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The XIXth National Meeting on Medicinal Chemistry: Verona, Italy

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The organizers dedicate this Special Issue to Professor Fulvio Gualtieri (University of Florence, Italy) on the occasion of his retirement.

An Historic Setting

Verona, the city of the legendary story of Romeo and Juliet, was host to the XIXth National Meeting on Medicinal Chemistry. The event, organized by the Medicinal Chemistry Division of the Italian Chemical Society under the auspices of the European Federation of Medicinal Chemistry (EFMC), took place at the GlaxoSmithKline R&D Auditorium, September 14–18, 2008.

Italian Chemical Society, Division of Medicinal Chemistry

European Federation for Medicinal Chemistry

An International Affair

There were 356 participants, 46 of whom (13%) were from countries outside Italy; 12 different countries were represented, with a significant number of attendees coming from England (14) and France (10). Furthermore, the participation of industry was consistent, with 67 attendees (17%) coming from several national and multinational companies.

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The meeting also represented an excellent opportunity for sponsors and exhibitors to present their activities and services, and to establish or extend contacts with the scientific community. Altogether, the event received the support of 12 sponsors, 3 media partners, and 11 exhibitors, which were an integral part of the meeting.

Awards

The opening day was initiated with welcome speeches by the chairpersons of the Scientific and Organizing Committee, the president of the EFMC (Prof. **Roberto Pellicciari**), and the representatives of GSK (Dr. **Emiliangelo Ratti**) and the University of Verona (Prof. **Roberto Corrocher**). The Awards ceremony was held in honor of Prof. **Giorgio Tarzia** (*University of Urbino*), recipient of the Giacomello Medal, and Prof. **Gianluca Sbardella** (*University of Salerno*) and Dr. **Maria Letizia Barreca** (*University of Perugia*), who were the recipients of the two Farmindustria (Italian Association of Pharmaceutical Industries) Prizes.

Inspiring Speakers

The opening lecture was given by Nobel Laureate **Richard R. Ernst** (*ETH Zürich*), who gave an enthusiastic and very attractive speech on who benefits from drug discovery—industry, society, or both?—and this concluded day one. The rest of the scientific program was articulated in seven half-day topic sessions with seven plenary and 21 main lectures highlighting important areas of medicinal chemistry:

- "Intelligent" therapeutics in oncology
- New insight into computer-assisted molecular design
- New drugs for the treatment of diabetes and other metabolic diseases
- New trends in medicinal chemistry
- Inflammation and respiratory diseases
- Analytical advances in metabolite identification
- Perspectives in the treatment of CNS diseases

"Intelligent" therapeutics in oncology

In this section, **Stephen Hanessian** (*Université de Montréal*) reported a new and interesting approach to cancer treatment with the hierarchical construction of drug-functionalized polyvinylalcohol/polyvinylamine polymers with encapsulated super-paramagnetic ion oxide nanoparticles (SPIONs). The drug is attached to the polymer through an appropriate linker, which is susceptible to the action of lysosomal esterases among other intracellular enzymes. An external magnet accelerates the uptake of the SPION–drug conjugate into human melanoma cells relative to those not exposed to the magnetic field. Cleavage of the labile ester (or related) bonds releases the active drug intercellularly. Such magnetically directed accumulation of the SPION–drug conjugates at the tumor site has the potential to effect selective delivery of chemotherapeutic agents by enhancing drug internalization relative to uptake by healthy cells.

Thomas Miller *(Merck Research Laboratories, Boston)* reported recent advances in the design of histone deacetylase (HDAC) inhibitors. HDAC represents an innovative target for anticancer drug development, and this is exemplified by the discovery and development of vorinostat (SAHA, Zolinza™), a novel hydroxamic acid derived inhibitor of HDAC.

In addition to histone acetylation levels, histone methylation patterns have been

demonstrated to play an important role in human cancer. In particular, histone lysine methyltransferases (HKMTs) and protein arginine methyltransferases (PRMTs) have been shown to be overexpressed in cancer cells, and their inhibition could revert epigenetic aberrations and restore the normal state or even sensitize cells to other antitumor drugs. **Gianluca Sbardella** (*University of Salerno*) described the discovery of new small molecules that are able to selectively inhibit lysine or arginine methyltransferases.

Steve Courtney (*Evotec, Oxfordshire*) described the fragment-screening and optimization process carried out at Evotec on heat shock protein 90 (Hsp90), an ATPase and chaperone protein which plays a key role in oncogenic transformation. This research culminated in the identification of a novel series of compounds endowed with a potent capacity to inhibit the growth of tumor cells.

Silvia Schenone (*University of Genova*) reported new pyrazolo[3,4-*d*]pyrimidine-based Src/Abl dual inhibitors with increasing enzymatic affinity in the nanomolar range. These molecules block cell-cycle progression and promote apoptosis in several cancer types. Some of these compounds also show an interesting inhibitory activity against imatinib-resistant strains related to T315I, E255K, and Y253F mutations in Bcr-Abl.

These compounds significantly decreased proliferation in a semisolid assay of cell clones expressing the wild-type and mutated Bcr-Abl genes, with LD_{50} values ranging between 1.0 and 1.6 μM. To improve the biopharmaceutical properties of the inhibitors, cyclodextrin encapsulation and liposomal entrapment were also performed, giving a marked improvement in the cytotoxic effect in thyroid cancer cells. Preliminary studies on cancer stem cells have also been carried out.

New insight into computer-assisted molecular design

The second section was dedicated to topics in computer-assisted molecular design. **Hugo Kubinyi** (*University of Heidelberg*) reviewed the successful applications of this approach, the first example of which was the discovery of the antihypertensive drug captopril, an angiotensin-converting enzyme (ACE) inhibitor. Since then, the improvement of this technology, together with the integration of other techniques such as protein crystallography and multidimensional NMR, has lead to the discovery of other drugs, which has, in the meantime, decreased the number of compounds to be synthesized. Nowadays, if a 3D structure of the biological target is available from protein crystallography or NMR studies, or can be modeled by homology, the final step is flexible docking followed by scoring and a careful visual inspection of the obtained results. In this manner, virtual screening has become a routine technique in the search for new leads, as illustrated by many successful applications.

Gabriele Constantino (*University of Parma*) then presented an application of molecular modeling for the discovery of inhibitors of 3-hydroxyantralinate dioxygenase (3-HAO), an enzyme of the kynurenine pathway of tryptophan metabolism responsible for the formation of quinolinic acid, an NMDA receptor agonist. Modulation of the level of this metabolite by inhibiting 3-HAO may represent a completely novel approach in the treatment of CNS diseases. Docking studies have aided in the discovery and optimization of new inhibitors, which in in vitro and in vivo models of neurodegeneration, have given very promising results.

Andrea Cavalli (*University of Bologna*) reported the application of a new metadynamic-based protocol in the study of three biological systems: glycogen synthase kinase-3β in complex with a selective ureidic inhibitor, estrogen receptor-α complexed with tamoxifen, and *E. coli* enoyl-ACP reductase in complex with triclosan. This protocol provides full mechanistic insight on protein–ligand recognition and docking processes, is able to clearly point to the crystallographic poses of ligand–protein complexes, and can unequivocally point to the transition state of the full undocking mechanism, giving an indication on the binding free energy and thus overcoming the main drawback from which docking simulations suffer.

Anna Vulpetti (*Novartis, Basel*) presented strategies for the development of kinase/protease inhibitors by structure-based drug design and fragment-based screening. Her talk was focused mainly on two different case studies:

1. The design and optimization of potent and selective CDK2 inhibitors through structure-based drug design (SBDD) and the helpful use of sequence and structure analysis for improving the compound selectivity profile over the kinase superfamily, and
2. The design and screening of a targeted library of fragments specifically selected for the S1 pocket of serine proteases.

New drugs for the treatment of diabetes and other metabolic diseases

This section was opened by **Pier Giuseppe Pelicci** (*IEO, Milan*) who gave an interesting talk on reactive oxygen species (ROS) and insulin signaling in the adipose tissue, critical determinants of aging and age-associated diseases. The effects of ROS on insulin signaling was investigated using $p66^{Shc}$-null mice as a model system; $p66^{Shc}$ is a redox enzyme activated by insulin specifically in adipocytes which generates mitochondrial ROS and promotes aging in mammals. This study demonstrated that $p66^{Shc}$-generated ROS regulate the effect of insulin on the energetic metabolism in mice, and suggest that intracellular oxidative stress might accelerate aging by favoring fat deposition and fat-related metabolic disorders.

This lecture was followed by the one given by **Uwe Grether** (*Hoffmann-La Roche, Basel*) on dual PPARα/γ agonists for the treatment of type 2 diabetes (T2D) and associated co-morbidities. Peroxisome proliferator activated receptor-α (PPARα) and -γ (PPARγ) have been identified as the primary molecular targets for the anti-diabetic thiazolidinediones (TZDs) and the lipid-lowering fibrates, respectively. This has provided new opportunities for the treatment of T2D, as the profile of a dual PPARα/γ agonist appears well-suited for addressing both hyperglycemia and the enhanced cardiovascular risk in diabetic patients. The results obtained in animal models look

very promising, and soon such drugs may be available to combat this disease, which is spreading exponentially around the world.

Federico Corelli (*University of Siena*) discussed anti-obesity therapy. He presented recent results obtained by his research group in the field of cannabinoid (CB) receptors, a new promising therapeutic target to counteract weight gain, an important indication, as a recent estimate reports about 800 million individuals suffer from being overweight. He amply discussed the SAR and pharmacological characterization of a series of 5-(pyrrol-1-yl)pyrazole-3-carboxamides: a new family of CB1 inverse agonists potentially useful in the treatment of obesity and other metabolic diseases.

New trends in medicinal chemistry

Graeme Robertson (*Siena Biotech, Siena*) opened this section by discussing how to achieve confidence in drug discovery and development. Target selection and candidate selection are two of the key operational decision points in drug discovery, in which each company uses certain selection criteria to make decisions on which targets to accept into their discovery pipelines and which compounds will pass into development. These steps help define the productivity of every company, but are decisions taken in the knowledge that given risks lie ahead. His talk covered various aspects on how progressing from a reductionist target-driven approach to a more holistic approach that encompasses early consideration of the chemistry–biology interface could play a role in addressing these developments in a drug pipeline.

Pierfausto Seneci (*University of Milan*) proposed pro-apoptotic treatments in cancer therapy. He described a structure-driven approach to potent Smac mimics/XIAP inhibitors with a favorable drug-like profile. The X-inhibitor of apoptosis protein (XIAP) binds caspases, preventing their activation and, as a consequence, cells are blocked from entering apoptosis. The second mitochondria-derived activator of caspases (Smac), a protein released from mitochondria, binds XIAP as a dimer at the same binding site of caspase 9 (BIR3 domain). Smac also interferes with the XIAP binding site of caspases 3 and 7 (linker-BIR2 domain), thus promoting both the extrinsic and intrinsic apoptotic pathways. The balance of this binding equilibrium is altered in various tumors that overexpress XIAP and, consequently, a caspase-dependent resistance to enter apoptosis. Thus, XIAP inhibition via the binding of Smac mimics is a validated mechanism for intervention in cancer therapy.

Alexander Alanine (*Hoffmann-La Roche, Basel*) presented the state of the art in multidimensional optimization and current tools in the prediction of DMPK, safety effects, and liabilities before advancing to in vivo studies. He also explored future trends toward tailored screening for molecules, moving away from the screen-all approach to selective assays and molecules (SAM) for refining high-quality drug candidates and optimal resource use, which is believed to result in enhanced success rates so heavily sought after in drug discovery.

Ersilia De Lorenzi (*University of Pavia*) discussed folding intermediates and transient oligomers as difficult protein targets to find new drugs for amyloidoses. Amyloidoses are a class of human

Fulvio Gualtieri was born in Rome on October 19, 1936. After obtaining a degree in chemistry from the University of Rome in 1960, he went on to become a lecturer in industrial organic chemistry (1964–1965) and subsequently an assistant professor in organic chemistry (1965–1969) at the University of Camerino. He undertook two postdoctoral fellowships in North America; the first at the Stanford Research Institute (Palo Alto, USA; 1969–1970) and the second at McGill University (Montreal, Canada; 1972). In 1975 he became a full professor of medicinal chemistry at the University of Palermo. In 1977, Professor Gualtieri returned to Camerino to serve as dean of the Faculty of Sciences (1977–1980). After three successful years, he moved to University of Florence, Faculty of Pharmacy, to assume the role of dean (1986–1995) and later to serve as director of the Department of Pharmaceutical Sciences (2000–2006).

In addition to his illustrious academic career, he has been an active member of the medicinal chemistry community over the years. He served as a member of the board of the Medicinal Chemistry Division of the Italian Chemical Society (1980–1986) and was later elected president of the same division (1991–1994). He also served as a long-time member of the editorial board of *Il Farmaco*. He was a member of the Chemistry Funding Committee for the Ministry of Education, University and Research (MIUR, 1988–1996). He was among the organizers of the 1st Camerino Symposium on Receptor Chemistry (1978) and, since then, is a permanent member of the Scientific Committee of the meeting that is still organized every year in Camerino or Noordwejikerhout or Cyprus, under the name Camerino-Noordweijkerhout-Cyprus Symposium. In 1980 he established the Summer School of Medicinal Chemistry (Urbino, Italy), which is known today as the European School of Medicinal Chemistry (ESMC), serving as director until 1986. From 1999 to the present day Professor Gualtieri has been coordinator of the National Research Project on Neurotransmitter Receptor Ligands. In 1999 he received the Giordano Giacomello award from the Medicinal Chemistry Division of the Italian Chemical Society for his research activities and contributions to the field of medicinal chemistry and pharmaceutical sciences. In virtue of his expertise, he has served as a member of editorial boards on several medicinal chemistry journals.

His research interests span from receptors to ion channels as therapeutic targets, and more recently to multidrug resistance. He has authored more than 150 articles in prestigious scientific journals and written several book chapters in addition to the various lectures given at national and international meetings.

diseases that arise from protein misfolding and subsequent aggregation into highly organized insoluble deposits known as amyloid fibrils. A multidisciplinary approach using spectroscopic and separatory techniques as well as imaging data partially elucidated the complex and highly dynamic pathway of protein misfolding and conformational transition that leads to fibrillogenesis. An improved knowledge of the molecular details would clearly result in a significant step forward in the development of more rational approaches, in which these species are pharmaceutical targets of small molecules capable of perturbing those equilibria that lead to fibril deposition.

Inflammation and respiratory diseases

In this section, **Vincenzo di Marzo** (*CNR Pozzuoli, Naples*) discussed the potential of endocannabinoid-based drugs with multiple sites of action against inflammation and hyperactivity. His talk was focused on the design of "hybrid" CB/TRPV1 agonists or CB antagonists/TRPV1 agonists, and of "dual" blockers of endocannabinoid degradation and TRPV1. Although cannabinoid (CB) receptors and the transient receptor potential vanilloid type-1 (TRPV1) channels belong to different receptor classes, they have much in common. They are often expressed in the same sensory and central neurons as well as in non-neuronal cells, and their pharmacological activation often results in similar beneficial effects via different mechanisms. Furthermore, they share, to a certain extent, the same endogenous agonists, known as endocannabinoids, in the case of CB receptors of type 1 and 2 (CB1 and CB2), and as endovanilloids, in the case of TRPV1 receptors. Therefore, it is conceivable that synthetic molecules that simultaneously target proteins of the endocannabinoid system and TRPV1 channels might be more efficacious.

Marcello Allegretti (*Dompè, L'Aquila*) reported on the most recent findings on the discovery of CXCL8 modulators. Due to its potent capacity as a chemoattractant, CXCL8 has been a very attractive target for chronic obstructive pulmonary disease (COPD) therapy, and many companies have developed their own clinical candidates. Reparixin, discovered at Dompè, acts as a noncompetitive allosteric inhibitor of both CXCL8 receptors, CXCR1 and CXCR2. Interestingly, it has also been shown to attenuate acute lung injury (ALI) in mice by CXCR2 inhibition. ALI is associated with high morbidity and mortality, and there are no specific treatments yet available. The role of CXCR2 in the regulation of polymorphonuclear leukocyte (PMN) recruitment in various animal models has been investigated, even if, up to now, no known small-molecule CXCR2 inhibitors have been shown to be efficacious in the proposed models. The results obtained with reparixin may open an avenue for therapeutic treatment.

The discovery of a novel range of nicotinamide-based PDE4 inhibitors that were specifically designed for inhaled delivery was discussed by **Mark Bunnage** (*Pfizer, Kent*), who described the medicinal chemistry and the human clinical data for UK-500,001. The efficacy of orally bioavailable PDE4 inhibitors in humans for the management of asthma and COPD have been reported over recent years; however, the clinical utility of these agents has so far been hampered by narrow therapeutic indices and adverse side effects. Delivery of PDE4 inhibitors by the inhalation route has the potential to secure the benefits of anti-inflammatory effects directly in the lung, whilst avoiding the systemically driven adverse side effects.

Paolo Tosco (*University of Torino*) presented a series of nitric oxide-donor aspirin-like molecules in which the NO-releasing moieties are joined to the phenol oxygen atom of salicylic acid by an ester linkage. Most of these compounds displayed in vivo anti-inflammatory activity similar to that of aspirin, with decreased or no associated gastrotoxicity. In addition to NO-dependent vasodilator properties, NO-independent platelet anti-aggregatory effects were observed. In vitro pharmacological characterization shows that derivatives behave as irreversible inhibitors of COX isozymes. With the aid of a computational study, the possible structural basis of the irreversible enzyme inactivation was also discussed.

Analytical advances in metabolite identification

This section commenced with the lecture of **John Lindon** (*Imperial College, London*), who focused on the analytical and statistical developments for metabolic biomarker characterization. Metabonomics analytical methodologies based on NMR spectroscopy and MS, the two most information-rich analytical techniques that give molecular structural information, were described, together with some recent chemometric technology developments, generally known as statistical spectroscopy, for biomarker identification and for integration of NMR and MS data sets. Some biomedical applications of this approach were illustrated, including drug toxicity, gut microbiome effects, dietary investigations, and measurement of an individual's response to therapy.

Identification of metabolites play a major role in the discovery and development of pharmaceutical compounds. This aspect was discussed by **Ellenia Bordini** (*GlaxoSmithKline, Verona*). The identification of drug metabolites can be divided into three discrete stages: metabolite generation, separation/isolation (collectively referred to as sample refinement), and identification. She reviewed the current state of the art employed for metabolite identification along with the USFDA guidance to industry on current approaches to safety testing of drug metabolites. MS-based techniques, such as stable isotope labeling, chemical derivatization, accurate mass measurement to enhance metabolite identification, and recent improvements in data acquisition and processing for accelerating metabolite identification were also described.

Malcom Clench (*Biomedical Research Centre, Sheffield*) discussed strategies for the "on-tissue" examination of xenobiotic, protein, lipid, and metabolite distribution and the use of normal scan, accurate mass, tandem mass spectrometry and ion-mobility separations in conjunction with MALDI-MSI (matrix-assisted laser desorption ionization mass spectrometry imaging). He also gave several examples from the analysis of formalin fixed paraffin embedded (FFPE) and fresh frozen tumor tissue, brain tissue,

whole-body animal sections, and plant sections. Particular emphasis was given to strategies combining multivariant statistics and bioinformatics approaches for the identification of analytes following MALDI-MSI or MALDI profiling experiments.

Giancarlo Aldini (*University of Milan*) reported the discovery of reactive carbonyl species (RCS)-sequestering agents. When RCS are massively generated, or when the detoxification systems are hampered, RCS covalently react with several macromolecules such as DNA and proteins, leading to cell and tissue damage. Hence, RCS are a potential drug target, and there is great interest in the search for novel bioactive molecules that are effective in detoxifying these compounds through a direct mechanism (RCS-sequestering effect), or by restoring/ameliorating the metabolic efficiency. Carnosine (β-alanyl-L-histidine, CAR), an endogenous histidine dipeptide, was recently identified as novel endogenous quencher of RCS. However, it has limited pharmacological use, as it is rapidly hydrolyzed by a specific serum dipeptidase (carnosinase). A series of CAR derivatives were prepared, characterized by high stability in human plasma, and by a near twofold increase in RCS-quenching ability relative to CAR itself.

Perspectives in the treatment the CNS diseases

Ceri Davies (*GlaxoSmithKline, Harlow*) introduced this section. He reviewed some of the challenges faced in drug discovery for neurological diseases: understanding the disease, target identification, diagnostic criteria, brain penetration, clinical evaluation, and treatment duration. Some case histories were used to exemplify the issue and how this has been resolved. Unmet medical need in the neurological disease area is immense, with better efficacy being the main objective for new treatments in nearly all CNS diseases. This is a major challenge for the pharmaceutical industry and is exemplified by the fact that few, if any, really new and effective mechanisms have been introduced into the market over the last 30–40 years. However, advances are being made, and the neuroscience sector continues to assess novel mechanisms in development projects. The hope is that these mechanisms are built on a better understanding of human disease and therefore possess greater probability of success.

In the last decade, corticotropin-releasing factor (CRF) has been shown to be the major biochemical modulator of the adaptive response of organisms to stress, responsible for the onset of anxiety and depressive disorders. Antagonists of the CRF type-1 (CRF-1) receptor have potential for the treatment of stress-related illnesses including depression. **Romano Di Fabio** (*GlaxoSmithKline, Verona*) reported an innovative series of drug-like CRF-1 receptor antagonists with a dihydropyrrole[2,3]pyridine structure. He disclosed compounds with high in vitro potency, excellent pharmacokinetics, and outstanding in vivo activity in animal models of anxiety.

N-methyl-D-aspartate receptors (NMDARs) are heteromeric ion channels formed by various combinations of subunits (NR1, NR2A–D, NR3). Among them, the NR2B subtype is commonly expressed in regions of the brain associated with particularly important neurological functions and represents a new interesting target for drug development. **Alba Chimirri** (*University of Messina*) illustrated how a combination of ligand-based and structure-based methodologies led to the identification of new ligands containing an indole nucleus that bind to the NR2B ifenprodil-like recognition site. The most active derivative has shown anticonvulsant and neuroprotective effects in vivo.

Rosaria Volpini (*University of Camerino*) discussed the role of purinergic receptors on neuroprotection and neurodegeneration and the perspectives for drug development. A series of adenosine A2A receptor (AA2AR) antagonists with an adenine structure were reported to have efficacy in various in vivo experimental models of Parkinson's disease and proved to reverse locomotor deficits induced by haloperidol and to induce controlateral turning behavior in treated rats. Furthermore, a number of polysubstituted adenosine derivatives have been characterized in vitro as partial and full AA3R agonists. This subtype seems to contribute to the neuroprotective action of adenosine, although the overall modulatory effects of A3 receptors on neurotransmission during cerebral ischemia are not yet well defined. The ability of the new AA3R agonists to decrease field excitatory postsynaptic potential (fepsp) depression in ischemic conditions was also reported.

More Science

In addition to the plenary and main lectures, 16 short communications and three poster sessions with 164 posters on display covered a wider range of further topics.

Italian Hospitality

Along with an exciting scientific agenda, an attractive social program was offered to the participants. Notably, the conference dinner was held on Tuesday evening at the famous Villa Mattarana. Delegates also had the opportunity to attend a concert of the Accademia Filarmonica Verona at the Sala Maffeiana on Wednesday.

Verona, with its history and monuments and palaces, represents a uniquely Italian meeting point for different European cultures and formed an exciting setting for stimulating scientific and human interactions. We would like to highlight that this National Congress has arisen from a close relationship between the academic world and industry. We hope that more joint initiatives of this kind will be proposed in the near future. In fact, the process of developing new drugs, today more than ever, is illustrated by the words "better, safer, faster"; industry and academia both should contribute to achieving these desirable results. Furthermore, the younger medicinal chemists attending this kind of event will hopefully find themselves stimulated and inspired to develop new research pathways. The Medicinal Chemistry Division of the Italian Chemical Society and the Organizing and Scientific Committees of this event worked hard toward these aims.

This year, the Scientific Committee of the 2008 Italian National Congress chose English as the official language. This

choice reflects a growing awareness of the need to share both national and international contributions more widely. At a challenging time for the field of chemistry, particularly for medicinal chemistry, we believe that the essential goal of events such as this should be to improve the global profile of medicinal sciences by promoting relationships among national and international academic and industrial pharmaceutical organizations. This can be done by promoting interdisciplinary approaches and by launching any possible initiatives, for young medicinal chemists in particular, to give them opportunities in the early stages of their careers.

Our Division has already undertaken this policy with the European School of Medicinal Chemistry (ESMC), which takes place in Urbino (Italy), being an example, where interdisciplinarity has always been a "must", and the use of English has been in place for a few years. It is sponsored by the EFMC, where the participation of PhD students from countries outside Italy is continuously increasing. The same approach is currently being used by another divisional activity, the "Summer Course on Pharmaceutical Analysis".

Internationalization, however, has always been a primary goal for our Division. An example is the well-established biannual "Joint Meeting on Medicinal Chemistry" jointly organized with eastern European countries. This meeting series started in Catania in 1999, and this year marks the 6th event, to take place in Budapest, organized by our Hungarian colleagues. In addition, several other such Joint Meetings have been organized in the past, in cooperation with the medicinal chemistry divisions of the respective chemical societies of England, France, Spain, and more recently, Switzerland.

There are many other events with an international profile that our Division has sponsored: the Camerino-Noordwijkerhout-Cyprus Symposium, Heterocyclic Structures in Medicinal Chemistry (Modello), Recent Developments in Pharmaceutical Analysis, and the first joint EFMC–American Chemical Society (ACS) meeting hosted last year in Siena, *Frontiers in CNS and Oncology Medicinal Chemistry*. All of this underscores the remarkable efforts of our Division, widely recognized as one of the most active in increasing internationalization.

Any effort to facilitate communication among researchers is a significant step in the right direction toward productive international collaboration.

Closing Remarks

We thank GlaxoSmithKline Verona (Italy) for their wonderful hospitality and cooperation. Thanks also to the exhibitors, media partners, institutions, and all those whose support made this meeting possible. Particular thanks to the speakers and poster presenters for their scientific contributions and to the attendees for their participation, which was particularly enthusiastic.

Just recently, the board of our Division, taking into consideration the success of NMMC 2008 and the interest shown by the participants, announced that the XXth National Meeting on Medicinal Chemistry (NMMC 2010) will take place in Padova, September 12–16, 2010. We challenge our successors in the hopes of an even larger turnout. Please stay tuned for upcoming details on NMMC 2010; we hope to see you there.

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