principal in this award account has grown to approximately \$115,000 at the present time. Only the income from the endowment has been used for minimal administrative fees, travel, per diem, a crystal plaque and a cash award for the recipient. Any remaining funds after the award presentation each year has been allowed to stay in the endowment account for the generation of future awards.

The ISAR and BMS have both expressed their delight with this joint project to honor one of the most talented and beloved members of the Society, Bill Prusoff. Bill has been a loyal member of the Society since its inception and can still be seen in front at all sessions, health permitting, asking questions. His many contributions to the development of antivirals that have progressed to clinical use are well known. He is considered to be the "father of antiviral chemotherapy" and his dedication to mentoring young scientists makes this award in his name truly appropriate.

The Awards Committee, supplemented by representation from BMS, has selected the recipient each year. The award is given to an outstanding young scientist (not older than 45 years of age) who has demonstrated dedication and excellence in the field of antiviral research (basic or clinical, synthetic or pharmacological) and who displays future potential for contributions to the field and to the Society. The award was intended to encourage young investigators in the field and, by definition, was intended for individuals who are not yet considered to be fully developed scientists. The ISAR membership is invited to submit nominations to the Awards Committee, following the published criteria, for the next year's award. Following a rigid selection process, similar to the Elion Award selection

process, the Committee would select the recipient and submit his/her name to the President of the ISAR for his/her letter notifying the recipient as well as BMS of the selection. The awardees are invited to make presentations of their work at the annual conference. The eligibility criteria and nomination process are presented on the ISAR web page, www.isar-icar.com.

Ralf Bartenschlager (University of Heidelberg; Heidelberg, Germany), the 2002 William H. Prusoff Young Investigator Lecture Award recipient said that while he “unfortunately never had the opportunity to meet Bill Prusoff in person”, he “certainly felt much honored to receive this award.” He commented that this award assured him that his work, “that is by large focused on basic research and basic virology, has an impact on the development of antiviral drugs to treat HCV infections.” Ralf indicated that having received this recognition by ISAR was a great honor for him personally.

The winner of the William H. Prusoff Lecture Award in 2006 was Tomas Cihlar, Senior Principal Scientist at Gilead Sciences (Foster City, CA) who received his Ph.D, at the Institute of Organic Chemistry and Biochemistry (IOCB) in Prague, Czech Republic under the mentorship of Antonin Holy. The 2006 awardee reflected on the first time that he met Bill Prusoff at lunch during the Atlanta ICAR along with Ming Chen, his first supervisor at Gilead and a former postdoctoral fellow with Bill at Yale University. Tomas said that he was “impressed with his enthusiasm” and that “Bill Prusoff is a role model for young scientists and, in fact, for everyone, regardless of age”. Tomas indicated that it was “personally a huge surprise to have been selected for the award and that it was a totally unexpected honor”. He said that it was “a significant recognition that cannot be ignored” and that it was “a very positive signal toward industrial antiviral research”.

ISAR Award for Outstanding Contributions to the Society

The success of the International Society for Antiviral Research has been due to the hard work and devotion of many individuals. However, occa-

sionally, the efforts of a single individual will stand out as a key factor in the Society’s success. The ISAR Award for Outstanding Contributions to the Society is therefore dedicated to one who has made significant contributions consistently over many years (i.e., for at least 10 years) that are considered to have been essential to the continuing success of the Society and its annual Conference. This rare award is only conferred by the ISAR Board upon considerable reflection of an individual’s extensive and unique contributions to the Society. It was decided that these contributions could include, but would not be limited to: administrative efforts, efforts considered essential to the success of the Society and its Conference, fund raising activities, active membership on ISAR committees, recruitment of new members, being an ambassador and promoter of the Society at multiple venues, promotion and/or presentation of the highest quality science at the Society’s annual meeting, promotion of the effective integration of Society members representing industry, academia, research institutes and government. Earl R. Kern of the University of Alabama at Birmingham, a Past President of the Society, was honored as the first recipient of the ISAR Award for Outstanding Contributions to the Society upon his retirement as the long-standing Chairman of the Conference Organizing Committee. The award was initiated with Board approval and presented to Earl in 2004 at the Tucson ICAR.

ICAR Poster Awards

In 1999, the ISAR leadership decided it should spend some of its surplus funds to establish competitive awards for excellence in scientific poster presentations at its annual Conference. The awards would be presented at the ICAR to recognize young investigators for their outstanding contributions to antiviral research. It was decided that the awards would be based on criteria that included: scientific excellence, innovative research methodology, clarity and organization of presentation materials, and competence of the investigator in responding to the poster audience. Award recipients were to be chosen by the Poster Award Subcommittee, a panel of ISAR members; with prizes presented at the annual ICAR banquet that included a monetary prize and a commemorative plaque to be sent to the recipients shortly after the meeting. First and second prize

awards were to be presented for winning posters in each of the following categories:

Category 1: Graduate student (Pre-Ph.D. or equivalent degree)

Category 2: Post-doctoral (up to 5 years post-Ph.D. or equivalent degree.)

Category 3: Young investigator (junior faculty member or the equivalent).

ISAR President Christopher McGuigan recently commented that the ICAR Poster Award Subcommittee, now chaired by Bob Buckheit, “does a great job in valiantly assessing the posters which is a lot of hard work during the conference. The quality of the competing posters is always extremely high and this is a great testament to our youth, who are the majority of the poster prize winners”.

Section Four – Thoughts and Comments on the ISAR’s Second Decade and on the Beginning of Its Third Decade

Reflections by Current and Past Presidents, Officers, Board Members, Committee Members, and original Co-Founders of the Society are provided in this section of the second ten years’ history to give a summary of where the ISAR has been and where it is headed in the future. This section is provided with a minimum of editing and is presented with intent to stimulate discussion and generate new ideas. The thoughts presented are not to be taken as opinions of the Board but as miscellaneous ideas provided purely as items of debate. This section also presents some thoughts and comments from many of our good friends and colleagues in the Society.

The bases upon which the ISAR was founded remain as strong and vibrant today as they were in 1987. The original goals to provide an interdisciplinary forum for scientists worldwide to meet together, to interact, to stimulate productive collaborations, and to provide the membership with comprehensive, state-of-the-art updates on the latest in preclinical and clinical antiviral drug research and development activities, are still sustained today as the primary and most rewarding benefits to be delivered by the ISAR through its annual Conference, the ICAR. As was the case after its first ten years, the ISAR faces many challenges ahead as it enters its third decade of operation. It must continue to recruit new active members into leadership positions who will energetically take up the challenges, bring new perspectives to the organization, and dedicate themselves to the hard task of building and maintaining the Society’s fundamental core activities during the next ten years. The field of antiviral research has achieved worldwide status and respect as a serious and important scientific discipline as the result of a new awareness of what can actually be accomplished to combat the economically disastrous and deadly viral diseases that confront mankind. It is up to the future ISAR membership to keep the Society at the forefront and in a leadership position in this important field.

One of the more serious challenges faced by the ISAR will be its ability to continue to attract new antiviral researchers (both preclinical and clinical

investigators) to the ISAR and its annual Conference. More and more specialized meetings are being held that focus on a single virus group or viral disease entity and these specialty meetings have drawn away many of the biomedical researchers who would normally attend the broader-scope ICAR. The large pharmaceutical companies sponsor or contribute heavily to those conferences that emphasize the clinical aspects of antiviral chemotherapy, primarily because these are the conferences that are heavily attended by physicians who treat patients and write prescriptions. A serious attempt needs to be made to increase the number of clinical presentations on the ICAR program and to initiate some incentives for young clinical researchers interested in antiviral research to regularly attend and participate in the annual Conference. This should be an immediate goal that needs to be met if the ISAR expects to grow and prosper into the future. With the shifting priorities and changes within the pharmaceutical industry, the ISAR funding base has significantly declined and there is a need to recapture the support of the larger pharmaceutical companies. The ICAR may need to be enlarged in order to attract more clinicians, more pharmaceutical company support, and more breakthrough scientific presentations and this may require another assessment of the annual meeting format. While most members have enjoyed the fact that there are no concurrent sessions at the ICAR, the only way to enlarge and expand the program may be to run concurrent sessions, extend the length of the conference, or schedule some evening sessions to accommodate additional presentation sessions or company-sponsored symposia. While the consensus of the ISAR leadership has been to expand the Society’s membership rolls, one of the reasons that the ICAR has been so successful in the past has been its limited scope and size. With an average of 325 to 450 attendees, the ICAR has allowed for frequent interactions among those attending the conference and the smaller size meeting has encouraged an *esprit de corp* and many long-lasting friendships among the ISAR members. Serious discussions and decisions lie ahead as to the future scope and format of the ICAR that will most benefit the ISAR and its membership.

A major challenge facing the ISAR is the identification and establishment of a strong new leadership. Many of the early stalwarts are retiring and need to be replaced. There is a current complacency among the membership: "Things are going well; they are doing a good job; let them keep it up." This complacency is demonstrated by the poor turnout in elections, poor participation in surveys, and poor response to requests for nominations for important ISAR awards. Only when things go wrong is there a stir among the membership of any group. The ISAR membership needs to take a more proactive role, interested individuals need to identify themselves and become strong advocates for the Society and not just rely on the same old few. Energetic new faces are needed in the Society's leadership to take the ISAR into its third decade with new perspectives and ideas to improve the Society and its associated ICAR.

Another challenge faced by ISAR is one of visibility. The Society needs to take and retain the leadership position on issues that are of national and international importance in the area of drug treatment for viral diseases. It needs a Public Relations Committee and an articulate spokesperson who will represent the ISAR and its membership with credibility and with professional persuasiveness to interact with the scientific community, with the mass media, with the funding agencies, and with the general public to inform and educate them about the importance of antiviral research, the activities of the ISAR, and the latest research results and advances reported at the annual ICAR that significantly impact medical science. Only then will the ISAR and its associated ICAR gain a greater recognition and respect outside of the organization as the principal professional society and scientific forum for antiviral drug research and development and as the one professional Society that speaks with authority for the entire antiviral research community worldwide. Many ISAR members have indicated a desire to see more innovative and "break-through" research reports presented at the ICAR that will represent the first news reports of advances in cutting edge medical science for public disclosure and dissemination. The challenge is for ISAR to convince the pharmaceutical industry that the ICAR is the premier international meeting on antiviral research, both preclin-

ical and clinical, at which to initially disclose the identities and activities of their newly developed antiviral drugs. The pharmaceutical companies have traditionally chosen the larger conferences, such as the annual ASM meeting, the ICAAC, or the annual IDSA meeting, to announce their newly developed drugs because of the greater publicity and numbers of attendees at those meetings. The availability of greater publicity opportunities at the ICAR through on-site interviews, through the internet, through traditional press releases to the media should be expanded and a more active participation by the membership and by the drug companies should be encouraged. The ISAR needs to take on an advocacy position with regard to its annual conferences and issues that impact the field.

The ISAR is still losing money on its annual conferences and the future success of the Society will largely depend upon the ability of the next generation of ISAR leaders to find new ways to increase the operating revenues and financial contributions to the Society and to find new contributors for the annual ICAR. At the same time, the Society will need to contain its expenses through cost-cutting measures that do not adversely affect the primary functions of the Society, i.e., the successful conduct of the ICAR, the encouragement of scientific interactions and collaborations among researchers throughout the year, the regular publication of the *ISAR News* and other valuable communications to the ISAR membership via the Society's website, and support for the ISAR's official journals published by Elsevier.

At the end of the second decade of its existence, the ISAR has really not grown as much as it should have over this period of time, especially with the advances in antiviral research that have been made over the past ten years. While the core of the active antiviral research community may already be represented by the ISAR, it is clear that there still needs to be a vigorous attempt to increase the Society's international membership. Amy Patick, the ISAR's President-Elect, said that she is strongly committed to "maintaining the Society's international flavor" and to encouraging the very productive collaboration of biologists and chemists worldwide. According to Erik De Clercq, the ISAR's official

journal *Antiviral Research* has grown significantly over the past ten years and, during the last year, it has received and published more and more manuscripts originating from investigators in China and other countries that have not been very heavily involved with the Society. The Society should look to the future and seek to expand its international representation by inviting antiviral researchers from these other countries to join the ISAR and participate in its annual ICAR. New trends in the science and demographics of antiviral research are often seen first by the Editorial Board of *Antiviral Research* and the Society should take particular note of these perceived changes and use this important information to its advantage. In addition, a concerted effort should probably be made to occasionally co-host meetings with the NIH, where government scientists have played an important role as advocates for antiviral research initiatives in the past, and with other antiviral research groups such as the Japanese Society for Antiviral Research, i.e., with national or regional societies that have similar research interests and goals to the ISAR, but whose members would rarely, if ever, attend the ICAR. Co-sponsorship of conferences would also provide greater visibility and potential membership recruitment opportunities for

the ISAR. Another possibility would be to time the ICAR to link up with or “piggyback” onto another related conference in an attempt to increase the cross-over meeting attendance. This was successfully done for many years between the ICAAC and the annual IDSA meeting, a strategy that allowed for significantly greater interplay between preclinical and clinical researchers.

In summary, the ISAR is now at an important crossroads in its history with many significant decisions to be made that will affect the Society’s future directions and the scope of the annual conference as it heads into its third decade. Many, if not most, of the original scientists who founded the Society and who led its successful first two decades have either already retired, or will soon be retired. It will be up to the next generation of antiviral research scientists to pick up the torch and run with it. It will, with a high degree of certainty, be both a challenging and a rewarding task for those who are seriously interested in the advancement and vitality of this important area of biomedical research and who are committed to adding new achievements to the legacy of the ISAR.

Conferences of the Society

	Date	Location	Conference & Program Organizers and Local Hosts*
I.	April 30 - May 3, 1985	Rotterdam, The Netherlands	Huub Schellekens* George Galasso Erik De Clercq TNO
II.	April 10 - 14, 1988	Williamsburg, VA	Earl Kern George Galasso Richard Whitley Bill Shannon SRI
III.	April 22 - 27, 1990	Brussels, Belgium	Erik De Clercq*
IV.	April 21 - 26, 1991	New Orleans, LA	Ken Soike*
V.	March 8 - 13, 1992	Vancouver, Canada	Steve Sacks*
VI.	April 25 - 30, 1993	Venice, Italy	Giorgio Palu* Fernando Dianzani* Earl Kern Richard Whitley Sistema Congressi
VII.	Feb. 27 - Mar. 4, 1994	Charleston, SC	David Gangemi* Earl Kern Richard Whitley Conference Table
VIII.	April 23 - 28, 1995	Sante Fe, NM	Gregory Mertz* Earl Kern Richard Whitley Conference Table
IX.	May 19 - 24, 1996	Urabandai, Japan	Shiro Shigeta* Kazuo Takahashi* Earl Kern Richard Whitley Tokyu Tourist Corp.
X.	April 6 - 11, 1997	Atlanta, GA	Raymond Schinazi* Earl Kern Richard Whitley Imidex, USA

XI.	April 5 - 10, 1998	San Diego, CA	Karl Hostetler* Doug Richman* Earl Kern Richard Whitley Conference Table
XII.	March 21 - 26, 1999	Jerusalem, Israel	Ehud Katz* Earl Kern Richard Whitley Kenes Ltd.
XIII.	April 16 -21, 2000	Baltimore, MD	George Galasso* Earl Kern Richard Whitley Courtesy Associates
XIV.	April 8 - 12, 2001	Seattle, WA	Larry Corey* Earl Kern Richard Whitley Courtesy Associates
XV.	March 17 - 21, 2002	Prague, Czech Republic	Antonin Holy* Earl Kern Richard Whitley Courtesy Associates
XVI.	April 27 - May 1, 2003	Savannah, GA	Earl Kern Courtesy Associates
XVII.	May 2 - 6, 2004	Tucson, AZ	Leroy Townsend* Earl Kern Courtesy Associates
XVIII	April 10 - 14, 2005	Barcelona, Spain	José Esté* John Drach Courtesy Associates
XIX.	May 7 - 11, 2006	San Juan, Puerto Rico	John Drach Jack Secrist Courtesy Associates
XX.	April 29 - May 3, 2007	Palm Springs, CA	Jack Secrist John Drach Amy Patick Courtesy Associates

* Local Hosts indicated by asterisks.

Presidents of the Society

1988-1990	Richard J. Whitley	University of Alabama at Birmingham, USA
1990-1992	Erik De Clercq	Rega Institute, Katholieke Univ., Leuven, Belgium
1992-1994	George J. Galasso	National Institutes of Health, Bethesda, MD, USA
1994-1996	Hugh J. Field	Cambridge University; Cambridge, UK
1996-1998	Earl R. Kern	University of Alabama at Birmingham, USA
1998-2000	John C. Martin	Gilead Sciences, Inc.; Foster City, CA, USA
2000-2002	Karen K. Biron	Glaxo Wellcome Company; RTP, NC, USA
2002-2004	John C. Drach	University of Michigan; Ann Arbor, MI, USA
2004-2006	John A. Secrist III	Southern Research Institute; Birmingham, AL, USA
2006-2008	Christopher McGuigan	Cardiff University; Cardiff, Wales, UK

Other Officers of the Society

President-Elect

2006-2008	Amy K. Patick	Pfizer Global R&D, La Jolla, CA, USA
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Secretary

1988-1994	Earl R. Kern	University of Alabama at Birmingham, USA
1994-2000	Koen Andries	Janssen Research Foundation, Belgium
2000-2003	Brent Korba	Georgetown University, Washington, D.C., USA
2003-2006	Amy K. Patick	Pfizer Global R&D, La Jolla, CA, USA
2006-2009	Joseph M. Colacino	PTC Therapeutics Inc., South Plainfield, NJ, USA

Treasurer

1988-1994	William M. Shannon	Southern Research Institute; Birmingham, AL, USA
1994-2003	John A. Secrist III	Southern Research Institute; Birmingham, AL, USA
2003-2009	John Morrey	Utah State University; Logan UT, USA

ISAR Award of Excellence

William H. Prusoff	Yale University	1988
Gertrude B. Elion	Burroughs Wellcome Company	1991
Richard J. Whitley	University of Alabama at Birmingham	1998
Erik De Clercq	Rega Institute, Katholieke Universiteit	1998

ISAR Award for Outstanding Contributions to the Society

Earl R. Kern	University of Alabama at Birmingham	2004
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Gertrude B. Elion Memorial Lecture Award

Michael Rossman	Purdue University	2000
Leroy B. Townsend	University of Michigan	2001
Antonin Holy	Academy of Sciences of the Czech Republic	2002
John C. Martin	Gilead Sciences	2003
Richard J. Whitley	University of Alabama at Birmingham	2004
Erik De Clercq	Rega Institute, Katholieke Universiteit	2005
Robert W. Sidwell	Utah State University	2006
Frederick G. Hayden	University of Virginia	2007

William H. Prusoff Young Investigator Lecture Award

Christopher McGuigan	Cardiff University	2001
Ralf Bartenschlager	Heidelberg University	2002
Johan Neyts	Rega Institute, Katholieke Universiteit	2003
Fabien Zoulim	Institute Universitaire de France	2004
Arianna Loregian	University of Padova	2005
Tomas Cihlar	Gilead Sciences	2006
Chris Meier	University of Hamburg	2007

