CRS Delivering Bioactives

Newsletter

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The CRS Newsletter is the official newsletter of the Controlled Release Society. The newsletter is published five times annually providing scientific and technical information pertinent to the controlled release community and news about society and chapter activities. Members can receive the newsletter via mail. The newsletter may also be viewed online at www.controlledreleasesociety.org.

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From the Editor

Bozena Michniak-Kohn, Ph.D.
Rutgers-The State University of New Jersey
Ernest Mario School of Pharmacy,
Piscataway, NJ, U.S.A.

As I write this section for our *Newsletter*, we have not reached summer officially on the calendar; however, the sun, humidity, and temperatures in New Jersey definitely make it feel as though the hot season is upon us. Exams are over, the students have left, and many of us are planning our getaways, as well as the proposals that need to be written soon. Many of us (whether academics or those in industry) apply or collaborate with those who apply for federal funding, and you may or may not have noticed that the NIH has issued new proposed rules that promote objectivity in research (*Federal Register*, Part II Health and Human Services Department, 42 CFR, Part 50, and 45 CFR, Part 94, May 21, 2010). Comments to the NIH must be received by July 20, 2010. These new regulations will impact many of us, since PHS funding involves small business grants (SBIRs and STTRs), clinical trials, and traditional research funding (R01s, R21s, etc.). Also, increasing numbers of professors are spinning off companies, or their funding portfolios have more studies funded by pharmaceutical, chemical, and personal care companies.

The NIH is proposing a new definition of "disclosure of significant financial interests" to an institution. This will mean that a "significant financial interest" could "directly and significantly affect the design, conduct, or reporting of PHS-funded research." The monetary threshold has been lowered from $10,000 to $5,000. The definition of an "investigator" who needs to report a "significant financial interest" will also be expanded to include not only the principal investigator, but also the subgrantees, contractors, collaborators, and consultants. For example, an institution may require an investigator to reduce their ownership interest in a company by some appropriate amount or to sell the ownership interest in its entirety. Depending on the particular situation, this will mean more scrutiny and work for institutions, as well as more paperwork for us all.

On a brighter note, we have a new issue of the *CRS Newsletter* for you to read while you soak up the sun, attend the CRS Annual Meeting in Portland, OR, or as a break in between writing NIH proposals. You can find out what our young scientists are organizing by reading the report of the CRS Young Scientists Committee chaired by Dody Reimer and Louise Rosenmayr-Templeton. Young investigators have the opportunity to attend several workshops, roundtables, and social events at the CRS Annual Meeting, with several sessions organized by the Young Scientist Mentor:Protégé Subcommittee.

There is a fascinating interview with CRS President Diane Burgess, articles on nanotechnology, as well as a report on the recent CRS elections. We welcome Profs. Kazunori Kataoka as vice president, Ijeoma Uchegbu as scientific secretary, and Michael Rathbone as member-at-large. Drs. Aron Anderson, Dennis Discher, Ken Howard, Tamara Minko, and Chris Porter have been elected to the CRS Board of Scientific Advisors—congratulations to all!

May all our annual meeting attendees have a productive and wonderful time in Portland this year! ■

Diane J. Burgess, Ph.D.
Board of Trustees Distinguished Professor
School of Pharmacy, University of Connecticut, Storrs, CT, U.S.A.

Communicating across the country or across the world may be easier and faster than it's ever been, and the days when face-to-face meetings were the norm may be gone. However, as the recent CRS Leadership Forum, held March 19–21, 2010, in Minneapolis, MN, demonstrates, there's still nothing like a sit-down, face-to-face meeting to get good ideas rolling and creative energy moving.

There was no shortage of innovative thinking when CRS committee chairs met with the CRS Board and our staff for a three-day event designed to brainstorm ideas for how CRS can better meet member needs now and be a stronger organization in the future. Topics covered at the forum included

- Volunteer Workforce: How to enhance the volunteer experience, what information committees need to be more effective, and how committee structures can be made more efficient and better engage volunteers.
- CRS Products: Membership, annual meeting, webinars, satellite meetings, website, and publications—ideas for how these specific CRS products can be enhanced to create greater member value.
- Building CRS: How to position our Society for the future.
- Interfacing Committees to Maximize Effectiveness: Establishing priorities and identifying opportunities for collaboration across committees.

One thing that was clear to all in attendance at the forum was the importance of member volunteers. As you can see by the subjects of our discussions, committee volunteers and leaders address issues vital to our Society. Yes, there are hard questions to be answered and challenging issues to be faced. Volunteer work for your organization is challenging, but the rewards, both personally and professionally, are equally as significant. Most importantly, volunteer work is fun and is a great way to network with your peers.

That's why CRS is dedicating time and attention to inviting members (like you!) to become involved in helping to imagine, plan, and implement the CRS of the future. You can explore volunteer opportunities right now by going online (www.controlledreleasesociety.org/main/about/form_Volunteer.cfm) and filling out a volunteer form. It is a small yet enormously important step toward playing a larger role in CRS and one I hope you'll take.

We will be holding a Volunteer Fair at the CRS Annual Meeting in Portland, OR. At the fair, members will have an opportunity to speak directly with committee members and chairs, as well as our staff and members of the CRS Board. This will provide a great opportunity to hear firsthand the roles and importance of various committees, what kind of volunteer commitment is involved, and how to put your particular talents and skills to service on behalf of CRS. The CRS Board is starting to implement the outcomes of the March Leadership Forum, and since so many great ideas were generated at this meeting, we will need a lot of new talent to help implement these ideas! We will be expanding the roles of some committees and establishing new committees, so there will be many opportunities for you to get involved. Items that received particular attention at the Leadership Forum were

1. Leadership development and volunteer engagement
2. Website development
3. Annual Meeting task force
4. Industry development

Speaking of service, I am very excited to announce the addition of a distinguished and highly regarded new recognition within CRS: the College of Fellows. This designation will be given in recognition of CRS members who have made outstanding contributions to their fields of study. Their contributions may be technical, scientific, and/or managerial in one or more fields of research, commercial development, regulatory science, education, and/or leadership. The first group of members inducted into the College of Fellows will be announced at the CRS Annual Meeting in Portland.

My experience as CRS president has in many ways been a series of affirmations—repeated experiences, like the CRS Leadership Forum, that remind me of the many brilliant, dedicated, and passionate people who make up our Society. This is why I feel proud and privileged to be a member of CRS—and why you should too.

There so many ways to get involved in CRS. Our CRS Chapters offer a unique opportunity to get involved at a local level. One of my goals this year has been to expand our Local and Student Chapters. I am writing to you from Beijing (I teach a summer course at Peking University, Health Science Center), and in less than two weeks we will have the inaugural ceremony for the CRS China Chapter in the city of Shenyang!

Get involved in CRS. Make a difference. Share your talents!

See you in Portland!

Diane J. Burgess ■

Interview with CRS President Dr. Diane Burgess

Brian Kilfoyle and Bozena Michniak-Kohn, Ph.D.
Ernest Mario School of Pharmacy, Rutgers-The State University of New Jersey, Piscataway, NJ, U.S.A.

Dr. Diane Burgess received her B.S. degree in pharmacy from the University of Strathclyde, U.K. (1979), and her Ph.D. degree in pharmaceutics from the University of London, U.K. (1984), specializing in colloidal pharmaceutics and microsphere technology under Prof. J. E. Carless. After graduating, she performed her post-doctoral research with Prof. S. S. Davis at the University of Nottingham, focusing on biopharmaceutics and animal testing. After completing her post-doctoral research, Dr. Burgess taught at the University of North Carolina at Chapel Hill as a visiting assistant professor (1985–1986) before moving to the University of Illinois at Chicago (1986–1992) as an assistant and then associate professor of pharmaceutics in the Department of Pharmaceutics. In 1993, Dr. Burgess moved to the University of Connecticut at Storrs, where she has remained ever since. In 2009, Dr. Burgess was appointed the Board of Trustees Distinguished Professor of Pharmaceutics because of her contributions to research, service, and teaching. Aside from her role as a professor at the University of Connecticut, Dr. Burgess teaches traditional Chinese medicine at Peking University in Beijing, China, every summer. Additionally, she consults for the pharmaceutical, food, cosmetics, and other industries.

Dr. Burgess is very committed to service, as she has been the president of the American Association of Pharmaceutical Scientists (2002) and is currently the President of the Controlled Release Society. She is only the fourth person to be president of both organizations, with the others being Dr. Joe Robinson, Dr. Gordon Amidon, and Dr. Vincent Lee. She has been the organizer and chair of numerous AAPS, CRS, and ACS conferences and workshops and has been a member of many NIH Study Sections. She is a member of the USP Advisory Panel on Performance Test – by Injection (2004–present) and the USP Biopharmaceutics Expert Committee (2005–2010).

Dr. Burgess is the current editor of the *International Journal of Pharmaceutics* (2009–present) and has previously been the editor for *AAPSPharmSci* (1999–2005) and the *Journal of Drug Delivery Science and Technology* (2003–2008). Additionally, Dr. Burgess serves on the editorial boards of seven international journals.

Dr. Burgess has received many awards throughout her career, including the Outstanding Teacher of the Year Award (2005 and 1992). She is a Fellow of the American Association of Pharmaceutical Scientists (2006) and was the first recipient of the CRSI Fellowship (2010) for outstanding contributions in the area of drug delivery.

Dr. Burgess has authored more than 130 refereed publications. She has given more than 350 research presentations at major international scientific meetings, more than 170 invited lectures and presentations, and 11 keynote addresses. Dr. Burgess has served as major advisor for 4 M.S. and 17 Ph.D. graduates, as well as 15 post-doctoral fellows. She is currently major advisor for 7 Ph.D. candidates and 2 post-doctoral fellows.

Research efforts in her lab focus on drug delivery systems and interfacial chemistry. Projects span the following areas: development of novel technologies; preformulation; materials science, formulation; stability assessment and prediction; transport; sterility assessment; biophysical assessment; cell culture and development of *in vitro* performance tests and *in vitro–in vivo* correlation. She is currently developing a miniaturized, implantable biosensor for metabolic monitoring, investigating and controlling tissue response to the implant. She is also investigating intracellular trafficking of DNA therapeutics.

Interview

Q ***Congratulations on receiving the Board of Trustees Distinguished Professor award from the University of Connecticut. What does this prestigious award mean to you?***

A Being designated a Board of Trustees Distinguished Professor is the highest honor bestowed on faculty at the University of Connecticut, and this appointment is given to only a small group of elite faculty members, and so I am very honored and humbled by this recognition. I am currently the only person that holds this title in the pharmacy school. This recognition is based on research, service, and teaching, with an emphasis on the research.

Burgess lab.

Q ***What are the current research interests of your group? Could you provide references so that if interested, our readers can further familiarize themselves with your work?***

A All of the main projects being worked on in my lab stem from a background in colloid and interfacial chemistry and applying that to drug delivery.

Much of my early work (which I continue) is on pure interfacial and colloid chemistry as applied to emulsion stability and optimizing formulation of microspheres and particles. This work focused on defining relationships between interfacial tension, rheology, and charge and emulsion stability. We're not just working on simple emulsions, but also multiple emulsions and nanoemulsions. In addition, we are applying these same principles to nanosuspensions and their stability and how surfactants interact on the particle surface to make them stable or not stable, as the case may be. This has resulted in a novel time- and resource-saving method for nanosuspension stabilizer selection; the current methods of nanosuspension stabilizer selection are based on trial and error.

Morais, JM, Rocha-Filho, PA, Burgess, DJ. Influence of phase inversion on formation and stability of one-step multiple emulsions, Langmuir 25(14): 7954-7961 (2009).

Verma, S, Huey, B, Burgess, DJ. A scanning probe microscopy method for nanosuspension stabilizer selection, Langmuir 25(21): 12481-12487 (2009).

Additionally, we are developing numerous novel drug delivery systems, including liposomes, microspheres, and nanoparticles for different disease applications, including using liposomal drug delivery for anti-AIDS in order to get the drug to the target cells.

Another project we are currently working on is developing a totally implantable biosensor to monitor glucose as well as other metabolites, such as oxygen, carbon dioxide, and lactate. This biosensor is primarily for diabetics, but also has applications in metabolic monitoring in general to understand metabolism and gain a better understanding of obesity and the progression of obesity to diabetes. This miniaturized (0.5 mm × 0.5 mm × 5 mm), totally implantable sensor is designed to interface with a PDA, iphone, or similar device that will have a patient-specific algorithm that will link to an insulin/glucagon pump to realize the much sought after concept of an "artificial pancreas." This devise will revolutionize diabetes management and enable avoidance of not only hypo- and hyperglycemic excursions, but also the more subtle deviations in glucose levels that lead to the many debilitating side effects of diabetes. Our group has been able to make such a biosensor become a reality through our pioneering work on biocompatible coatings. We have developed a multifunctional coating for our biosensor that allows rapid diffusion of analyte into the sensor and, at the same time, slow release of anti-inflammatory drug out to control the foreign body response.

Moussy, F, Kreutzer, D, Burgess, D, Koberstein, J, Papadimitrakopoulos, F, Huang, S. Implant coating for control of tissue/implant interactions, US Patent 6,497,729 and WO Patent (Canada, European Countries) (2002).

Bhardwaj, U, Sura, R, Papadimitrakopoulos, F, Burgess, DJ. PLGA/PVA hydrogel composites for long-term inflammation control following s.c. implantation, Int. J. Pharm. 384(1-2): 78-86 (2010).

Vaddiraju, S, Burgess, DJ, Jain, FC, Papadimitrakopoulos, F. Enhanced glucose sensor linearity using PVA hydrogels, JDST 3(4): 863-874 (2009).

Vaddiraju, S, Tomazos, I, Burgess, DJ, Jain, FC, Papadimitrakopoulos, F. Emerging synergy between nanotechnology and implantable biosensors: A review, Biosens. Bioelectron. (2009).

Vaddiraju, S, Burgess, D J, Jain, F C, Papadimitrakopoulos, F. The role of H_2O_2 outer diffusion on the performance of implantable glucose sensors, Biosens. Bioelectron. 24(6): 1557-1562 (2009).

Bhardwaj, U, Papadimitrakopoulos, F, Burgess, D J. Development of a vehicle for localized and controlled drug delivery for implantable biosensors, JDSAT 2(6): 1016-1029 (2008).

Bhardwaj, U, Sura, R, Papadimitrakopoulos, F, Burgess, D J. Controlling acute Inflammation with fast-releasing dexamethasone-PLGA microsphere/PVA hydrogel composites for implantable devices, J. Diabetes Sci. Technol. 1(1): 8-17 (2007).

Patil, S D, Papadimitrakopoulos, F, Burgess, D J. Concurrent delivery of dexamethasone and VEGF for localized inflammation control and angiogenesis, J. Control. Release 117(1): 68-79 (2007).

Galeska, I, Kim, T-K, Patil, S D, Bhardwaj, U, Chattopadhyay, D, Papadimitrakopoulos, F, Burgess, D J. Controlled release of dexamethasone from PLGA microspheres embedded within polyacid-containing PVA hydrogels, AAPS J. 7(1): E231-E240 (2005).

Patil, S D, Papadimitrakopoulos, F, Burgess, D J. Dexamethasone-loaded poly(lactic-co-glycolic) acid microspheres/poly(vinyl alcohol) hydrogel composite coatings for inflammation control, Diabetes Technol. Ther. 6(6): 887-897 (2004).

In 2001, I took a sabbatical at the FDA to work with them on the regulation of controlled release parenteral delivery systems. I continue this work with the FDA and the USP to

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look into developing performance testing methods for controlled release parenterals to ensure the safety and efficacy of these products. We are currently working with the United States Pharmacopeia to validate and ensure transfer of the *in vitro* release testing methods that we have developed for controlled release parenterals for adaptation into a USP monograph.
Zolnik, B S, Raton, J-L, Burgess, D J. Application of USP apparatus 4 and *in situ* fiber optic monitoring to microspheres release testing, Dissolution Technol. 12(2): 11-14 (2005).

Zolnik, B S, Leary, P E, Burgess, D J. Elevated temperature accelerated release testing of PLGA microspheres, J. Control. Release 112(3): 293-300 (2006).

Zolnik, B S, Burgess, D J. Evaluation of *in vivo – in vitro* release of dexamethasone from PLGA microspheres, J. Control. Release 127: 137-145 (2008).

Bhardwaj, U, Burgess, D J. A novel USP apparatus 4 based release testing method for dispersed systems, Int. J. Pharm. 388(1-2): 287-294 (2010).

Q ***Could you briefly describe the role of controlled release in your work, with a possible emphasis on the anionic liposomal delivery systems and PLGA microspheres?***

A All of my research is either focused on controlled or targeted delivery, with a greater focus on controlled delivery. The multifunctional coating for our biosensor contains microspheres that are programmed to slowly release anti-inflammatory drug and different tissue response modifiers to prevent the foreign body response. This needs to be done in a controlled manner over the entire lifetime of the sensor, or the inflammation will kick in as soon as the drug release finishes. If inflammation and fibrous encapsulation results, then the sensor cannot function, because the analyte will not be able to diffuse to the sensor (analyte being the glucose) due to the thick layer of fibrotic cells around the sensor (the sensor is effectively entombed or walled off from the body fluids).

Bhardwaj, U, Papadimitrakopoulos, F, Burgess, DJ. Development of a vehicle for localized and controlled drug delivery for implantable biosensors, JDSAT 2(6): 1016-1029 (2008).

Bhardwaj, U, Sura, R, Papadimitrakopoulos, F, Burgess, DJ. Controlling acute inflammation with fast-releasing dexamethasone-PLGA microsphere/PVA hydrogel composites for implantable devices, J. Diabetes Sci. Technol. 1(1): 8-17 (2007).

We are using anionic liposomal delivery systems for siRNA delivery and the delivery of other gene therapeutics. In addition, we have developed a method that involves the conjugation of semiconductor quantum dots to the gene therapeutic, as well as the gene delivery system, in order to monitor and, thus, understand intracellular trafficking of these DNA therapeutics. The intent here is that this knowledge will allow researchers to make improved delivery system designs that will overcome the barriers to effective delivery of gene therapeutics. For the liposomal work we are doing with siRNA and other gene delivery, we are interested in the therapeutic being contained within the liposome until it is taken up inside the cell and then for it to be released from the endosome. Further, for those gene therapies in which uptake into the nucleus is necessary, we are working on that as well.

Patil, SD, Rhodes, DG, Burgess, DJ. Bio-physical characterization of a novel anionic liposomal delivery system, Biochim. Biophys. Acta 1711(1): 1-11 (2005), doi:10.1016/j.bbamem.2005.03.004. (Top 10 most downloaded articles of 2005 in BBA.)

Patil, SD, Rhodes, DG, Burgess, DJ. DNA-based therapeutics and their delivery systems: A comprehensive review, Published online at www.aapspharmsci.org/articles/aapsj0701/aapsj070109/aapsj070109.pdf, AAPS J. 7(1): article 9 (2005) (2007 Outstanding Manuscript Award, *AAPS Journal*.)

Srinivasan, C, Papadimitrakopoulos, F, Burgess, DJ. Dual fluorescent labeling method to visualize plasmid DNA degradation, Bioconjugate Chem. 20(1): 163-169 (2009).

Srinivasan, C, Lee, J, Papadimitrakopoulos, F, Silbart, LK, Zhao, MH, Burgess, DJ. Labeling and intracellular tracking of functionally active plasmid DNA with semiconductor quantum dots, Mol. Ther. 14(2): 192-201 (2006).

Our laboratory is also working on QbD (quality by design) of liposomes in order to gain a better understanding of the design space of these products to facilitate their regulation and translation into safe and efficacious products. We're looking at QbD for liposomes, but there are different types of liposomes, including those that release immediately, those that release in a controlled fashion, and those that only release when they are taken up into cells. We are looking to develop *in vitro*-release testing methods that will be able to mimic the *in vivo* performance of all of these different types of liposomes.

Q ***Could you provide a little more detail about your work on implantable biosensors in collaboration with Dr. Fotios Papadimitrakopoulos and Dr. Faquir Jain?***

A It's a glucose oxidase-based system that is used to measure the glucose, i.e., it is an electrochemical sensor. With the help of Dr. Jain, we've been able to fit all of this onto a tiny silicon chip (0.3 mm in diameter × 3.0 mm in length), and the sensor can be injected into the body with a hypodermic needle. My laboratory is primarily involved in preventing the foreign body response (as described above) to the sensor and in the eventual linking of this sensor with an insulin delivery device.

Patil, SD, Papadimitrakopoulos, F, Burgess, DJ. Concurrent delivery of dexamethasone and VEGF for localized inflammation control and angiogenesis, J. Control. Release 117(1): 68-79 (2007).

Bhardwaj, U, Sura, R, Papadimitrakopoulos, F, Burgess, DJ. Controlling acute inflammation with fast-releasing dexamethasone-PLGA microsphere/PVA hydrogel composites for implantable devices, J. Diabetes Sci. Technol. 1(1): 8-17 (2007).

Additionally, there is a biosensor video at the following web address that those who are interested may want to check out (www.youtube.com/watch?v=YPnubyqB9Ws).

Q ***What types of* in vitro *performance tests for controlled release colloidal systems are you working on?***

A We're mainly looking into *in vitro* release testing methods, but depending on the delivery system, a performance indicator test may also include other methods, such as particle size analysis and stability. For regulation purposes, we need to have a release test, but to get a product on the market, we also need to understand a lot of other CMC issues.

With the microspheres, we have developed an appropriate *in vitro* release test, and we've been able to establish *in vitro/in vivo* correlations between the *in vivo* release in small animals and the *in vitro* release in the USP 4 system that we've further developed (modified flow-through cell). We've also developed a modification to the USP 4 flow-through cell for liposomes and nanoparticles. Essentially we have modified the cell to make the flow-through more applicable for the different types of delivery systems. The different modifications for these different delivery systems allow application of this method to these delivery systems, avoiding errors such as product aggregation and sampling errors. In addition these modifications can allow simulation of conditions in the subcutaneous and intramuscular tissues. Although specific apparatuses have been designed before with the oral and transdermal routes in mind, till now there have not been any methods that were specifically designed for parenteral controlled release systems. As these types of delivery systems are becoming increasingly popular for the new biological classes of compounds, as well as for poorly soluble small molecule drugs, the need for appropriate testing methods is becoming urgent.

Zolnik, S, Raton, J-L, Burgess, DJ. Application of USP apparatus 4 and *in situ* fiber optic monitoring to microspheres release testing, Dissolution Technol. 12(2): 11-14 (2005).

Zolnik, BS, Leary, PE, Burgess, DJ. Elevated temperature accelerated release testing of PLGA microspheres, J Control. Release 112(3): 293-300 (2006).

Zolnik, BS, Burgess, DJ. Evaluation of *in vivo–in vitro* release of dexamethasone from PLGA microspheres, J. Control. Release 127: 137-145 (2008).

With my students and my collaborator Prof. Papadimitrakopoulos after graduation May 2009, when I was named Board of Trustees Distinguished Professor.

Bhardwaj, U, Burgess, DJ. A novel USP apparatus 4 based release testing method for dispersed systems, Int. J. Pharm. 388(1-2): 287-294 (2010).

Q ***What do you regard as the most significant achievement(s) of your scientific career thus far?***

A In terms of science and scientific breakthrough, the work we are doing with the FDA and USP is very important and helpful to the pharmaceutical industry and to the regulatory authorities to facilitate the acceptance of safe and efficacious products for human as well as veterinary health care. This is very satisfying, as our efforts in this area can have a large impact, helping to bring safe and effective medicines onto the market.

My group is working diligently to develop our glucose biosensor, but that's only one product, and if we can get it onto the market (which we hope), I think it would be revolutionary, because you'd be able to get continuous monitoring of glucose from this and it would eventually be able to act as an artificial pancreas. It's going to be implanted, it's really tiny, and it's not very invasive to the patient. With a wireless communication to a PDA, a signal can be sent to a doctor's office or the parent of a child with diabetes. Also, an algorithm can be put into the PDA that calculates, based on the patient's glucose profile, how much insulin or glucagon is needed, effectively closing the loop and working as an artificial pancreas. This is not on the market yet, but I hope that it will be one of the most significant things that I do.

In terms of pure science, a lot of the work I've done on emulsion stability, though not realizing a product, has been utilized by many other scientists in various fields. In particular, this work has applications in diverse areas, including pharmaceutical science, cosmetic science, and other consumer products.

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Another huge aspect of what I do is service. I was president of AAPS in 2002, and I am the current president of CRS. This work consumes a lot of my time, but I think it's a very important and valuable contribution to the general scientific community and, in particular, to our community of controlled release and drug delivery. Being the editor of journals is also a significant contribution to the scientific community in general. I am currently editor of the *International Journal of Pharmaceutics*.

I also teach traditional Chinese medicine at Peking University in Beijing, China, during the summer, so I do a lot of different things.

Q ***Could you tell us a little bit more about teaching traditional Chinese medicine? How did you get involved in this? How different is the environment to that in the U.S.?***

A This summer elective program is designed to provide American pharmacy as well as other science majors from the University of Connecticut with an understanding of traditional Chinese medicine. As alternative medicine is becoming a more sought-after option in the U.S. and around the globe, such programs are extremely useful. This program is designed to give the students an understanding of not only another pharmacy culture, but also another culture in general. Students learn about the Ying-Yang theory, the Five Channel theory, acupuncture, and herbal medicine. They also spend almost half of their time learning basic Mandarin. I developed this program with colleagues at Peking University and specifically want to acknowledge Dean Junyi Lui and Professor Xiaoda Yang in the School of Pharmaceutical Sciences, as well as Mr. Xu You at the Peking University Study Abroad Office. In China, traditional Chinese medicine is practiced side-by-side with modern Western medicine, both in the large modern hospitals and in the local pharmacies.

Q ***What scientists have played an important role in your scientific development?***

A There are many people who have had a profound effect on my scientific development. While I was an undergraduate at Strathclyde, Professor Alexander (Sandy) Florence (a past president of CRS), Professor John Stenlake, and Dr. Tony Whateley encouraged me to go into the sciences and to pursue my Ph.D. My Ph.D. supervisor Professor John Carless and my postdoctoral supervisor Professor S. S. Davis taught me important skills. Since I've been in the U.S., people that have influenced me include Professor Les Benet (the founder of AAPS), Professor Larry Augsburger, Professor Kinam Park (the editor of *JCR*) and Professor Ron Borchardt.

With a group of study-abroad Connecticut students in Beijing, China.

Q ***When you finished graduate school, why did you decide to stay in academia instead of pursuing a career in industry?***

A Actually, when I went to graduate school it was in order to pursue a career in industry. I worked for a while in industry after my bachelors degree and realized that to get on in industry I would need to get a Ph.D., so I went to study for my Ph.D. with the intention to work in industry. When I was conducting my Ph.D. studies I did some teaching and that got me interested again in teaching. When I was in high school, I thought I wanted to be a chemistry teacher, but then I got into pharmacy. I liked being a pharmacist but wanted to give industry a try, and I was encouraged by Professor Florence, Professor Stenlake, and Dr. Whateley to do a Ph.D. My older sister was doing a Ph.D. in pharmacology at the time, and she was also very influential in encouraging me in this direction.

When I was working as a teaching assistant, I thought that I liked the idea of teaching, so I decided to do a postdoc. During my postdoctoral experience, I was able to do some lecturing, and this convinced me to pursue an academic career. Following my postdoctoral studies I secured an assistant professor position at the University of Illinois, and the rest is history.

Q ***If you were to give advice to a recent or soon-to-be graduate, what would it be?***

A I think a very important thing is networking. One can achieve that through a scientific society such as CRS, by volunteering and getting involved in committees. Such volunteering will facilitate important networking with peers outside your place of work. As you progress in your career, these colleagues can help you, and you can help them, in many, many ways. Professional volunteer work provides a place to learn separate from your place of work. Through this kind of activity, one can also make a contribution to the society in general. I believe that it is important to always contribute to more than one area, so that if one thing isn't working there is always another option.

Q ***What personal attributes have allowed you to excel in your scientific career?***

A Work ethic. I have a very, very strong work ethic. Good communication skills, both orally and written; these are essential. Another important ingredient is compassion. Smile, be compassionate, and use your judgment to separate right from wrong. Always help others regardless of their station.

Q ***Outside of your scientific endeavors what hobbies do you enjoy?***

A I like sports, including running, bike riding, and skiing (downhill, cross-country, back country). Running is the main one because it's the easiest one to do when I travel a lot. When I was at the CRS meeting in Hawaii, I ran the Kona Kailua marathon, and I came in third in my age group (I think it was the under 20's…).

Q ***As the president of the Controlled Release Society, what important role(s) do you think the Society has played since its inception?***

A The CRS is responsible for bringing people together and educating them. Through this we can develop better products for consumers, whether they are healthcare products, veterinary products, or cosmetic products, etc. One of the great things is that it is an international organization.

Q ***What can readers expect at the upcoming conference in Portland, Oregon?***

A I think it will be a very exciting meeting with great science and an outstanding program. Portland is a beautiful venue with a lot to offer in terms of hiking, biking, coastline, and mountains. It's a phenomenal place for outdoor activities and even has skiing on Mt. Hood in the summer! It's a wonderful place with a lot of fantastic restaurants and is also near Oregon wine country. What more could you want?

Q ***It seems appropriate that the conference will be held in Oregon, the retirement home of Dr. Jorge Heller. Could you talk about the legacy of Jorge Heller and some details on the Controlled Release Society 2010 Fellowship to honor him?***

A He was the founder of the *Journal of Controlled Release*, which is one of the most important contributions that our Society has made. When you go to different parts of the world, everyone has heard about the Controlled Release Society because our journal is a top journal in our field, and everyone wants to publish his/her research in this journal. Dr. Heller's science, his industrial career, and his ability to get products to the market was exceptional. He was very interested in education, which makes this fellowship for a postdoctoral researcher a very nice way to honor our beloved and great scientist. ■

Spotlight on the

2010 CRS Annual Meeting & Exposition Host City

Portland, Oregon, U.S.A.

What to do with an hour or two of free time while in Portland…

- Saturday Market (open Sunday's, too). Artists, crafters, food vendors, and more! Under the Burnside Bridge, Portland.
- Peruse the millions (literally) of new, used, rare, and out of print books at Powell's City of Books, 1005 Burnside, Portland.
- Savor a relaxing cup of coffee or tea…there's a coffee/tea shop on almost every corner in Portland.
- Take a walk along Governor Tom McCall Waterfront Park, West Bank of the Willamette River, downtown Portland.
- Indulge in a decadent cupcake at Cupcake Jones, Pearl District, 307 NW 10th Ave., Portland.
- Search out that favorite vinyl or CD at the oldest record store in the Pacific Northwest; Music Millennium, 3158 E. Burnside St., Portland.
- Sip a cool beer on a hot summer day at one of Portland's 36 brew pubs.
- Gaze at amazing hand-made jewelry, pottery, clothing, leather goods, artisan glass, children's toys, and exotic woodwork, at the Real Mother Goose, 901 S.W. Yamhill, Portland.

www.controlledreleasesociety.org/meeting

RiverPlace Marina with Portland Skyline by Edward Nugent, courtesy of Travel Portland.

Welcome to the 37th Annual Meeting & Exposition of the Controlled Release Society

Personalized Medicines and Products for the Next Generation

July 10–14, 2010
Oregon Convention Center
Portland, Oregon, U.S.A.

Peninsula Park Rose Garden courtesy of Travel Portland/Steve Terrill.

Welcome to the "City of Roses," Portland, OR, and your opportunity to experience a bit of fresh air and copious amounts of fresh thinking!

The 2010 CRS Annual Meeting & Exposition promises to be one of the freshest on record, with many new programs planned. The largest new program is CRS Innovation Sunday and the CRS Partnering Sessions. The Young Scientist program has also expanded, with a new workshop being presented on Monday, as well as an expanded Mentor/Protégé program. Several networking events are also being introduced: Women in Science Luncheon, Networking Night at BridgePort Brewing Company, and an After Party immediately following the Closing Banquet. The biggest networking experience of all can be found in the Exposition/Poster Hall starting Sunday evening and running through Wednesday afternoon. All programs and events have been thoughtfully planned to provide extra value for the CRS annual meeting attendee's experience.

2010 CRS Annual Meeting & Exposition Schedule*

All meetings and events take place at the Oregon Convention Center unless otherwise stated.

Saturday, July 10

08:00 – 18:00	Educational Workshops I, II, and III Nanomedicine: From Materials Design to Clinical Applications Characterization of Nanoparticles and Microparticles Using State-of-the-Art Techniques Enhancing Bioavailability of Poorly Soluble Drugs via Melt Extrusion Technology: From Formulation to Commercialization
08:30 – 16:45	Young Scientist Workshop I Improving the Solubility of Poorly Soluble Drugs

Sunday, July 11

08:00 – 12:00	Young Scientist Workshop II True Stories; Career Development
08:00 – 17:00	Career Center Open
08:00 – 17:00	CRS Partnering
09:00 – 14:30	Releasing Technology Workshops
09:00 – 11:00	Tablet Manufacturing Roundtable Discussion (followed by Focus Group)
09:00 – 11:00	Oral Drug Delivery Roundtable Discussion (followed by Focus Group)
11:30 – 13:30	First Timer's Meeting/Volunteer Fair
12:30 – 14:55	Soapbox Sessions
12:30 – 15:00	Young Scientist Roundtable Discussion
13:00 – 15:00	Nanomedicines Roundtable Discussion (followed by Focus Group)
14:00 – 16:30	CRS Innovation Sunday Open Forum
16:30 – 17:30	Pearls of Wisdom Sessions Bioactive Materials/Young Scientist (joint session) C&DP Veterinary
16:45 – 17:30	State of the Industry Keynote
17:30 – 19:00	Grand Opening of the Exposition and Welcome Reception

Monday, July 12

07:00 – 09:30	Young Scientist Workshop III Team Working and Motivation
08:00 – 09:00	Plenary Session – *Raju Kucherlapati, Harvard Medical School, U.S.A.*
08:00 – 17:00	Career Center Open
08:00 – 16:30	CRS Partnering
09:00 – 10:00	Networking – Exposition/Poster Hall
09:00 – 17:00	Exposition/Poster Hall Open
10:00 – 12:00	Scientific Sessions/Mini-symposia Mini-symposium: Theranostics: Diagnosis and Treatment in One Box

	New Chemistries for Drug Delivery
	Non-parenteral Delivery of Biologics
	Novel Materials and Release Systems
	Ophthalmic Medicines
	Prediction and Application of IVIVC for Veterinary Species
	Transdermal
12:00 – 13:30	Women in Science Luncheon
12:00 – 14:00	Networking – Exposition/Poster Hall
13:00 – 14:00	Poster Session I – Authors Present
14:00 – 15:00	Plenary Session – *Ramin Najafi, NovaBay Pharmaceuticals, U.S.A.*
15:00 – 15:30	Networking – Exposition/Poster Hall
15:30 – 17:30	Scientific Sessions/Mini-symposia
	Mini-symposium: Biomarkers: The Needle in the Haystack
	Nanoparticles and Fibers for Controlled Release Systems
	Peptides and Proteins
	Polymers in Medicine
	Pulmonary Delivery
	Translational Studies
17:30 – 19:00	Vet Get Together
	Technological Innovations in Drug and Vaccine Delivery in Animal Health – Challenges and Opportunities
18:00 – 22:30	Networking Night/BridgePort Brewing Co. (organized by the Young Scientist Committee)

Tuesday, July 13

07:00 – 08:00	Get Up Get Educated!
08:00 – 09:00	Plenary Session – *Frank Szoka, University of California-San Francisco, U.S.A.*
08:00 – 09:30	Mentor Protégé Meet and Greet
08:00 – 16:00	CRS Partnering
09:00 – 10:00	Networking – Exposition/Poster Hall
09:00 – 17:00	Exposition/Poster Hall Open
10:00 – 12:00	Scientific Sessions/Mini-symposia
	Encapsulation for Environmental Protection
	Medical Devices
	Mini-symposium: siRNA/Micro-RNA
	Oral Delivery I
	PEGylated Technologies
	Vaccines
11:45 – 12:45	Highlights of Student Posters
12:00 – 14:00	Networking – Exposition/Poster Hall
13:00 – 14:00	Poster Session II – Authors Present
13:30 – 14:30	CRS Members Meeting/Awards Ceremony/ College of Fellows Induction
14:30 – 15:15	Plenary Session – *Hiroshi Maeda, Sojo University, Japan*
15:15 – 15:30	Networking – Exposition/Poster Hall
15:30 – 17:30	Awards Showcase
15:30 – 17:30	Scientific Sessions
	DNA Delivery
	Encapsulation of Cells and Microorganisms
	Intracellular Trafficking
	Liposomes
	Oral Delivery II
	Tumor Targeting
18:30 – 23:00	Closing Banquet and After Party – Portland Art Museum

Wednesday, July 14

08:00 – 09:00	Plenary Session – *Mauro Ferrari, University of Texas-Houston, U.S.A.*
08:00 – 13:00	CRS Partnering
09:00 – 10:00	Networking – Exposition/Poster Hall
09:00 – 13:30	Exposition/Poster Hall Open
10:00 – 12:00	Scientific Sessions/Mini-symposia
	Blood Brain Barrier
	Environmentally Friendly and Biodegradable Controlled Release Systems
	Mini-symposium: Biomedical Photonics: *In Vivo* Diagnostics of Malignancy with Targeted Delivery Tools
	Mini-symposium: Stem Cells – Yes, We Can!
	Nanomedicines I
	Hydrogels
12:00 – 13:30	Networking – Exposition/Poster Hall
12:30 – 13:30	Poster Session III – Authors Present
13:30	Exposition/Poster Hall Closes
13:30 – 14:30	Plenary Session – *Nicholas Peppas, University of Texas-Austin, U.S.A.*
14:30 – 16:30	Scientific Sessions/Mini-symposia
	Biomaterials
	Biomedical Imaging
	Mini-symposium: Vaginal Drug Delivery: Past, Present, and Future
	Nanomedicines II
	Tissue Engineering

**Program subject to change. Final program available onsite.*

If you have not yet registered, we invite you to do so at **www.controlledreleasesociety.org/meeting**.
The registration deadline is June 30, 2010. (Onsite registration available).

Enhance your professional development with CRS!

Vaccine Development—CRS-IPTS Educational Workshop

To be held immediately prior to the 15th International Pharmaceutical Technology Symposium

September 11-12, 2010
Kervansaray Lara Hotel, Antalya, Turkey

Novel Methods for Developing Clinically Relevant Product Specifications

Workshop co-sponsored by the American Association of Pharmaceutical Scientists and the Controlled Release Society. To be held immediately prior to the FIP Pharmaceutical Sciences World Congress 2010 in association with the AAPS Annual Meeting

Saturday, November 13, 2010
Morial Convention Center, New Orleans, Louisiana, U.S.A.

CRS Product Development Forum – Poorly Soluble Drugs

January 27–28, 2011
Doral Golf Resort and Spa, Miami, Florida, U.S.A.

38th Annual Meeting & Exposition of the Controlled Release Society

July 30–August 3, 2011
Gaylord National Resort and Convention Center
National Harbor, Maryland, U.S.A.

39th Annual Meeting & Exposition of the Controlled Release Society

July 14–18, 2012
Centre des Congrès de Québec
Québec City, Canada

CRS
Delivering Bioactives

Cell-Specific Delivery of Hydrophobic Cargo Using Targeted Mesoporous Silica Nanoparticles as Drug Delivery Vehicles

Jessica M. Rosenholm,[1,2] Emilia Peuhu,[3,4] Annika Meinander,[3,4] Rasmus Niemi,[3] John E. Eriksson,[3,4] Cecilia Sahlgren,[3,4] and Mika Lindén[1]

Summary
Targeted drug delivery is one of the key aims in medical science today. The application of nanotechnology in drug delivery has raised the expectations of achieving this goal, and this field is likely to change the focus of the pharmaceutical and biotechnology industries in the future. By employing nanotechnology, it may be possible to deliver, or even co-deliver, drugs in a cell- and tissue-specific manner. Targeting is especially relevant in the context of cancer therapies, as most of the commonly used anticancer drugs have serious side effects due to unspecific action on healthy cells. Moreover, drug delivery will play a vital role in realizing the potential success of newly identified therapeutic agents, a significant percentage of which are poorly soluble in water (1). Here we show that poly(ethylene imine)-mesoporous silica hybrid particles can specifically target cancer cells under co-culture conditions with normal cells, using folic acid as the targeting ligand. Moreover, the intracellular drug delivery ability combined with the targetability of this system was verified using two hydrophobic fluorophores as model drugs, which made it possible to follow the intracellular release using confocal fluorescence microscopy, as well as to quantify the intracellular delivery using flow cytometry.

Introduction
Since the beginning of the new millennium, much research has focused on applying mesoscopically ordered nanoporous silica materials as drug delivery systems (2), as these materials can carry large amounts of a broad chemical spectrum of different payloads as a consequence of their high specific surface area and pore volume. Current efforts, thus, lie in also introducing cell specificity to these materials. However, successful intracellular delivery does not only require the drug delivery system to be internalized by the right population of cells, but also the ability of the system to release its cargo into the cytoplasm once taken up by the cell. Simultaneously, premature leaking of cargo before cellular internalization is not desirable. Therefore, we designed a hybrid system in which we combined the high adsorption capacity and biodegradability of the silica matrix for carrying and protecting the cargo with some advantageous properties of poly(ethylene imine) (PEI). Hyperbranched PEI, thus, was grown from the particle surface to act as a "molecular barrier" to prevent the cargo from premature release, as well as to provide suspension stability to the particulate system, create a net positive charge to promote cellular uptake, and provide a large amount of terminal reactive groups for further functionalisation, as well as to introduce possible "proton sponge" and "endosome buffering" capacity for facilitating the escape of the active agent from the cellular compartments into the cytoplasm (3). Furthermore, the sol-gel–based material synthesis allowed for *in situ* incorporation of fluorescent labels, making the particles traceable in a biological environment.

Results and Discussion
Fluorescent mesoporous silica nanoparticles (MSNs) with hyperbranched PEI grown from the particle surface were created (Figure 1). In order to design a cancer-targeting system, folic acid moieties, a ligand for a cell surface receptor that is over-expressed in cancer cells, were covalently attached to the PEI layer. When folic acid (FA) is attached to PEI-MSNs, an efficient cell-specific uptake can be achieved in HeLa cells, a commonly studied cervical cancer cell line (Figure 2). Confocal fluorescence microscopy studies in combination with flow-cytometry (FACS) analysis confirmed that both the number of particles per cell and the number of cells that had internalized the FA-PEI-MSNs were much higher for cancer cells over-expressing the folate receptor (FR) compared with low-folate

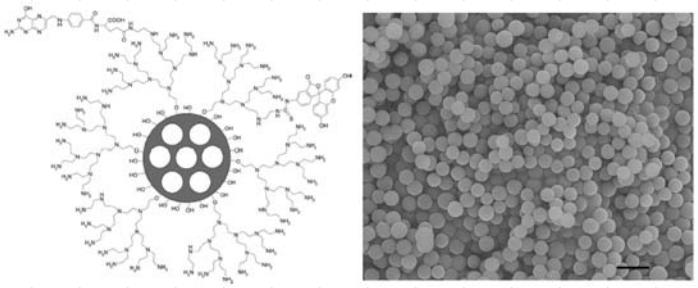

Figure 1. *Scanning-electron microscopy (SEM) image (scale bar 1 μm), as well as a schematic representation of the nanoparticle design. The fluorescent label can be attached either to the particle surface, inside on the pore walls, or incorporated* in situ *during synthesis.*

Scientifically Speaking Rosenholm continued on page 14

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Scientifically Speaking Rosenholm continued from page 13

receptor-expressing non-cancerous cells, epithelial HEK 293 (4). The extracellular fluorescence was quenched prior to the measurements in order to exclude particles just adsorbed onto the outer cell membrane from the analysis, as a surface with a high positive charge promotes non-specific adhesion of particles to cells. Moreover, the particle uptake by the HeLa cells decreased dramatically in the presence of free FA, confirming that receptor-mediated particle internalization is the dominant mechanism for particle endocytosis (4). The particle uptake was further studied under co-culture conditions, as factors including cell-density could have an influence on particle uptake. These results are shown in Figure 2C. The green fluorescing particles were co-localized with the blue-stained FR-high HeLa cells, while very little green fluorescence was observed in the red-stained FR-low HEK 293 cells. This is a positive proof for successful *in vitro* targetability of the developed particles to cancer cells.

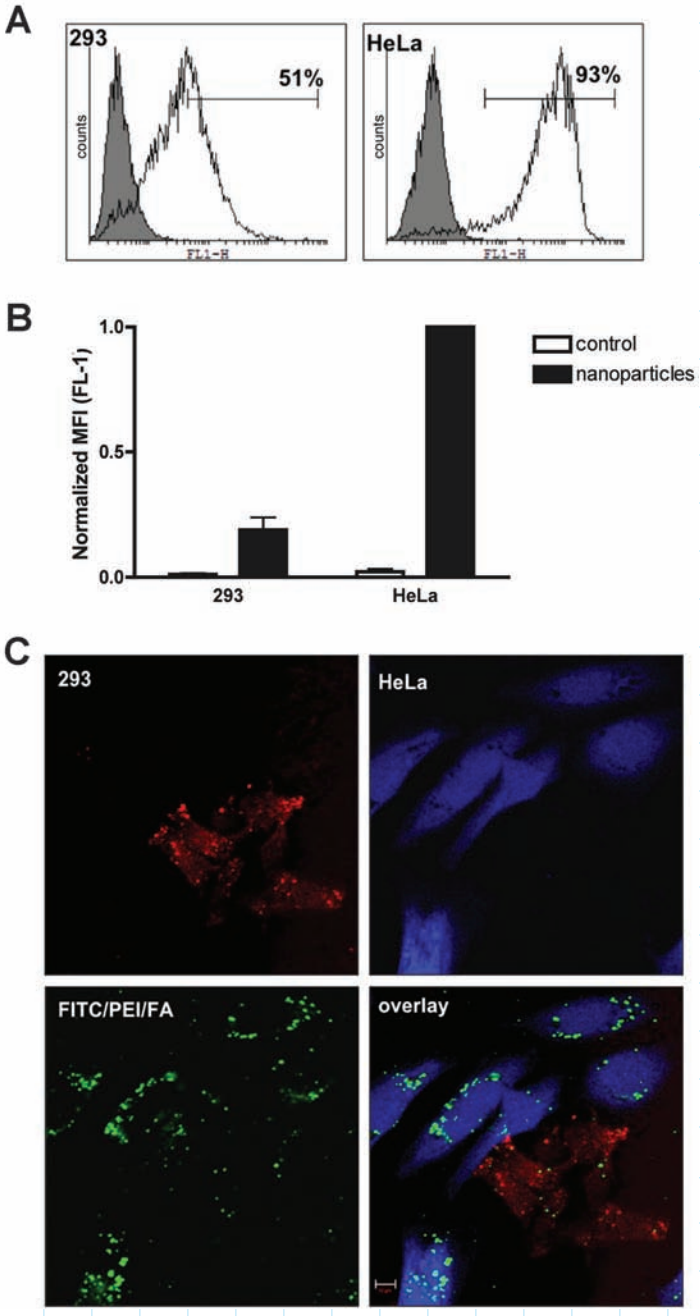

Figure 2. *Cell-specific internalization of silica nanoparticles.* ***A*** *and* ***B****, HeLa cells or 293 cells were incubated with particles for 4 hr, after which the extracellular fluorescence was quenched. Percent FITC-positive cells (****A****) or mean number of particles per cell expressed as mean fluorescence intensity (MFI) of FITC (****B****) were measured.* ***C****, Cell-specific endocytosis of FA-PEI-MSNs in co-cultures of HeLa and HEK 293 cells. The cells were labelled with blue CMAC (HeLa) or CellTracker Red (HEK 293) and plated together overnight prior to incubation with the particles. The endocytosed particles with FITC-label (green) inside blue- or red-labelled cells were detected by confocal microscopy. Scale bar 10 µm. From Rosenholm et al. (4).*

The drug delivery ability of the nanoparticulate system was demonstrated by loading the particles with two hydrophobic fluorophores, DiI (red) and DiO (green), as drug models of poorly water-soluble compounds, a property shared also by many anticancer agents. Thus, the intracellular release process could easily be followed by confocal fluorescence microscopy (Figure 3), as well as quantified using FACS (Figure 4B). Both molecules could be delivered into HeLa cells without any leakage prior to endocytotic uptake (5). Furthermore, both fluorescent dyes could be co-delivered (Figure 4A), suggesting the ability to administer multiple therapeutic agents simultaneously. As a final control, DiO-loaded nanoparticles were incubated with both HeLa and HEK 293 cells. Minimal fluorescence was observed in HEK 293 cells, while intracellular DiO was easily detected within HeLa cells by fluorescence microscopy (Figure 4C) and FACS,

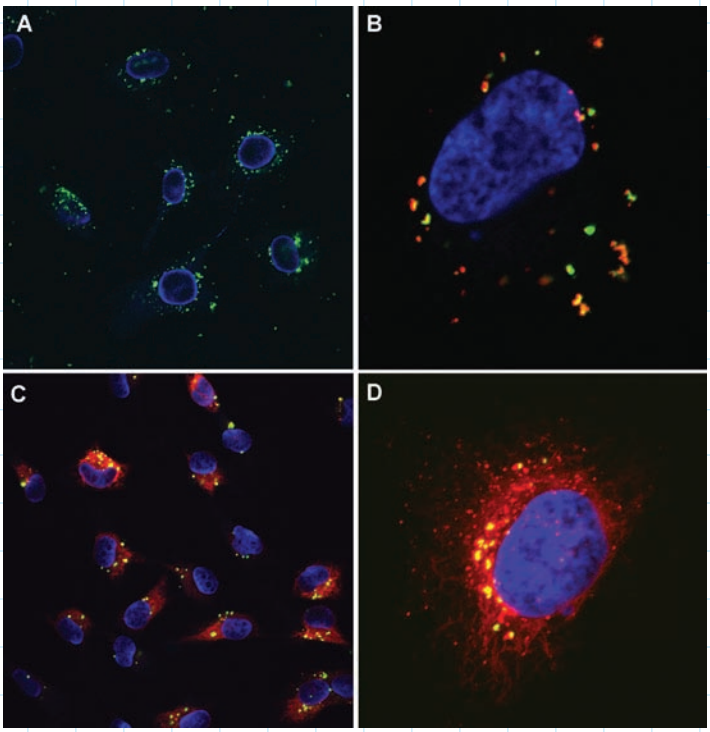

Figure 3. *Nanoparticle-mediated delivery of hydrophobic dye DiI (red) into HeLa cells.* ***A****, FITC-labelled particles (green) without cargo;* ***B****, DiI-loaded particles compartmentalized inside the cell, prior to payload release;* ***C****, DiI released into the cytoplasm while particles remain compartmentalized; and* ***D****, close-up of a cell (3D image) after 24 hr of incubation.*

suggesting specificity of the delivery between healthy and cancerous cell populations.

At present, system efficiency has been evaluated with cytostatic agents *in vitro* with very promising results, and current research focuses on evaluating targetability, pharmacokinetics, toxicity, and particle degradation in animal tumour models *in vivo*.

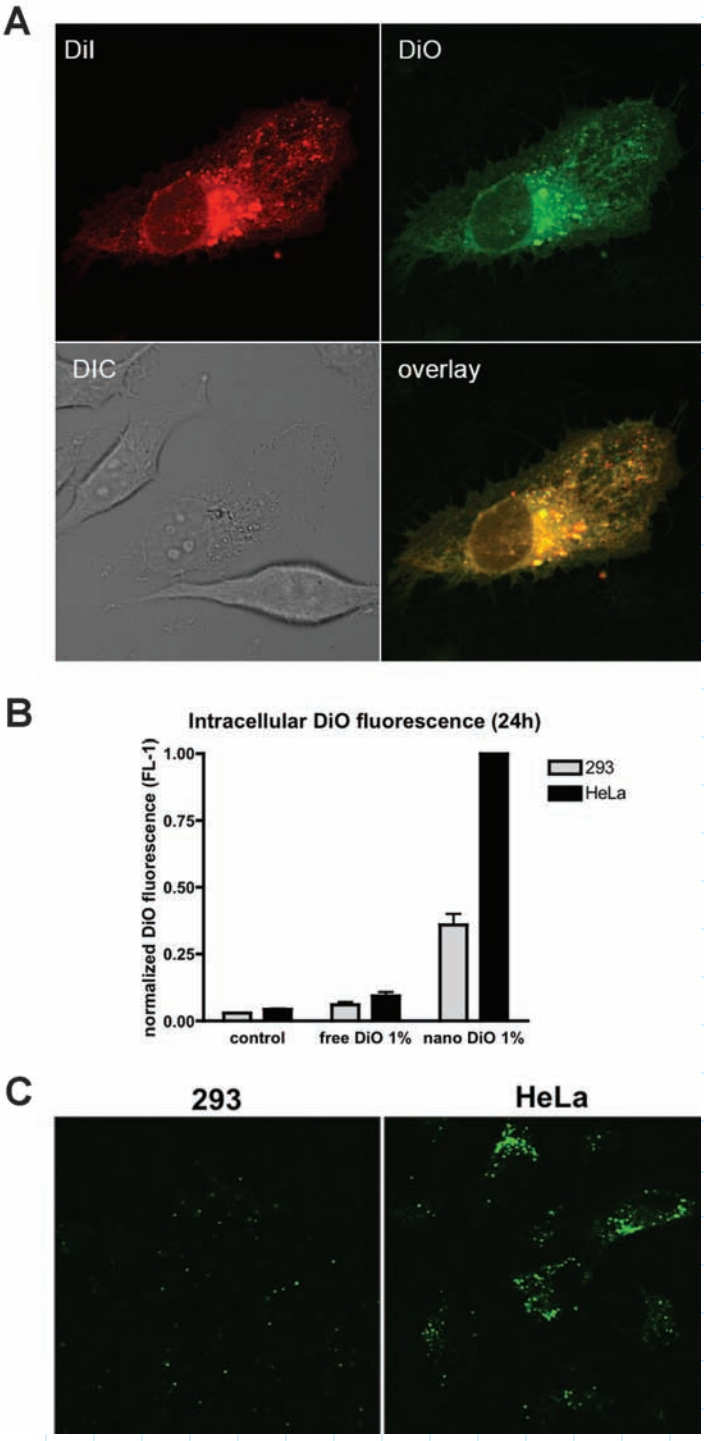

Figure 4. *Co-delivery of two compounds and targeted nanoparticle-mediated delivery of DiO.* ***A,*** *HeLa cells incubated with DiI+DiO-loaded (total 1 wt%) non-fluorescent nanoparticles.* ***B*** *and* ***C,*** *HeLa cells and HEK 293 cells incubated for 24 hr with free DiO or non-fluorescent FA-PEI-MSNs loaded with the corresponding amount (1 wt%) of DiO. Extracellular fluorescence was quenched, and the intracellular DiO fluorescence was measured. From Rosenholm et al. (5).*

Conclusions

To conclude, we have successfully demonstrated targeted nanoparticle-mediated intracellular delivery of two hydrophobic fluorophores that were not internalized in free form. The nanoparticles were taken up by receptor-mediated endocytosis, followed by accumulation in the endosomal compartment. In addition to the selectivity of the developed nanoparticles for the cancer cells, the incorporated cargo was able to escape from the endosomes into the cytoplasm, which is essential for successful intracellular delivery. In view of the hydrophobicity of many anticancer drugs, the presented carrier system constitutes a promising candidate for targeted drug delivery for cancer treatment.

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Irinotecan Sustained Release Nanoparticles: An Innovative Nanoparticle Formulation for Oral Administration of Cancer Treatments

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Summary
Oral chemotherapy is a great challenge due to poor pharmacokinetics and distribution. We have designed an oral formulation using a sustained release nanoparticles (SRN) technology. *In vivo* studies in a mice bearing tumor model show a better tolerance of the irinotecan (IRN)-SRN formulation compared with an oral solution, along with similar efficacy results.

Introduction
Oral chemotherapy is a great challenge, and important advantages can be expected from this route of administration, including better patient compliance and acceptance and also significant cost savings, both in terms of treatment costs and lost wages incurred by patients and family during physician visits. Using sustained release formulation technologies, oral chemotherapy can maintain an optimum concentration of drug in circulation, which can provide prolonged exposure to cancerous cells, which can, in turn, improve efficacy, prevent or limit resistance, and decrease adverse effects.

BioAlliance Pharma has developed a strong expertise in drug delivery systems and particularly in nanoparticle technology. Our objective is to use this knowledge to develop new formulations for the oral route using SRN technology. This technology allows us to encapsulate the active ingredient in a polymeric network of polyisohexylcyanoacrylate (PIHCA) nanoparticles. Our IRN-SRN is the first formulation designed for cancer treatment by the oral route.

IRN is a well-known DNA enzyme, topoisomerase I, which is currently administrated by the intravenous (iv) route mainly for metastatic colorectal cancer treatment. IRN is a prodrug that is converted into its active metabolite, SN-38, by carboxylesterase in the liver, intestinal tract, and some tumors. To date, the development of oral IRN formulations appears to have been limited by the lack of tolerance induced by this route (severe diarrhea), due to rapid absorption and high conversion in SN38. Therefore, we have designed an oral nanoparticle formulation of IRN that could lead to a better controlled conversion of IRN into SN-38 in the gastrointestinal tract and could reduce the adverse effects. IRN-SRN is formulated as an oral suspension of IRN-loaded polymeric nanoparticles with a size between 200 and 400 nm.

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Experimental Methods
The nanoparticles were obtained by polymerization of isohexylcyanoacrylate (Monorex®, BioAlliance Pharma) in a medium containing the raw materials (surfactant and cyclodextrin) and the active ingredient, IRN hydrochloride, under magnetic stirring. IRN encapsulation rates and nanoparticle sizes were determined. A range of IRN concentrations was studied, from 1 to 2 mg/mL, to determine the optimal IRN content.

Oral IRN-SRN was assessed for maximum tolerated dose (MTD) in a nude mice bearing human HT29 tumor model. For this purpose mice bearing tumors were treated with 50, 100, 200, and 300 mg/kg of IRN-SRN p.o. once a day for five consecutive days. The efficacy study was performed in mice bearing the same HT29 tumor model and treated with IRN-SRN at 30, 100, and 300 mg/kg and free IRN at 100 mg/kg p.o. once a day for five consecutive days and free IRN at 20 mg/kg iv once a week for 2 weeks. Mice body weight and tumor growth inhibition were monitored.

Results and Discussion
Optimization of the IRN-SRN Formulation. After polymerization, the average size measured was 310 nm (±59 nm) with a polydispersity index (PI) of 0.002, which means a very narrow size distribution. Within the range of IRN concentration tested, between 1 and 2 mg/mL, the particle sizes ranging from 300 to 400 nm were not affected by the concentration of IRN. The highest encapsulation rates were obtained for 1.5 mg/mL of

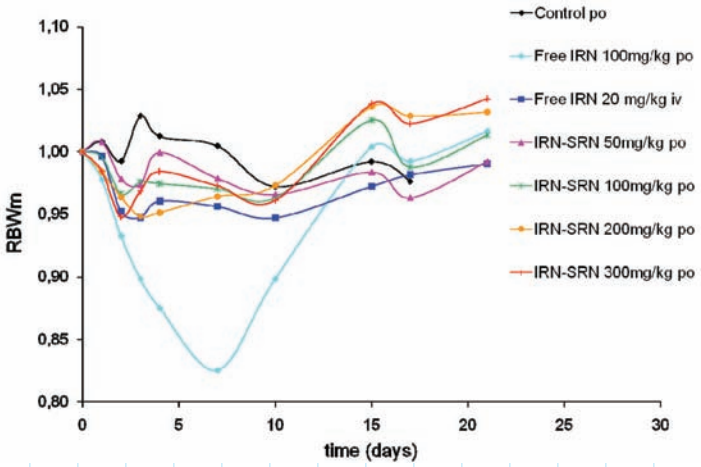

Figure 1. *Mean relative body weights of nude mice bearing HT29 tumors (50, 100, 200, and 300 mg/kg of IRN-SRN and 100 mg/kg of IRN p.o. once a day for five consecutive days and 20 mg/kg of IRN iv once a week for 2 weeks).*

IRN, but a decrease appeared for IRN concentrations of 1.75 and 2 mg/mL.

***In Vivo* Experiments.** Figure 1 presents the MTD results obtained for mice bearing human HT29 tumors. All IRN-SRN dosages given orally were well tolerated without any loss of weight and no mortality. The MTD of oral IRN-SRN was not achieved even at the highest feasible dose of 300 mg/kg. The MTD for free IRN p.o. was 100 mg/kg with an important weight loss (>15%).

As the IRN-SRN oral formulation was well tolerated, we evaluated the efficacy of the formulation on tumor growth (Figure 2). The IRN-SRN taken p.o. showed significant dose-dependent tumor growth inhibition, 84 and 75% at 300 and 100 mg/kg, respectively (day 11). These results were similar to the tumor growth inhibition (88%) observed with free IRN p.o.

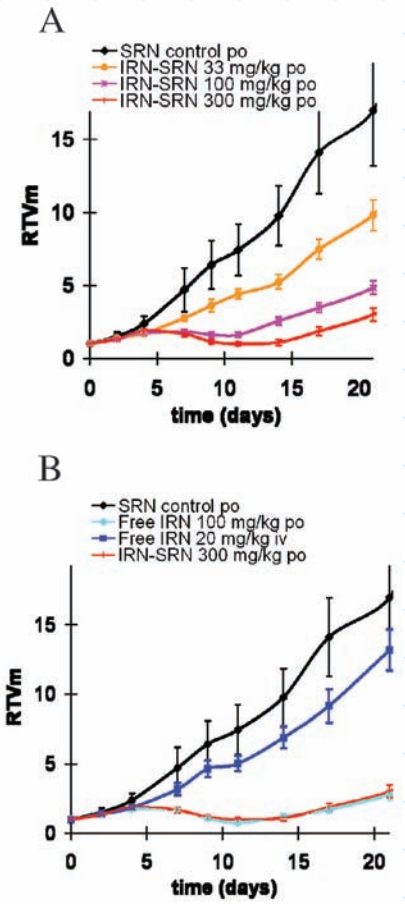

Figure 2. *Tumor growth inhibition of nude mice bearing HT29 tumors.* ***A,*** *Dose effect of 33, 100 and 300 mg/kg of IRN-SRN p.o. once a day for five consecutive days.* ***B,*** *Comparison between 300 mg/kg of IRN-SRN and 100 mg/kg of IRN p.o. once a day for five consecutive days and 20 mg/kg of IRN iv once a week for 2 weeks.*

Conclusions

A stable and reproducible formulation of irinotecan-loaded slow-release nanoparticles was prepared. This new oral formulation of IRN-SRN demonstrates a better tolerance compared with free IRN and a similar antitumor efficacy and allows higher oral dosing of IRN without any sign of adverse effect. Drug release kinetic in *in vitro* and pharmacokinetic studies are ongoing to determine the expected slow release and exposure profile of this new oral formulation of IRN. The proof of concept with this first oral formulation allows us to plan for further anticancer drug development by oral route.

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A Novel Approach to Follow the Intracellular Fate of Pharmaceutical Nanocarriers

Tatyana Chernenko,[1,2] Rupa Sawant,[3] Christian Matthäus,[1] Luis Quintero,[4] Vladimir Torchilin,[3] and Max Diem[1]

Introduction

Diverse nanocarrier systems have been developed over the years that enhance the therapeutic effect of encapsulated drugs. These systems range from inorganic materials, such as iron oxide and silica nanoparticles, to biodegradable and biocompatible polymeric particles (1,2). Polymeric micelles are self-assembly nanoparticles that effectively solubilize and transport poorly soluble chemotherapeutics. Their small size also allows for extravasation into the tumor interstitium, thus enhancing drug bioavailability (3). Various surface modifications of such nanoparticles facilitate even greater accumulation in the targeted tissue. These modifications involve, in particular, cell-penetrating peptides, which significantly increase intracellular penetration of pharmaceutical nanocarriers. One such peptide is the TAT peptide (TATp), an 11-mer fragment of transactivating transcriptional activator (TAT) from HIV-1 (3).

With the increasing diversity and potential of drug delivery systems, it is essential to monitor the impact of nanocarriers on sub-cellular metabolic processes and organelles, since the delivery of a drug usually involves nanoparticulate internalization. Hence, the translocation and degradation patterns of a specific nanodelivery system must be ascertained. We have employed vibrational spectroscopy coupled with optical microscopy to provide a non-invasive method for cellular and sub-cellular imaging. This method relies on biochemical mapping of all the inherent cellular components, as well as the introduced system of interest, thus circumventing the use of extraneous labels or dyes that may potentially alter the system under investigation (4,5)

The technique is based on the identification of molecular vibrations that are characteristic of different functional groups contained within molecules. For cells, these vibrational fingerprints arise from functional groups contained within proteins, nucleic acids, phospholipids, and carbohydrates, the basic building blocks of mammalian cells. Vibrational spectra may be obtained by illuminating the specimen either with broadband infrared radiation and monitoring its absorption or with narrowband visible light from a laser and detecting scattered photons. The latter approach detects inelastically scattered photons and is known as the Raman effect. We utilize this technique to identify the presence of nanocarrier systems introduced to a cell and map their concentration and distribution. Here, we describe the results obtained with polymeric micelles made of polyethylene glycol-phosphatidylethanolamine (PEG-PE) conjugate.

Results and Discussion

In order to distinguish sub-cellular organelles from the nano-delivery system introduced, we exploit isotopic labeling by deuterium. The stretching vibrations of CD_2 groups exhibit strong and isolated bands in the region of the spectrum (2,050–2,275 cm^{-1}) outside of the biochemical fingerprint range (800–1,800 cm^{-1} and 2,800–3,100 cm^{-1}). Deuteration does not alter the chemical properties of a molecule appreciably and is non-invasive to the cell if the deuterium atoms are covalently bonded to the carbons of the aliphatic side chains of the phosphatidylethanolamine (d_{70}-DSPE). A spectrum of air-dried deuterated PEG-PE micelle aggregates is shown in Figure 1, where the highest peak intensity came from the C-D stretching vibrations of the aliphatic side chains at 2,103 and 2,175 cm^{-1}.

Images were acquired from cells fixed after incubation with deuterated micelles. Raman spectral images were collected from cells in phosphate-buffered saline aqueous media by raster scanning the cells through the focal point of the laser (488-nm excitation wavelength) and collection of backscattered Raman spectra from each pixel. The instrumentation and additional data acquisition parameters have been previously reported (5). All spectral data sets, comprising between 10,000 and 22,500 individual pixel spectra, were analyzed using a multivariate color decomposition algorithm known as vertex component analysis (VCA) (6). It decomposes all spectra in a dataset in terms of the most dissimilar spectra, known as endmembers. The abundance of each endmember in every spectrum can be represented by a

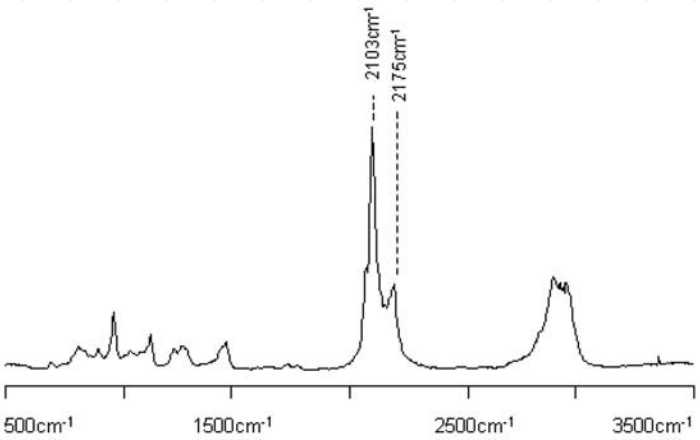

Figure 1. *Raman spectrum of deuterated micelles dried on CaF_2 windows.*

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monochrome abundance plot. An overlay of such abundance plots for different endmembers creates a pseudo color image of a cell. Three of the endmembers include the cell body, which has spectrum pertaining to intracellular proteins, depicted in blue. Green regions delineate the membrane-rich organelles, while the red clusters show the aggregated micelles.

Incubation of cell culture with micelles for 1 hour showed their distinct aggregation at the periphery of the cells (Figure 2, top panel). The corresponding endmember spectra for the three cellular entities—the cell body, membrane-rich organelles, and exogenous nanoparticles—are shown in Figure 3. After incubation for 1 hour, the micelle-containing medium was changed with fresh medium, in order to prevent any further micelle internalization. In this way the degradation patterns could be established. As degradation proceeded, there was an observable migration of the micelles toward the perinuclear region. After 3 hr, the micelle-specific signals were also seen to co-localize with regions high in endoplasmic reticulum (ER) and Golgi apparatus, shown in green in Figure 2 (middle panel). Close examination of both the green and red abundances revealed the formation of tight clusters, with increasing incubation time of the cell culture in fresh medium. This was consistent with the previously observed studies of biodegradable nanoparticles being sorted into Golgi-associated late endosomes (7). These inclusions completely disappeared by 23 hr of incubation in fresh medium (Figure 2, bottom panel), as indicated by only two spectral members, one for the nucleus and cell body (blue) and another for ER- and Golgi-rich regions (green). This shows complete digestion of the introduced nanoparticles, which was observed via a decrease in micelle-specific signal with increasing incubation time, with the amount of internalized micelles decreasing exponentially during degradation. This metabolic activity was apparent from the changes in the peak heights and ratios in the C-H stretching intensities, portraying the engulfment and sorting of the phospholipid-rich vesicles.

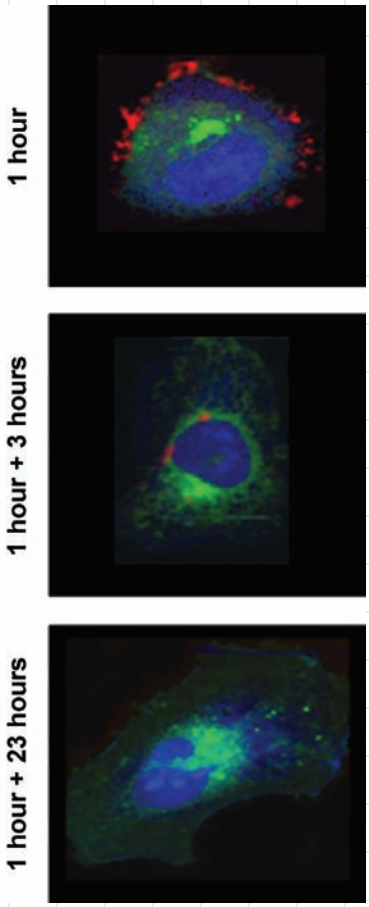

Figure 2. *Time-course degradation experiment with TATp-modified micelles. Top row: 1 hr of incubation with D-PE TATp-modified micelles. Middle row: 1 hr of incubation with micelles followed by 3 hr of incubation with fresh medium. Bottom row: 1 hr of incubation with micelles, followed by 23 hr of incubation in fresh medium. The VCA algorithm produced three distinct spectral members that correspond to the cell body and nucleus (blue), membrane-rich organelles (green), and internalized micelles (red).*

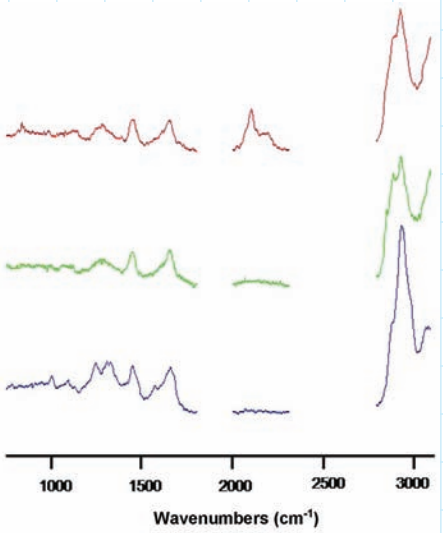

Figure 3. *Typical endmember spectra, generated by VCA, which corresponds to cellular images in Figure 2. The blue spectrum corresponds to the nucleus and cell body, the green spectrum corresponds to the membrane-rich organelles, such as ER, Golgi, and mitochondria, and the red spectrum shows deuterated micelles.*

These results demonstrate that Raman microscopy can be used for monitoring sub-cellular trafficking of nanoparticulate drug delivery systems. Degradation patterns of a particular nanovehicle may be established, delineating its effects on diverse cellular processes. Raman microscopy, thus, has become a valuable, non-invasive tool to study the kinetics of diverse nanocarrier systems, with potential for *in vivo* applications.

Acknowledgments

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CRS Election Results for 2010


Kazunori Kataoka


Ijeoma Uchegbu


Michael J. Rathbone


Aron B. Anderson


Dennis E. Discher


Ken Howard


Tamara Minko


Chris Porter

The following candidates have been elected to serve on the CRS Board of Directors. They will begin serving their terms at the conclusion of the 2010 CRS Annual Meeting & Exposition, July 10–14, in Portland, OR. Thanks to all of the members who participated in this year's election process.

Kazunori Kataoka has been elected to the office of vice president. Kataoka is a professor of biomaterials at the Graduate School of Engineering, University of Tokyo. He has been appointed to a joint position, since 2004, in the Graduate School of Medicine, University of Tokyo, as a professor and chair of the Division of Clinical Biotechnology at the Center for Disease Biology and Integrative Medicine. He received his Ph.D. degree (1979) in polymer chemistry at the University of Tokyo. He was a visiting professor at the University of Paris XIII (1992 and 1996), and Ludwig-Maximilian University (LMU), Munich (2008). He has received several awards, including the Award of the Japanese Society for Biomaterials (1993), CRS Outstanding Paper Award (1995), Award of the Society of Polymer Science, Japan (2000), Clemson Award in Basic Research, Society for Biomaterials, USA (2005), and CRS Founder's Award (2008) for his outstanding contribution on the development of polymeric micelles as nanocarriers in drug and gene delivery. He has more than 400 publications and is on the editorial boards of 12 international journals. He has served as an associate editor (2003–2006) and editor (2006–2008) of the *Journal of Controlled Release*.

Ijeoma Uchegbu has been reelected to the office of scientific secretary. Uchegbu obtained her Ph.D. degree in drug delivery from the School of Pharmacy, University of London, in 1994 and, after a period of post-doctoral study and a lectureship, was appointed to a personal chair in drug delivery at the University of Strathclyde in 2002. In 2006 she was invited back to the London School of Pharmacy to take up a chair in pharmaceutical nanoscience, the post she currently occupies. Uchegbu recently served as Chair of the Academy of Pharmaceutical Sciences of Great Britain (2005–2007) and was appointed British Pharmaceutical Conference Science Chair in 2009. Uchegbu's group has been awarded a number of prizes, including the Woman of Outstanding Achievement Award in Science Engineering and Technology awarded by the U.K. Department for Business Innovation and Skills in 2007.

Michael J. Rathbone has been elected to the member-at-large position. Rathbone is associate professor of pharmaceutics, School of Pharmacy, Griffith University, Australia. Previously he was the director of research at InterAg, where he spearheaded the company's modified release drug delivery research and directed InterAg's national and global collaborative research activities. Rathbone obtained his undergraduate degree in pharmacy at Leicester Polytechnic, U.K., and his Ph.D. degree in pharmaceutics from the University of Aston, Birmingham, U.K. Rathbone's research interests are in the area of systemic drug delivery via mucosal sites, the development of modified release drug delivery systems, and veterinary drug delivery. Rathbone has published more than 100 scientific and professional papers, review articles, book chapters, and scientific abstracts and is the co-inventor of 11 patents/patents pending. He has co-edited 8 special theme issues of the journal *Advanced Drug Delivery Reviews* and 4 books on modified release drug delivery. Rathbone has been a member of the Controlled Release Society for 15 years and, in that time, has served on the Board of Governors, Board of Scientific Advisors, and as an *ad hoc* member of the Board of Directors. He has held the positions of chair of the CRS Committee Focusing on Veterinary Products and of the Education Committee. He is currently the series editor of CRS books and serves on both the Young Scientist and Membership & Development Committees.

The following candidates have been elected to serve on the CRS Board of Scientific Advisors. They too will begin serving their terms at the conclusion of the 2010 CRS Annual Meeting & Exposition, July 10–14, in Portland, OR.

Aron B. Anderson is currently chief scientific officer at SurModics, a company focused on drug delivery, medical device, and *in vitro* diagnostic technologies. Anderson has worked at SurModics since 1991, where he has contributed to the development of technology for blood-compatible coatings and a variety of drug delivery platforms. He has helped develop drug-eluting stent coatings, drug delivery implants for ophthalmic disease, and biodegradable polymer drug delivery systems. Anderson is a named inventor on 15 U.S. patents and is an author of more than 30 presentations and publications in the areas of controlled release systems and biocompatible materials. He serves on the Board of Directors of the University Enterprise Laboratories in St. Paul, MN, a partnership between the University of Minnesota, the city of St. Paul, and local industry that serves as an incubator for start-up life science technology companies. Anderson received a B.S. degree in chemical engineering from the University of Minnesota in 1985. He received an M.S. degree in 1987, and a Ph.D. degree in 1991, both in chemical engineering, from Stanford University. He has been a member of CRS since 1999.

Dennis E. Discher is a professor at the University of Pennsylvania in chemical and biomolecular engineering and in the graduate groups of cell and molecular biology and physics. He received a Ph.D. degree from the University of California, Berkeley, in 1993, and was a U.S. National Science Foundation International Fellow at the University of British Columbia. His group at the University of Pennsylvania pioneered the development of polymer vesicles and elongated worm-like micelles for drug delivery, with seminal papers in *Science*, *Nature Nanotechnology*, *Macromolecules*, and the *Journal of Controlled Release*. Discher has coauthored nearly 150 publications, with more than 7,000 citations, in topics ranging from polymer matrix effects on stem cells to protein folding, with papers published in *Cell*, *Science*, the *Journal of Cell Biology*, and *Nature Physics*. His honors and service include a Presidential Early Career Award for Scientists and Engineers from the U.S. National Science Foundation, the Friedrich Wilhelm Bessel Award from the Humboldt Foundation of Germany, a Best Paper Award (2004) in the *Journal of Controlled Release*, and membership on the editorial board for *Science*.

Ken Howard received a Ph.D. degree in pharmaceutical science from the University of Nottingham, U.K., in 1995 in the field of mucosal vaccination. He was a research fellow at the Department of Pharmacy, University of Geneva, Switzerland (1995–1997), CRC Institute for Cancer Studies, University of Birmingham, U.K. (1998–2001), and School of Pharmacy, University of London, U.K. (2001–2004), before joining the Aarhus University interdisciplinary Nanoscience Center (iNANO) in Denmark, where he is now associate professor. Howard is co-founder of the iNANO drug delivery initiative based within a highly interdisciplinary setting, with a focus on nanomedicine and nanoparticle delivery systems and tissue engineering. He is co-founder and CEO of an Aarhus University spin-out "Nanoference," providing delivery solutions for RNA interference-based therapeutics. Howard is the course organizer of both a nanomedicine and a Ph.D. drug delivery course at Aarhus. His key research areas include drug delivery, nanomedicine, gene therapy, RNAi therapeutics, inflammatory and cancer disease treatments, and vaccines. He has published approximately 30 papers and is the co-inventor of 8 patents.

Tamara Minko is a professor and chair of the Department of Pharmaceutics at Rutgers, The State University of New Jersey. She is also a member of the Cancer Institute of New Jersey, New Jersey Center for Biomaterials, Environmental and Occupational Health Sciences Institute. Her current research interests include drug delivery; biopharmaceutics; nanotechnology; molecular targeting; antisense oligonucleotides, siRNA, and peptide delivery; mechanisms of multidrug resistance; intracellular fate and molecular mechanisms of action of anticancer drugs; bioimaging; macromolecular therapeutics; preclinical evaluation of anticancer drugs; tumor hypoxia; and modulation of cell death mechanisms during hypoxia. Minko is author and co-author of more than 360 publications (peer-reviewed papers, books, and textbook chapters and conference proceedings/abstracts). Many of her papers are well cited and published in prestigious journals with high-impact factors, including *PNAS*, *Nature Nanotechnology*, *Cancer Research*, *Advanced Drug Delivery Reviews*, and the *Journal of Controlled Release*. Minko is an AAPS Fellow, recipient of numerous awards, editor of *Pharmaceutical Research*, member of the editorial boards of several scientific journals, and a member of the Study Sections at NIH, DOD, the American Heart Association, and other national and international review panels.

Chris Porter is professor of pharmaceutics at the Monash Institute of Pharmaceutical Sciences and associate dean (research) of the Faculty of Pharmacy and Pharmaceutical Sciences at Monash University, Melbourne. He completed his undergraduate pharmacy degree and graduate studies in drug delivery at the University of Nottingham in the United Kingdom before moving to Australia and Monash in 1992. Subsequently, Porter's research program has focused on understanding and quantifying drug absorption, distribution, and elimination profiles and on developing the models and techniques to probe these interactions. A major interest has been the issues and problems surrounding the absorption of poorly water-soluble, highly lipophilic drugs and, in particular, the use of lipid-based delivery systems to enhance oral bioavailability and stimulate lymphatic transport. More recently, his interests have also expanded into the mechanisms of cellular transport of lipophilic drugs and the potential utility of dendrimers as drug delivery systems. Porter has published more than 100 peer-reviewed papers in these areas. Porter is a Fellow of the Royal Australian Chemical Institute, is a member of CRS, AAPS, and ASPET, and sits on the editorial boards of *Pharmaceutical Research*, the *Journal of Pharmaceutical Sciences*, and the *Journal of Pharmacy and Pharmacology*. ■

Vet Activities at the 37th CRS Annual Meeting & Exposition in Portland, OR, U.S.A.

Michael Rathbone[1] and Jim Riviere[2]

Sunday, July 11, will see two top scientists, one from the human area and one from the animal arena, debate interspecies differences in IVIVC in a Pearls of Wisdom session entitled "Of Mice and Men: Can Parenteral Product Specifications Be Extrapolated Across Species?" Moderator Ramesh Panchagnula (Pfizer Animal Health, India) will have his hands full separating Marilyn Martinez (CVM FDA, U.S.A.) and Diane Burgess (University of Connecticut, U.S.A.) as they do battle to convince the audience one way or the other. Who will present the stronger argument? It's difficult to know given the equal balance of arguments for this topic.

Mike Rathbone (Griffith University, Australia) and Jim Riviere (North Carolina State University, U.S.A.) will co-chair the vet track scientific session that will be held on the afternoon of Monday, July 12. The session has been designed to be of general interest to both human and animal drug product developers, as it covers the prediction and application of IVIVC for veterinary species, including presentations on the topics of dogs, GastroPlus absorption, pharmacokinetic, pharmacodynamic simulation software, and transdermal penetration models, all of which are used by human scientists in their research and development studies. Although the same *in vitro* constraints and challenges face both human and veterinary scientists when developing *in vitro–in vivo* correlations, substantial *in vivo* challenges are faced by veterinary formulation scientists in their IVIVC efforts due to the different animals they deal with, which differ vastly in anatomical, physiological, and pharmacological handling of drugs (even within a species). Four invited speakers will address various challenges in this area, with the goal of identifying current issues, defining existing challenges, and presenting recent solutions in an attempt to shed light on solutions to the complex array of issues associated with this topic. Prof. Mark Papich (North Carolina State University, U.S.A.) will talk on "The Potential Application of IVIVC for Drugs in Veterinary Species—Where It Works and Where It Doesn't." Dr. Marilyn Martinez (CVM, FDA, U.S.A.) will follow with a presentation on "Establishing *In Vivo/In Vitro* Relationships for Oral Dosage Forms in Dogs—Issues, Challenges and Examples." The "Use of GastroPlus Models in Veterinary Research and Development" will be discussed by Assoc. Prof. Steven Sutton (College of Pharmacy, University of New England, U.S.A.), and the session will close with an informative presentation by Prof. Jim Riviere (on the "Use of *In Vitro* Dermal Penetration Models to Estimate *In Vivo* Absorption of Topical Dosage Forms." This really is a not-to-be-missed scientific session.

Vet activities at a CRS Annual Meeting & Exposition are not just restricted to scientific sessions. On Monday evening the Vet Get Together will be held, during which speaker Dr. Keith Marotti (Pfizer Animal Health, U.S.A.) will provide an overview of his experiences on the challenges, opportunities, and technological innovations in drug and vaccine delivery in animal health. The Vet Get Together provides a conducive environment to talk shop and presents the opportunity to increase your network of animal-health colleagues from industry, academia, and regulatory areas.

Jim and I look forward to catching up with old friends, mixing with colleagues, and making new contacts in Portland in July. See you there! ■

We would also like to extend an invitation for you to attend the Vet Committee Meeting in Portland. This is an open meeting, and anyone can attend—we would love to have your input in the Veterinary Group of CRS. Topics for discussion include a special issue of *JCR* on veterinary controlled release, the formation of an animal health focus group, and webinars.

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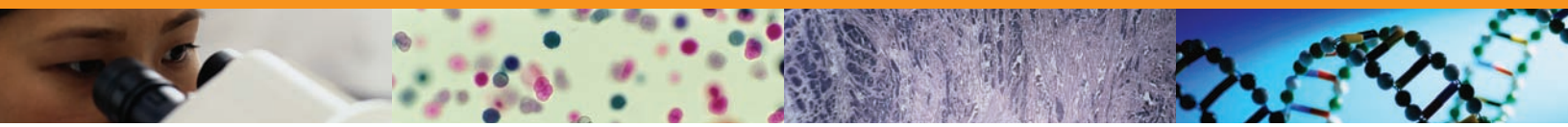

New Trends in Food Science for Encapsulation of Health Ingredients

Igor Bodnár
NIZO Food Research, Ede, The Netherlands

Health ingredients are often encapsulated when used in food products. In this area of protect and deliver ingredients there are clearly three trends visible, which are further described in this article: self-assembly, mild processing, and intestinal delivery.

One of the main trends in the food industry is to provide consumers with healthier foods that remain pleasant and convenient. Pleasure is the first restriction, since consumers will not accept an unpleasant food for repetitive purchase (in contrast to less-pleasant medications). Convenience is the second restriction: an easy dosage and prolonged shelf life are key to consumers. Fresh products, such as fruit and fish, are often pleasant and healthy, but their restricted shelf life of a few days leads us to fill the garbage bin every so often. Therefore, more and more extra ingredients with claimed or associated health benefits are being included in processed foods.

Health ingredients often are sensitive compounds that need extra protection in order to withstand the processing of the food, as well as to remain active over a significant shelf life. These ingredients are not always very tasty, so they need to be kept away from the taste buds during consumption. Furthermore, health ingredients often only fulfill their health function when absorbed by the intestinal lumen, which requires protection up to the point of gastric transit.

All of the above indicate good opportunities for encapsulation technologies to provide the right protection. Currently the encapsulation technologies most often used within foods are spray drying, spray chilling, extrusion, and fluid bed technology. For many applications these technologies fulfill the requirements, albeit every application/ingredient combination requires its own encapsulation solution, leaving ample space open for further development.

There are, however, various important aspects in which the current technologies have their shortcomings. First, there is the point of particle size, where current technologies usually render particles in a size range of 10 µm to a few hundred micrometers. This size range is clearly inappropriate for use in liquids or beverages, due to sedimentation or creaming of the encapsulates. One possible way to overcome this shortcoming is to make use of self-assembly. Second, there is the point of heat load during preparation of the capsules. Most technologies make use of aqueous solutions, where the water is usually evaporated at elevated temperatures, easily above 70°C, that are detrimental, for example, for heat-sensitive anti-oxidants or probiotics. Therefore, there is a clear shift toward mild processing, in which encapsulates can be formed under only slightly elevated or even ambient temperatures. Finally, there is a clear shift from pure protection of ingredients in a product toward the controlled delivery of health ingredients in specified parts of the intestines. The last point is not a shortcoming per se of the current technology. It is more a shift in interest to what happens to foods from a structural point of view during digestion, especially as it applies to the material science of coatings. In the following sections, these three trends are further described.

Self-assembly

One of the first ideas that comes up when self-assembly is discussed in connection with particle size is "micro-emulsions." Micro-emulsions are spontaneously formed emulsions, where very small droplets, <0.1 µm, are formed based on the characteristics of the interfacial layer (the surfactants) between the oil and water phase. Due to the interaction between energy (in favor of a few, larger droplets) and entropy (in favor of more, smaller droplets), very specific systems can exhibit this behavior. However, up until now there have been no good food-grade systems available. This is also reflected in the fact that even recent reviews in this area talk about "the potential" of micro-emulsions in the food area (1).

Another possibility for using self-assembly in foods is to make use of peptides. The idea is based on Mother Nature's approach to delivery of high levels of calcium to the neonate in milk (2). By selecting the right milk peptides, small (20–200 nm) particles can be spontaneously (re-)formed in which various minerals are embedded in the form of nano-clusters that are stabilized by the peptides. The addition of minerals to food often leads to negative effects, such as taste, instability of proteins, and accelerated oxidation of fats. These self-assembled particles are tasteless, however, and do not interfere with the stability of other ingredients in the product. In Figure 1 examples are given of encapsulates with Ca^{2+}, Fe^{3+}, and Cu^{2+}. In this non-optimized experiment some sedimentation is still visible, but most of the particles remain stable in solution. This is a fine method of fortification of, for example, beverages with minerals, while the minerals do not produce the negative effects of taste and destabilization of other ingredients.

Consumer and Diversified Products continued on page 24

Consumer and Diversified Products continued from page 23

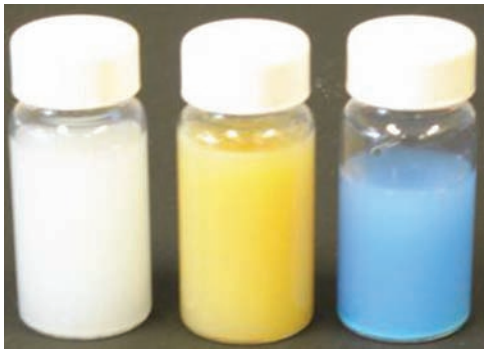

Figure 1. *Self-assembly of peptides with encapsulated (left to right) Ca^{2+}, Fe^{3+}, and Cu^{2+}.*

Mild Processing

One of the detrimental factors in the production of encapsulates is the amount of heat to which the encapsulated ingredient is exposed. With spray drying the inlet temperature is often as high as 180°C, and an outlet temperature easily above 80°C is needed to evaporate the water. Unfortunately, these elevated temperatures can give rise to severe losses of materials such as anti-oxidants or to a significant reduction in viable counts of micro-organisms such as probiotics.

For the encapsulation of probiotics, which are themselves in the order of a micrometer, it is often required that these probiotics be agglomerated into particles of tens of micrometers before coating technologies can be applied. This first step in the coating process is often detrimental for micro-organisms: hydration and dehydration of probiotics, including the heat treatment to which they are exposed during spray drying, for example, kills most of them. New mild-processing technologies based on spouted bed technology have been developed by Glatt so that high levels of survival during the first step of the encapsulation process can be achieved. Dry probiotic powders can be used, avoiding the hydration-dehydration step, and near ambient temperatures are used, minimizing the heat load. However, whether encapsulation of probiotics will be sufficient to ensure a long shelf life is still being debated (3).

Another novel technology under development that can create encapsulates using mild processing is electrospinning. Here (sub-)micrometer-sized droplets and fibers are formed under the influence of a high electric field under ambient conditions. Although a high electric field could be considered somewhat harsh, it seems that probiotics can survive this treatment (4). In our lab we are currently also working on the encapsulation of anti-oxidants, and in this area mild processing seems to offer interesting benefits.

Intestinal Delivery

Since health ingredients will often only fulfill their health function when absorbed by the intestinal lumen, there is a need to protect these ingredients during consumption and gastric transit. The science community is embarking on massive study of the changes in structures during digestion; during the Food Colloids conference last March in Granada, a large part of the presentations was devoted to this topic. Within food science it is believed that this approach can help us to change the digestion of fats and, thereby, fight obesity (5).

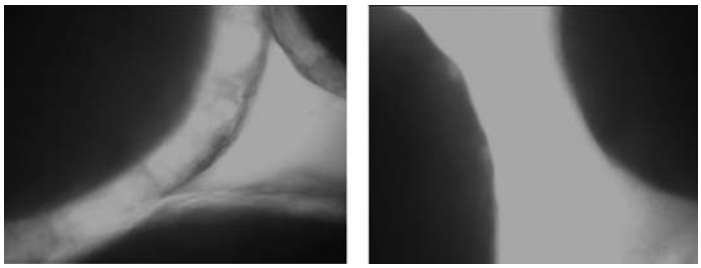

Figure 2. *Enteric coating based on whey proteins under simulated gastric (left) and intestinal (right) conditions.*

Food-grade enteric coatings are being developed that can protect ingredients during gastric residence and release them in the intestines (6). This broadens the field of possible useful health ingredients that would otherwise not withstand the harsh conditions of the stomach. An example of an enteric coating based on whey protein technology is shown in Figure 2, where the coating (approx. 50 µm) is still intact under simulated gastric conditions and has disappeared under simulated intestinal conditions.

Conclusions

To create healthier foods, healthy ingredients often are added to foods during processing. These ingredients, however, are often sensitive to temperature, as well as the food environment and often need to be delivered in the gut in order to have optimal functionality. Current encapsulation technologies offer a wide range of possibilities. However, there are areas where these technologies have shortcomings, such as particle size and heat load during production. Therefore, new trends in encapsulation are evolving within the food industry. Here three of these trends—self-assembly, mild processing, and intestinal delivery—have been discussed to show the benefits for the food industry.

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CRS Young Scientist Committee

Who are CRS young scientists? They are scientists under the age of 40 or new to the delivery of bioactives and other functional materials in the past five years.

The Young Scientist Committee (YSC), chaired by Dody Reimer (Northern Lipids, Canada) and Louise Rosenmayr-Templeton (Tower Pharma Consulting, Austria), strives to provide students, early career scientists, and new colleagues with the following:

- Educational opportunities at the CRS Annual Meeting in the form of workshops, presentations, and discussion sessions on scientific, product development-related, and career development topics.
- Career development initiatives such as one-on-one mentoring of young scientists by seasoned CRS experts as part of our Mentorship Program (now managed by the Young Scientist Mentor:Protégé Subcommittee).
- Networking events that enable younger CRS members to meet and mingle with CRS experts from academia, industry, government, and their peers in both formal and social settings.

Established Initiatives and Events

For many years the YSC has organized full- and half-day complimentary workshops on the Saturday and Sunday prior to the start of the CRS Annual Meeting & Exposition. These workshops are designed to give young scientists an introduction to and overview of a particular area of relevance to the development of pharmaceutical products. Past topics have included micro- and nanoencapsulation, intellectual property, regulatory aspects of pharmaceutical sciences, and the world of veterinary drug delivery. At this year's CRS Annual Meeting & Exposition in Portland, OR, the Saturday workshop will focus on the challenges of formulating poorly soluble drugs, and Sunday's workshop will give young scientists the opportunity to hear first-hand experiences of working in the CRS arena from experts in academia and industry.

The CRS Career Center, offered during CRS Annual Meetings, assists new college graduates and experienced scientists in finding positions in academia, government, and industry. Many of the YSC's events offer a much-needed platform for networking among professionals and an opportunity to mingle with peers and meet established scientists from academia, government, and industry.

Another highly successful initiative is the CRS Young Scientist Mentorship Program (YSMP). It is designed to advance the personal and professional development of students and new professionals through the establishment of one-on-one relationships between them and experienced members of CRS. The YSMP is an outcome of a successful pilot program that involved four mentor-protégé pairs in 2007–2008. Since then, the number of active pairings has grown substantially. The YSMP is now organized and managed by a subcommittee of the YSC, the Young Scientist Mentor:Protégé Subcommittee chaired by Mike Rathbone (Griffith University, Australia) and Ozgen Ozer (Ege University, Turkey).

Current and future activities associated with the YSMP include

- Development of induction workshops to provide protégés with guidance and information that support their year of involvement.
- Provision of mechanisms for online support so protégés are aware of their responsibilities and requirements.
- Design of web-based material providing further mentorship advice.
- Development of exciting and innovative CRS Annual Meeting & Exposition activities specifically for protégés on topics related to mentorship.
- Provision of regular *CRS Newsletter* articles on topics of interest to mentors and protégés.
- Design of a coaching program to be delivered at a future CRS Annual Meeting.

YSMP events in Portland include a workshop on team working and motivation conducted by Buket Aksu (Ken Blanchard Training Companies and Santa Farma Pharmaceuticals, Turkey). The Mentor/Protégé Meet and Greet Session will provide a forum where those interested in the program can sign up and be matched with a suitable mentor and/or protégé.

Newer Initiatives and Events

The Young Scientist Roundtable was held for the first time at the 2009 CRS Annual Meeting & Exposition in Copenhagen. It contrasted the pros and cons of a career in industry to one in academia by allowing young scientists in small groups to "interview" experienced members from big pharma, specialty pharma, and universities. This year's roundtable will provide an overview of the challenges faced when trying to deliver compounds by the ocular route. Its goal is to facilitate understanding and stimulate discussion on a route of delivery that has seen an explosion of research activity in recent years.

A Young Scientist CRS Sub-group on LinkedIn has been set up and is managed by Sarah Eccleston (Encap Drug Delivery, Scotland). It allows young scientists working in the areas of controlled release and drug/bioactive delivery to share views, initiate discussions, find out about events, and make contact with others in the field—all, in a quick and easy way. If you are not already a member, join today and keep up with the latest information and widen your network.

New social events for young scientists at the 2010 CRS Annual Meeting & Exposition in Portland include the Young Scientist Networking Night at the BridgePort Brewing Company organized by the YSC. In conjunction with the Membership Committee, an After Party has been planned with younger

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members in mind immediately following the Closing Banquet. These events have been organized in response to a gap identified through membership surveys to provide networking opportunities for younger CRS members. Both events are ticketed and require advance registration.

To fulfill the 2010 educational initiative of the YSC, the following workshops and special events have been planned for Portland.

Saturday, July 10

Young Scientist Workshop I: Improving the Solubility of Poorly Soluble Drugs

Chairs: Raid Alany, University of Auckland, New Zealand, and Ron Ortiz, Upsher-Smith Labs, U.S.A.

Technological advances in drug discovery have revolutionized the efficiency of lead identification. However, the promise of new chemical entities (NCEs) as suitable drug treatments can only be fulfilled if they can be successfully formulated and administered *in vivo.* One of the major barriers to the development of many NCEs is their poor solubility in aqueous media. This complimentary Young Scientist workshop will introduce the audience to the science underpinning the technologies for improving drug aqueous solubility. The secrets to successfully formulating a poorly soluble drug using a number of formulation strategies will be discussed. Examples of commercialized delivery technologies will be presented. The program includes

Session 1: Advances in Technology

Introduction to Poorly Soluble Drugs, **Ali Rajabi-Siahboomi,** Colorcon, U.S.A.
Technologies for Delivering Poorly Soluble Compounds, **Dan Smithey,** Agere Pharmaceuticals, U.S.A.
Solid State Modification to Improve Drug Solubility, **Paolo Gatti,** Eurand, Italy
Optimization and Development of a Cyclodextrin-based IV Formulation of a Poorly Water-Soluble Compound, **Sid Patil,** Millenium Pharmaceuticals, U.S.A.
Recent Advances on Nano-suspensions, **Rajeev Gokhale,** Abott Laboratories, U.S.A.
Formulating Poorly Soluble Drugs Using Liposomes, **Tom Redelmeier,** Northern Lipids Inc., Canada
Advances in Formulations of Poorly Soluble Drugs Using Self-microemulsifying Drug Delivery Systems (SMEDDS), **Anja Graf,** University of Auckland, New Zealand
Spray-dried Dispersions (SDDs) for Solubilization: Immediate and Controlled Release Applications, **Brett Caldwell,** Bend Research, U.S.A.
Panel Discussion

Sunday, July 11

Young Scientist Workshop II: True Stories: Career Development

Chairs: Jeffrey James, Molecular Profiles Ltd., U.K., and Jonathon Zhao, Cordis Johnson & Johnson, U.S.A.

The career landscape for the young scientist in controlled release and delivery is varied and challenging. While post-graduate programs continue to provide a platform for professional growth, how does the young scientist make use of such growth for achievement and career development? The True Stories workshop will provide young scientists with the information needed to "fast-track" their career decisions, from both academic and industrial perspectives. The workshop will feature stories from speakers who have "been there and done that," from putting their CV together all the way through to starting their own successful company! Informally, the True Stories workshop offers you, the young scientist, a feel for the types of issues, technical and non-technical, that may occur during career development. This workshop aims to uncover issues experienced by those in the industry, with an emphasis on the important information that you cannot get from a textbook! The program includes

The Choice Between Industry and Academia, **Sarah Eccleston,** Encap Drug Delivery, U.K., and **Teresa Virgallito,** Microtek Laboratories, U.S.A.
University Funding: Is Release Too Controlled?, **Thomas Rades,** University of Otago, New Zealand, and **Vladimir Torchilin,** Northeastern University, U.S.A.
Starting a Controlled-Release Company, **Andy Lewis,** Critical Pharmaceuticals, U.K., and **Ronald J. Versic,** Ronald T. Dodge Company, U.S.A.
Leaving the Lab Coat Behind: Non-technical Roles in Controlled Release, **Claire Madden Smith,** Molecular Profiles, U.K., and **Kurt Fegely,** Colorcon, U.S.A.
Do's and Don'ts: Applying for Positions in the CR Arena, **Vinay Chattre,** Northern Lipids, Canada, and **Andrew Parker,** Molecular Profiles, U.K.

Young Scientist Roundtable: Ophthalmic: CRS 20/10 – 20/20 Vision

Discussion Facilitator: Raid Alany, University of Auckland, New Zealand

Recent advances in the understanding of the genetics and biology of ophthalmic disease hold the potential to deliver an increasing number of novel ocular drugs to the clinic. However, due to the complexities associated with eye anatomy, as well as management of related diseases, virtually all new therapeutics will require tailored and specialized drug delivery systems. The core of this roundtable is an introduction to the current state, challenges, and emerging solutions in ophthalmic drug delivery systems. It will include an overview of ophthalmic anatomy and physiology and bring you up-to-date on the various advances in medical materials, polymers, and devices designed to meet the challenges of treating diseases of the anterior and posterior eye. Young scientists will be provided with the opportunity to

actively participate in the roundtable and ask questions leading to increased insights, vision of new directions, and, possibly, the birth of new ideas. Whether you are new to this exciting area of drug delivery or have many years of experience, join the discussion with experts from industry and academia on the challenges of controlled ocular delivery.

Controlled Ocular Drug Delivery System in Posterior Disease, **Hovik Gukasyan,** Pfizer, U.S.A.
Controlled Drug Delivery in the Anterior Part of the Eye, **Ilva Rupenthal,** University of Auckland, New Zealand

Note: One-half hour prior to the start of the Young Scientist Roundtable, you will be introduced to the CRS Young Scientist Mentorship Program. This brief presentation will provide details on the 2010–2011 program, how to join, what is expected from those who enroll in the program, and how you will benefit from participating. For those interested in becoming a CRS protégé, forms will be available, and details on where to find mentor biographies will be announced.

Bioactive Materials/Young Scientist Pearls of Wisdom

What can you expect during a Pearls of Wisdom session? Just about anything! Controversial topics, outrageous points-of-view, and audience participation emphasize that change and innovation don't necessarily mean consensus! Structured in debate format with a motion and evidence followed by a counter-motion and evidence, the presenters conclude and open the floor to lively audience participation.

An Innovative Scientist Is Better Off in Industry

Moderator: Clive Wilson, University of Strathclyde, Scotland
Pro Presenter: **Mike Rathbone,** Griffith University, Australia
Con Presenter: **David Brayden,** University College Dublin, Ireland

Monday, July 12

Young Scientist Workshop III: Team Working and Motivation

Chairs: Ozgen Ozer, Ege University, Turkey, and Michael Rathbone, Griffith University, Australia
Speaker: **Buket Aksu,** Ken Blanchard Training Companies and Santa Farma Pharmaceuticals, Turkey

This complimentary young scientist three-hour workshop will provide you with information and insight into team working. Team-working skills are essential tools for a young scientist's future successes, whether their goal is to work in industry or academia. Attend this workshop and increase your team-building knowledge while taking advantage of networking opportunities with your peers and Buket Aksu.

***NEW!* Networking Night at BridgePort Brewing Company**

Organized by the Young Scientist Committee

Join your colleagues at the BridgePort Brewing Company for an evening of networking, food, and brewery tours! Founded in 1984, BridgePort is Oregon's oldest craft brewery and is known for its award-winning ales, stouts, IPAs, and porters. Ticket and advance registration are required.

Tuesday, July 13

Get Up! Get Educated!

How to Write Great Papers!

Speakers: **Kinam Park,** *Journal of Controlled Release* editor-in-chief and Purdue University, U.S.A., and **Jaap van Harten,** Executive Publisher, Elsevier, The Netherlands

Would you do yourself a disservice by not giving your good science a great manuscript? Do you want to save time, energy, and potential disappointment? Get up early and attend this morning seminar to learn from the insiders exactly what editors and publishers are looking for in a good paper and how to avoid common pitfalls.

Young Scientist Mentor/Protégé Meet and Greet

Chair: Michael Rathbone, Griffith University, Australia

This is a must-attend session for anyone enrolled in the 2010–2011 CRS Young Scientist Mentorship Program. At this session you will be introduced to your mentor and be given the opportunity to discuss how you are going to interact over the next 12 months, what your career ambitions are, and what you want out of the program. Attend this meeting and gain your first CRS mentorship experience.

***NEW!* Closing Banquet and After Party**

The Closing Banquet and After Party will be held at the Portland Art Museum's historic Kridell Ballroom. The Portland Art Museum is internationally recognized for its permanent collection and ambitious special exhibitions drawn from the museum's holdings and the world's finest public and private collections. After the program and the passing of the gavel from current CRS President Diane Burgess to President-Elect Mark Tracy, the evening kicks into high gear with a new event for 2010—the After Party! Dance the night away with Portland's own Swingline Cubs, a high-energy, eight-piece band that churns out R&B, Motown, and other classics. A late-night snack buffet, one drink ticket, and a bar featuring Oregon microbrews round out this special night! *Ticket and advance registration are required.* ■

Overview of the 2010 CRS Annual Meeting & Exposition Events Organised by the Young Scientist Mentor:Protégé Subcommittee[1]

Michael J. Rathbone[2] and Padma V. Devarajan[3]

This year's CRS Annual Meeting & Exposition will see a host of events organised by the Young Scientist Mentor:Protégé Subcommittee that support the CRS Mentorship Program. These events are described in this article.

On Sunday, July 11, at the Young Scientist workshop, Co-chair of the Young Scientist Mentor:Protégé Subcommittee, Assoc. Prof. Mike Rathbone will give a presentation that divulges all the details about the CRS Mentorship Program. Based on previous years, this presentation promises to be both educational and amusing as Dr. Rathbone's personal advice on career development is progressively revealed throughout the presentation.

On Monday, July 12, Buket Aksu will present a workshop entitled "Team Working and Motivation." The workshop has an early start at 7:00 a.m., but don't let that put you off, as this free three-hour educational workshop will provide you with information on, and insight into, aspects of team working and motivation that you will never have considered before. Buket Aksu hails from Turkey and is a senior specialist in the field of self-establishment skills like "multidirectional personal leadership," "multidirectional leadership," and "emotional leadership." She has organized numerous training courses for many foundations, universities, and non-profit organizations. Her professional affiliations include being a trainer in the Ken Blanchard Training Companies and a director in Santa Farma Pharmaceuticals. Buket is a member of many national and international trade associations and also represents Turkey at EUFEPS (European Federation for Pharmaceutical Sciences) as a member of the Executive Board.

Why is this workshop important to attend? Being a member of a team is a part of our life, because none of us is as smart as all of us. In addition, when you think about it, none of us has the option of not being a member of any team. At the very least we are a member of a team, like a family, a student in a class in a pharmacy school, or an employee in a company in business life.

What can this workshop teach you? Even though a team may have stars as its members, it sometimes does not succeed, so this workshop will teach you:

- The features of a good team.
- How to be a good team member.
- How you can effectively perform in a team environment.
- Strategies to treat each team member as an individual to maximise performance.
- The characteristics of effective teams and how you can recognize them.
- The four stages of team development.
- How to identify the different stages of team development.
- How to establish good communications between team members.
- When and how to show empathy toward team members.
- How to motivate yourself and the team.
- The strategies that will keep teams focused on achieving success.
- What the role of motivation is in our life.

Don't forget to come as a willing participant, as Buket is renowned for her inclusion of active participation in her workshops. She incorporates challenging exercises and fun games that provide the opportunity to reinforce what you are being taught as the workshop goes along. Attend this workshop and expand your education, take advantage of networking opportunities with fellow peers, and simply have a fun three hours with Turkey's authoritative presenter Buket Aksu.

Finally, at 8:00 a.m. on Tuesday, July 13, a two-hour CRS Mentorship Program Meet and Greet Session begins. At that session, 2010–2011 Protégés will have the opportunity to meet their Mentors for the first time. This session will reveal to each Protégé who their Mentor is and provide them the opportunity to meet and greet their Mentor in a unique face-to-face environment. Come prepared with your goals and ambitions, pre-consider your career development challenges, and bring along the list of questions you are longing to know the answers to in order to progress and forward your career.

The Young Scientist Mentor:Protégé Subcommittee wishes you an enjoyable and scientifically rewarding 2010 CRS Annual Meeting & Exposition in which you will expand your global networks, make new friends, and leave more educated than when you first arrived! ■

1 Subcommittee members: Michael Rathbone and Ozgen Ozer (co-chairs), Sudip Das, Teresa Virgaletto, Padma Deveran, and Pithi Pal Singh.

2 Associate Professor in Pharmaceutics, School of Pharmacy, Griffith University, Australia 4222. E-mail: m.rathbone@griffith.edu.au.

3 Professor and Head, Department of Pharmaceutical Sciences and Technology, Institute of Chemical Technology, Mumbai 400019, India. E-mail: pvdevarajan@gmail.com.

CRS 2010 Mentor Protégé Meet

The CRS Mentor Protégé Meet
An opportunity to meet and greet
This year (2010) plans an additional treat!!

A winner in life to be, we all aspire
Charge ourselves, our bellies on fire,
Without success we often retire….

A one man/woman show, it works no more,
Those are stories in folklore
Being a team member, together you soar!!!

Team spirit is what we present
A powerful method to assure your ascent,
To rise on to the "SUCCESS CRESCENT"!

The role leader to lead you through
The experienced and skilled Buket Aksu
Some fun and some learning will be the brew!

Welcome to the Mentor Protégé meet,
A session not just to meet and greet
A learning experience complete!!!!

Erratum

CRS Newsletter
Volume 27, Number 2, 2010

In the Scientifically Speaking article "Tracking the *In Vivo* Fate of High Molar Mass Poly(vinyl alcohol) Using Multispectral Fluorescence *In Vivo* Imaging" by Schädlich et al. (pages 15–16), the image published for Figure 6 is incorrect. The correct image and caption are provided below.

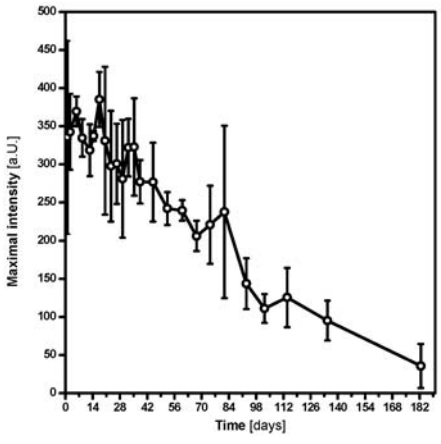

Figure 6. *Maximum intensity values of the PVA-TMR signal for 26 weeks after i.p. administration* (n = *3).*

3rd Annual Meeting of the CRS Australian Chapter Held in Tasmania

Pegah Varamini and Pavla Simerska
University of Queensland, Brisbane, Australia

The 3rd Annual Meeting of the Australian Chapter of the Controlled Release Society (AUS-CRS) was held on Thursday, December 10, 2009, at Wrest Point Convention Centre in Hobart, Tasmania. The meeting was organized in conjunction with the Australasian Pharmaceutical Society Association (APSA) Conference, as in previous years.

The AUS-CRS meeting was opened by Istvan Toth (founder and first president of AUS-CRS, University of Queensland, Australia) and followed by Robin Polt's (University of Arizona, U.S.A.) outstanding plenary lecture. The high-quality programme continued with lectures from national and international invited scientists, including 10 renowned speakers from different universities and institutions throughout Australia (Leslie Yeo, Tracy Brown, Colin Raston, Mary Chebib, Pall Thordarson, David Craik, Wim Meutermans, Spomenka Simovic, Lisa Kaminskas, and Ross McKinnon). Moreover, two esteemed international guests, Michael Weiss (University Halle Wittenberg, Germany) and Raid Alany (University of Auckland, New Zealand) supported the AUS-CRS meeting by attending and reporting on their scientific achievements.

Mary Chebib gives a lecture on "Subtype-Selective GABA Receptor Ligands for Memory and Anxiety." (Photo by Mehfuz Zaman)

All of the speakers were able to meet with the AUS-CRS Committee and get to known each other at the AUS-CRS conference dinner held the night before the meeting at the Custom House Waterfront Hotel. Istvan Toth also discussed other activities during the Annual General Meeting of AUS-CRS, highlighting the poster prize winners from the 2nd Annual Meeting of AUS-CRS, how to join AUS/NZ-CRS workshops, and budgets.

Moreover, according to the elections being organized following the CRS model, some changes were made to the AUS-CRS Committee:

1. Istvan Toth (founder and first president of AUS-CRS) stepped down from the presidency due to other commitments and nominated Ben Boyd to become the new president and Michael Rathbone the vice president of AUS-CRS.
2. Ben Boyd was elected as the new president of AUS-CRS.
3. Michael Rathbone was elected as the new vice president of AUS-CRS.
4. Pavla Simerska was re-elected as the scientific secretary of AUS-CRS.
5. Allan Coombes stepped down from the secretary position due to other commitments.
6. Daniela Traini was elected as the new secretary of AUS-CRS.

Ben Boyd, new AUS-CRS president. (Photo by Mehfuz Zaman)

A large number of students and academics presented their CRS-related results during a poster session. The posters were judged by invited speakers who selected the winners of the 2009 AUS-CRS poster prizes that were provided by our sponsors (contributions toward attendance of the 2010 CRS Annual Meeting & Exposition in Portland, OR, and the 2010 AUS-CRS Annual Meeting or workshop).

Four student prizes were awarded for the best posters in the controlled release field:

1st Prize: The University of Queensland, School of Pharmacy Prize, a $1,000 contribution toward attending the 2010 CRS Annual Meeting in Portland, was awarded to Mehfuz Zaman (University of Queensland) for "Toll-like Receptor 2 Targeting Fully Synthetic Lipopeptide Group A Streptococcus (GAS) Vaccine."

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1st Prize: The University of Sydney, Faculty of Pharmacy Prize, a $1,000 contribution toward attending the 2010 CRS Annual Meeting in Portland, was awarded to Mette U. Anby (Monash Institute of Pharmaceutical Sciences) for "Using Polymers to Enhance the Utility of Lipid-based Delivery Systems."

2nd Prize: Queensland University of Technology, Pharmacy Prize, a $500 contribution toward attending the 4th Annual Meeting of the AUS-CRS or 3rd AUS/NZ-CRS Workshop, was awarded to Adel S. Abdelrahim (University of Queensland) for "Design, Synthesis and Biological Evaluation of a Novel Anionic Liposaccharide-based Drug Delivery System."

3rd Prize: Griffith University, School of Pharmacy Prize, a $200 contribution toward attending the 4th Annual Meeting of the AUS-CRS or 3rd AUS/NZ-CRS Workshop, was awarded to Makan Khoshnejad (University of Queensland) for "Modified Influenza Virosomes for Gene Delivery."

Ben Boyd awarding the 1st poster prizes to Mette U. Anby (left) and Mehfuz Zaman (right).

Poster winners and AUS-CRS Committee (left to right): Mette U. Anby, Makan Khoshnejad, Adel S. Abdelrahim, Ben Boyd, Mehfuz Zaman, Pavla Simerska, and Istvan Toth.

We are sincerely grateful to Istvan Toth for establishing the Australian Local Chapter of CRS and for all of his efforts during his presidency and, of course, to our generous sponsors who contributed to the poster prizes and program of the 3rd AUS-CRS Annual Meeting: ATA Scientific, Davies Collison Cave, Griffith University, Monash University Institute of Pharmaceutical Sciences, Phosphagenics, Queensland University of Technology, The University of Queensland, and The University of Sydney. ■

News and Upcoming Events for CRS Canadian Chapter

Jake Barralet
McGill University, Montreal, Canada

We welcome Dr. Damon Smith (Labopharm) to the Board. Damon is our first industrial board member and provides a link for our corporate members to the Board. We look forward to working together. Patricia Comeau is a Ph.D. student at McGill University and bravely agreed to be the student board member. Patricia is responsible for our Canadian Research Focus section and has already done a great job in highlighting new papers from Drs. Amsden and MacLachlan. Read the latest research focus with Dr. MacLachlan on siRNA delivery as reported in *Nature Biotechnology* on the CRS Canadian Chapter (CC-CRS) web-page. If you have just had a paper accepted that you would like featured please e-mail me at jake.mcgill2@gmail.ca.

We can confirm student travel awards will be available for the CSPS in Richmond, BC, Canada, this June and for the CRS meeting in Portland, OR. To receive a travel award you must be a student registered at a Canadian Institute, a member of the CRS Canadian Chapter, and have an abstract accepted. Details to follow. If your students are not members, please encourage them to join.

We can now confirm that the first meeting of the CRS Canadian Chapter will be held in Montreal in May 2011 (date to be confirmed). Our meeting will be held in partnership with CSPS, CSPT, and NHPRSC. The meeting chair will be Dr. Damon Smith, CC-CRS scientific secretary. We will also be hosting a reception at CSPS this June and will have a meeting open to all members to discuss the 2011 meeting and the 2012 CRS Annual Meeting in Quebec City. If people have thoughts on invited speakers for Montreal 2011 or wish to participate in co-organisation, please e-mail me.

For our Quebecers, more immediately, there will be a local meeting of CSPS and the CRS Canadian Chapter on April 22, at 6:30 p.m. at the Université de Montréal, Faculty of Pharmacy, on "The Brain: The Next Frontier." Where Prof. Lecanu from the Research Institute of the McGill University Health Centre will discuss challenges in drug delivery to the brain. All members are welcome. ■

Misuk Bae Receives Student Service and Leadership Award

Misuk Bae and Dr. Barrett Rabinow (Baxter Healthcare).

Misuk Bae, Ph.D. student and past president of the CRS Student Chapter-Illinois has received of the 2009 Chancellor's Student Service and Leadership Award from UIC (University of Illinois at Chicago). This award honors students who have made an outstanding contribution to the university through campus and community services. Bae was recognized for establishing the Controlled Release Society Student Chapter-Illinois (CRS-IL), of which she served as president from 2007 to 2009 and on the organizing committee for the CRS symposium Recent Advances in Parenteral Drug Delivery.

We express our heartfelt congratulations to her on her achievement. It is very well deserved, and she is listed under the Rising Stars column in the winter issue of the *UIC Pharmacist*. ■

UKICRS Symposium 2010: Controlled Release in Drug Delivery: Right Time, Right Place

Jitinder Wilkhu and Behfar Mohgaddam
Aston University, Birmingham, U.K.

The 2010 UKICRS Annual Meeting was held Wednesday, April 14, at the University of Hertfordshire and focussed on controlling release in drug delivery at the right time and right place. We called upon a range of experts to share their thoughts on the challenges and tribulations of such work. It was a great meeting, and we had over 100 attendees, which gave us a lively atmosphere and plenty of discussions.

Keynote speakers (left to right): Dr. Emma McConnel, Dr. Marina Levina, Dr. Woei Ping Cheng, Dr. Sam Pygall, Dr. Annalisa Mercuri, Prof. Clive Wilson, Dr. Peter Seville, Dr. Ryan Donnelly, Abdul Basit, Dr. Liam McAuley

The day opened with a talk by Prof. Clive Wilson (J. P. Todd Professor of Pharmaceutics at the University of Strathclyde) discussing the "Outs and Ins of Ocular drug delivery." The main areas of research covered in the talk included how things move in the body and ocular diseases such as conjunctivitis and glaucoma. Moreover, emphasis was placed on how and why we try to reach the smallest size for delivery to the eye via eye drops, where research was analysed using gamma scintigraphy.

Our second speaker of the morning was Dr. Peter Seville (senior lecturer in pharmaceutics at Aston University), whose talk emphasised "Better Particles by Design: Using Spray-drying

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Technology to Develop Inhalable Particles." The aims of the research involved enhancing aerolisation properties, developing modified release particles, and, in turn, generating inhalable protein formulations. The main technique used to carry out the research involved the use of a spray drier, where different formulations were compared with each other. In conclusion, by spray drying the enzymatic activity of dry-powder inhalers can be increased.

After a midsession coffee break, the next speaker was Dr. Annalisa Mercuri (post-doctoral researcher at Norwich University), who presented a talk based around the "Dynamic Gastric Model." General points regarding the modified USP method based on media adaptation were discussed, as well as whether a predictive *in vitro* model can be used to assess APIs and drug content.

Coffee break.

Postgraduate speakers (left to right): Dr. Hamid Merchant, Rita Haj Ahmad, Dr. Lizzy Ahmed, Dr. Liam McAuley.

Oral drug delivery was the next hot topic to be highlighted by Lizzy Ahmed (Ph.D. student at Nottingham University). What is a floating system and how can supercritical fluid technology be used when examining oral vaccine delivery? In addition, the benefits of oral drug delivery in terms of it being an easy process, green, and excluding the use of organic solvents were emphasised. Further aims of the research involved particle formation in a broad spectrum of sizes and how encapsulation efficiency is affected.

Poster first award winner I. A. Palmer.

Poster second award winner Manal Alsaadi.

Poster session.

With a talk including many images of the digestive systems of several animals, Hamid A. Merchant (Ph.D. student at the School of Pharmacy, London) discussed the mission to characterise the GI tracts of the Guinea pig and rabbit for oral drug delivery. The main features of the talk included the importance of different GI tracts and how parameters such as pH, fluid volume, and lymphoid follicles vary between different animals. Emphasis was given to the challenges of pre-clinical studies and which model best fits the human GI system.

Disrupted by rumbling stomachs, lunch was in the cards at the University of Hertfordshire, and with great timing, as the next talk was based on drug delivery to the colon. The title "Its a Dirty Job, but Somebody Has to Do It" suggested that lunch was served at the right time. Dr Abdul Basit (senior lecturer in pharmaceutics at the School of Pharmacy, London) embarked on an epic adventure through the colon with a video of his own colon to set the scene for the talk. The main features of the talk included colon function and physiology, with delivery strategies to overcome the challenges, such as the routes through the GI tract to get to the colon for effective drug delivery. Opportunities such as local and systemic therapies were discussed, and the use of radio-labelling drugs and following them via gamma scintigraphy were used.

Aston drug delivery research group.

Dr. Ryan Donnelly (senior lecturer in pharmaceutics at Queen's University Belfast) explained the use of hydrogel microneedle arrays for transdermal and intradermal drug delivery. The talk explained how we can exploit transdermal and intradermal routes to pass through the stratum corneum and how important a balance in lypophilicity and hydrophobicity is crucial with the drug. Enhancement strategies such as drug modification, stratum corneum modifications, and how electrically assisted drugs can be bypassed or removed were discussed. The main features of the talk included the applications and benefits of these routes of delivery and the advantages of microneedles used to penetrate the stratum corneum.

The last speaker before the last coffee break was Dr. Emma McConnel (research scientist in formulation development at Merk, Sharp and Dohme). She talked about the challenges of investigating gastroretention in early development. She discussed how this method can improve drug delivery and mentioned how much it can vary from person to person because of different diets and habits and other differences in people. Through *in vitro* and *in vivo* studies, she explained how this development could be achievable.

After a break for refreshments, Marina Levina (senior manager, product development at Colorcon) started her talk on the topic of "Improving 1st Time Right Order Oral Drug Delivery Using Hydrophilic Matrices." She explained the theory of delivery of the drug by hydrophilic matrices and clarified its advantages followed by a demonstration of its formulation and process.

Dr. Liam McAuley (research scientist in formulation development at Merk, Sharp and Dohme) gave the closing talk of the day, introducing the latest improvements in transdermal delivery. After an introduction on drug delivery to the skin and skin structure, he explained the methods that may cause enhancement in skin penetration. He also talked about the importance of studying diffusion and the instruments and method that has been used for it, such as ATR-FTIR spectroscopy. ■

Welcome New Members

Amirhossein Aarabi
Hamdy Abdelkader
Akwete L. Adjei
Tauseef Ahmad
Hibah Aldawsari
Manal Alsaadi
Aws Alshamsan
Erhan I. Altinoglu
Zohreh Amoozgar
Pavlos Anastasiadis
Mette Uhre Anby
Alhassan Aodah
Karthik Arumugam
Husain Attarwala
Jongsuep Baek
Gaurav Bajaj
Pavan Balabathula
Amrita Banerjee
Abdulgader Baoum
Derek W. Bartlett
David Bassett
Ziya Bayrak
Anna Bershteyn
Saritha Bhandary
Sampada Bhaskar Upadhye
Himanshu Bhattacharjee
Ziyad Binkhathlan
Elijah M. Bolotin
Daniel Bonner
William Bowtle
Ana L. Braga
Barbara Buchan
Rachel Buchanan
Matt Burke
Sara E. Butler
Rosa Canifax
Brenda F. Canine
Brian A. Carr
Denis Carr
Domenico G. Cassara'
Sajeev Chandran
Park C. Woo
Chin-Tin Chen
Dexiang Chen
Xianfeng Chen
Bo Chi
Chuda Chittasupho
Amit Ashok Chivate, Sr.
Daniel Cho
Eunbi Cho
Bo G. Choi
Michael Chorny
Young B. Choy
Changju Chun
Jin-Hwa Chun
Justin Clark
Meredith Clark
Yvonne Cuppok
Mark Cupta
Claudia Da Silva Bitencourt
Praveen Date
Nicole Daum
Eileen Dawson
J. C. DeBraal
Coralie Deladriere
Peter DeMuth
Enrica De Rosa
Neha Desai
Rita De Santis
Dipti Deshpande
Marie-Luce De Temmerman
Sanju Dhawan
Abdenour Djemai
Dejan Djuric
Michael Doschak
Anisha D'Souza
Howard Epstein
Dongmei Fan
Silvia Ferrati
Susan Fetherston
Stefan Fischer
Andrew Flynn
Maria S. Flynn
Astrid Franken
Andrew Fu
Ju Y. Fu
Jitendra Gangwal
Zahra Ghalanbor
Amir Ghassemi
Ariel Gilert
Robert W. Glenn
Randy Goodall
Adam Gormley
Sven Gottschalk
Furio Gratiatica
Manish Grover
Bing Gu
Dalapathi Gugulothu
Micael A. Guillot
Hovhannes Gukasyan
Ece Gulcur
Mette Guldbrandt
Sridhar Gumudavelli
Chunqiang Guo
Himanshu Gupta
Joshua Gustafson
Michael F. Haller
Meeree Han
Qin He
Randy Hecht
Susan K. Heimbecher
Heather Herd
Thomas P. Herringson
John D. Higgins
Robert E. Hirche
Simone R. Hoertner
Yuhua Hu
Bonnie Huang
Hsin-Hui Huang
Keng-Shiang Huang
Tina Huang
Yi-Cheng Huang
Robert Huber
Abu Huq
Delwar Hussain
Fady Ibrahim
Mayumi Ikeda
Darrell J. Irvine
Takuya Ishii
Esmaiel Jabbari
Yuly Jaimes
Shardool Jain
Hoon S. Jeh
Kihyang Jeong
Weihang Ji
Hulin Jiang
Xuan Jiang
Tuo Jin
Anil Jindal
Byeong Jin Jeon
Russell N. Johnson
Todd Johnson
Sung Joon Hong
Steffi K. Joschek
Hsin-Yeh Jsou
Xiang Jun
Hyun C. Jung
Bhagwati Kabra
Deepali Kaduskar
Pardis Kalantarian
Minsum Kang
Seung-rae Kang
Harry Karmouty-Quintana
Frederick R. Kettinger
Ali Khademhosseini
Ashkan Khalili
Fatima A. Khatib
Azadeh Kheirolomoom
Yoon K. Joung
Arum Kim
Beob S. Kim
Dong-Wan Kim
Hyesung Kim
Jae K. Kim
Jang I. Kim
Jung H. Kim
JungHyun Kim
Pyung H. Kim
Seungki Kim, Sr.
Yoon K. Kim
Yuki Kimura
George Kirilov Mihov
Jutarat Kitsongsermthon
Fu-Hsiang Ko
Douglas M. Kolodny-Hirsch
MinJi Koo
Isha Koonar
Erez Koren
Alexander Koshkaryev
Neeraj Kumar
Ruchita V. Kumar
Sunny Kumar
Suresh Kumar Swaminathan
Vikesh Kumar Shukla
Sangamesh G. Kumbar
Noble Kuntworbe
Takuro Kurita
Brandon Kwong
Michel Lafleur
PoHong Lai
Nate Larson
Beom S. Lee
Byung-Heon Lee
Chen-Chang Lee
Dongwon Lee
Hanchen Lee
Kyuri Lee
Sang J. Lee
Soo H. Lee
Wen-Chuan Lee
Young S. Lee
Jun Li
Susanna Lin
John Lind
Albert Lindner
Steven R. Little
Hui W. Liu
Ye Liu
Yu Liu
Seong L. Lo
Yu-Li Lo
Yu-Wen Lo
Giovanna Lollo
Matthew Lorincz Skiles
Deborah Lowry
Wan-Liang Lu
Weiyue Lu
Yael Lupu
Ling Ma
Yuh-Fun Maa
Peter Mack
Sindhuri Maddineni
Achuthamangalam B. Madhankumar
Parveen Madher
Alamelu Mahalingam
Ian Major
Keith R. Marotti
Helena M. Cabral Marques
Charlie E. Martin
Jonathan O. Martinez
Adrian Mason
Pietro Matricardi
John McDermott
Arlo McGinn
Alyn McNaughton
Huan Meng
Qinggang Meng
Todd R. Meyer
Larisa Mihoreanu
Mary Miller
Maureen Mistry
Birgitte Moelholm Malle
Ole Moeller Dall
Behfar Moghaddam
James J. Moon
Emilia Moradi
Javier O. Morales
Joshua Moskowitz
Anindita Mukerjee
Sheetal R. Muley
Mirela Nadler Milbauer
Lekha Nair K.
Hideaki Nakamura
Hye Y. Nam
Kyungwan Nam
Pei-Sze Ng
Dai H. Nguyen
Vinit Nigudkar
Vijayalakshmi Nirmalkumar
Sakae Obara
Sangkwon Oh, Sr.
Carmen M. Ortega-Plaza
Ullrich Oswald
Santhosh K. Pabba
Maria Palmira Gremiao
Jun Pan
Chun G. Park
Jiwon Park
Junsung Park
Myeong C. Park
Brijeshkumar I. Patel
Dhavalkumar Patel
Roshni Patel
Ines Nobre Peca
Jason Perry
Elaine Peters
Thida Phoeung
Dakrong Pissuwan
Pallavi V. Pople
Tyrone M. Porter
Jay Prakash Jain
Sandhya Pranatharthiharan
Robert Price
Eleanor Pritchard
Hussaini Syed Sha Qhattal
Hong Qi
Rong Qi
Bin Qin
Yao Qin
Nicoletta Quattrocchi
Ali Rafati
Venkataraju M. P. Raju
M. Ramesh
Shasha Rao
Abhijit Ray
Thimma Reddy Thatiparti
Hwa P. Rim
Joseph Riolo
Edgardo Rivera-Delgado
Hongwein M. Rivers
Brian A. Riviere
Emilie Roger
Lisa C. Rohan
Shraddha Sadekar
Preety Sahdev
Tarsem Sahota
Asami Sano
Poonam Saraf
Malisa Sarntinoranont
Vipin Saxena
Ehud Segal
Jeong M. Seo
Sangkyo Seo
Sameer Sharma
Dnyanesh Shelar
Namdev Shelke
Jie Shen
Yuri Shimatani
Jeff Shimizu
Rajesh R. Shinde
Satoshi Shirakawa
Nava Shterman
Sukhjeet Singh
Bram Sluetter
Christine Smid
Luis Solorio
Sejin Son
Priya Srinivasan
Stephan T. Stern
Xingfang Su
Kaoxiang Sun
Nathalie Symens
Terence Ta
Christine Talling
Ko Tanaka
Jaidev S. Tantry
Olena Taratula
Jimmy L. Taylor, Jr.
Hiroto Terashima
Sumalee Thitinan
Anitha Thomas
Bruce Thurmond
Fei Tian
Ron Tomer
Udaya S. Toti
Sylvie Trifilieff Riolo
Reginaldo Trindade
Tsuimin Tsai
Kenji Tsukigawa
Salit Tzaban
Pieter Vader
Rita Vanbever
Pegah Varamini
Dries Vercauteren
Abhilasha Verma
Anita Verma
Prinda Wanakule
Chih-Kuang Wang
Chung-Huei K. Wang
Jian-Cheng Wang
Qing Wang
Qun Wang
Shu Wang
Tao Wang
Yan Wang
Ellen K. Wasan
Andrew Watkins
Florence Wauters
Christian Weber
Jennifer Weiser
Jessica Wen
Jitinder Wilkhu
Lauren Wiser
Juan Wu
Shih-Kwang Wu
Zimei Wu
Sixing Yang
ALaa Yassin
Iman Yazdi
Dong-jin Yoo
Sun-Mi Yoon
Toru Yoshitomi
Jian You
Weien Yuan
William Yuen
Emanuela Zacco
Mehfuz Zaman
Sara Zargar-Shoshtari
Vladimir Zarnitsyn
Monica Zepeda
Mingzhen Zhang
Qiang Zhang
Xuan Zhang
Yilin Zhang
Yong Zhang
Yulong Zhang
Hugh Zhao
Arturas Ziemys
Hans Zou
Evgenia Zuser

In the News

Compiled by Steven Giannos
Industrial Editor

May 2010

Nativis, Inc. Presents Breakthrough Technology to Treat Brain Cancer and Other Serious Diseases

Business Wire: May 13, 2010 – LA JOLLA, CA – Nativis Inc., a life science company based in La Jolla, CA, has unveiled its groundbreaking technology to treat diseases in new ways. For the past eight years, Nativis has been developing drug signal therapy, a platform technology based on the pioneering work of several Nobel laureates. A drug signal is a recording of the photon field that surrounds the solvation shell of a molecule in solution. Nativis has developed the technology to capture the unique photon fields (or drug signals) of active pharmaceutical ingredients (API) or drugs at the atomic level. It then uses its patented technology to deliver the signal in a solution to treat serious diseases in new, safe, and more effective ways. Drug signal therapy promises to transform the treatment of diseases, including those for which there are no known cures, like brain cancer.

Nativis is using its drug signal therapy to overcome the physical hurdles that have limited the effectiveness of traditionally administered drugs. Many drugs in wide use for treating cancer are unable to successfully treat brain tumors because they are incapable of permeating the blood-brain barrier. The blood-brain barrier, a physiological separation of circulating blood and spinal fluid, successfully protects the brain from common infections, but it also hinders the delivery of diagnostics and therapeutic agents. Early preclinical trials have shown that Nativis' technology can safely pass through the blood-brain barrier.

The first application of Nativis' drug signal technology is Digitax, which is used to target glioblastoma brain tumors, one of the most aggressive and difficult cancers to treat. Digitax is a taxane-based drug signal captured from the cancer-fighting chemical drug Taxol. The Digitax drug signal provides the therapeutic equivalent of Taxol. Digitax delivered orally in a water-based solution is effective in safely crossing the blood-brain and other barriers and has been proven to reduce and eliminate tumor growth in preclinical studies.

This new technology epitomizes the concept of green chemistry and has the potential to replace the current process of producing drugs in traditional manufacturing plants, which would reduce the environmental footprint. For more information visit www.Nativis.com.

Alnylam Scientists and Collaborators Publish Research on Key Mechanism for Delivery of RNAi Therapeutics with Lipid Nanoparticles (LNPs)

Business Wire: May 11, 2010 – CAMBRIDGE, MA – Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), a leading RNAi therapeutics company, has announced the publication of pre-clinical research in the journal *Molecular Therapy* revealing key mechanisms related to the systemic delivery of RNAi therapeutics using lipid nanoparticles (LNPs). The new study (Akinc et al., *Molecular Therapy*, doi:10.1038/mt.2010.85, 2010), performed in collaboration with scientists at the Max Planck Institute of Molecular Cell Biology and Genetics and AlCana Technologies, Inc., describes a mechanism for endogenous apolipoprotein E (ApoE)-mediated targeting of LNPs to the liver, demonstrates alternative ligand-directed targeting strategies for liver delivery of RNAi therapeutics, and highlights potential targeting approaches for delivery to tissues and cell types beyond the liver.

"In recent months, we have made tremendous progress in the delivery of RNAi therapeutics, a critical determinant for advancement of this promising new class of medicines to patients and for realizing the fullest potential of this technology," said Akin Akinc, Ph.D., associate director, research at Alnylam. "In particular, the findings published today reveal key mechanisms for the delivery of LNP-encapsulated siRNAs to the liver, and more generally, suggest strategies for achieving targeted delivery to tissues and cell types beyond the liver. These mechanistic findings, along with our recent work on the discovery of next-generation LNPs, demonstrate the considerable progress made both in our understanding and in our utilization of LNPs for the delivery of RNAi therapeutics."

Preliminary results from this study were previously presented at the Advances in Biopharmaceuticals Keystone Symposium in January 2010, demonstrating that ApoE is an endogenous targeting ligand for neutrally charged ionizable LNPs (iLNPs) but not certain cationic LNPs (cLNPs). Further, iLNPs were engineered with the carbohydrate *N*-acetylgalactosamine (GalNAc) to achieve targeting to the asialoglycoprotein receptor (ASGPR) as an alternative targeting strategy for the hepatic delivery of RNAi therapeutics.

LNP formulations represent one of several approaches Alnylam is pursuing for systemic delivery of RNAi therapeutics. Additional approaches include novel lipidoid formulations, including cationic LNPs (cLNPs), mimetic lipoprotein particles (MLPs), siRNA conjugation strategies, and single-stranded RNAi, among others. Alnylam is currently enrolling patients in a Phase I clinical program with its systemic RNAi therapeutic

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ALN-VSP for the treatment of liver cancers. In addition, Alnylam intends to initiate a Phase I trial in the first half of 2010 for an additional systemic RNAi therapeutic, ALN-TTR01, for the treatment of transthyretin (TTR)-mediated amyloidosis. ALN-VSP and ALN-TTR01 both utilize a first-generation LNP formulation known as stable nucleic acid-lipid particles (SNALP), which contains an ionizable lipid and has been developed in collaboration with Tekmira Pharmaceuticals Corporation. Alnylam is also advancing its second-generation LNP platform in its ALN-TTR02 and ALN-PCS programs, currently in pre-clinical development.

CEA-Leti Announces TARGET-PDT Study Aimed at Improving Photodynamic Therapy for Cancer Treatment

Business Wire: May 11, 2010 – GRENOBLE, FRANCE – CEA-Leti has announced the launch of the TARGET-PDT project designed to increase the effectiveness of photodynamic therapy (PDT) for treating cancer by developing a novel nano-carrier–based approach.

PDT is a minimally invasive treatment that destroys cancer cells with a combination of a photoactive drug known as a photosensitizer and a specific wavelength of light. When the photosensitizers are activated by the laser light, they produce a form of oxygen that destroys illuminated cancer cells.

Focusing on using PDT against bone cancer and head-and-neck squamous cell carcinoma, which is a tumor of the oral cavity, the project will study the delivery and targeting of photosensitizers encapsulated in lipid nano-particles. For both cancer forms, current treatment regimes often result in low cure rates and show serious side effects or poor functional outcome. The nano-carriers offer a high payload that will include antibodies targeting specific tumor biomarkers.

PDT has already shown significant potential for improving cancer treatment because it offers strictly focused application, biocompatibility with other forms of treatment, the option for repeated use, excellent cosmetic or functional outcomes, and fast recovery. Indeed, there typically is a modest enhanced accumulation of the photosensitizer in tumor tissues, and an additional selectivity is mainly provided by the confined illumination of the target area. However, the use of PDT has been restrained by the limited effectiveness of the photosensitizers upon reaching the tumor and the potential damage to healthy cells near the tumor. Improved targeting of the photosensitizer and nano-particles is necessary to prevent damage to the surrounding healthy tissue.

CEA-Leti, which is coordinating this European project, expects the nano-carrier–based approach will significantly improve delivery and targeting of the photosensitizer, enhancing concentrations at the tumor site even after systemic application. The TARGET-PDT project will allow the partners to study all aspects of PDT treatment: nano-carrier size and payload, photosensitizers such as chlorines and phthalocyanines, targeting method, and types of laser irradiation. The experimental approach will be developed into a preclinical validation to deliver an optimized combination for first clinical "nano-PDT" at a later stage. By using nanotechnology-based photosensitizer delivery systems, the project will set the stage for improved control of the therapy and more comfort for cancer patients.

CEA-Leti is coordinating TARGET-PDT as part of its research program on organic nanocarriers and delivery systems for clinical applications like molecular imaging and drug delivery. The partnership includes highly complementary partners. In addition to CEA-Leti, the European industrial leader in PDT, other partners in the project include the German company biolitec AG; University Hospital Zurich, which is recognized for it clinical PDT capabilities; French academic laboratories belonging to the Centre National de la Recherche Scientifique (CNRS) and the Anticancer Research Center; and Centre Alexis Vautrin in Nancy, France, which specializes in PDT from bench to bedside. For more information, visit www.leti.fr.

Cipher Achieves Major Milestone with FDA Approval for CIP-TRAMADOL ER

PRNewswire-FirstCall: May 10, 2010 – MISSISSAUGA, ON, CANADA – Cipher Pharmaceuticals Inc. (TSX: DND) has received approval from the U.S. Food and Drug Administration (FDA) for CIP-TRAMADOL ER, the company's extended-release tramadol product for the treatment of moderate to moderately severe chronic pain in adults.

"This represents our second FDA approval—a major achievement for the Company that reflects a significant amount of effort and dedication from our team, led by Dr. Jason Gross," said Larry Andrews, president and CEO of Cipher. "We are excited about the opportunity for CIP-TRAMADOL ER in the large and growing U.S. pain market. There were more than 28 million tramadol prescriptions written in 2009, only 5% of which were for once-daily formulations, indicating there is a substantial opportunity for a new entrant. We believe our product's unique capsule formulation comprising an immediate-release tablet and sustained-release beads, combined with having no food effect, will make it an attractive alternative for clinicians and chronic pain sufferers."

QRxPharma Successfully Completes Comparative Phase I Proof-of-Concept Study for MoxDuo® CR Tablet Formulation

PRNewswire: May 10, 2010 – BEDMINSTER, N.J. and SYDNEY – QRxPharma (ASX: QRX and OTCQX: QRXPY) announced today the successful outcome of a Phase I trial for MoxDuo CR, a controlled-release (CR) Dual-Opioid™ designed to provide 12 hr of pain relief in patients suffering from moderate to severe chronic pain (including cancer, lower back, osteoarthritis, and neuropathic). The purpose of the trial was to determine which of the various experimental formulations provided the optimum duration of drug levels in the blood.

"The successful outcome of this trial reinforces QRxPharma's intellectual property that defines MoxDuo CR as a novel,

controlled-release formulation for sustained pain relief. We are now one step closer to addressing the needs of chronic pain patients and entering the multi-billion dollar chronic pain market," said Dr. John Holaday, managing director and chief executive officer, QRxPharma. "QRxPharma remains on track to finalising the MoxDuo CR tablet by the end of this year and to be in a position to initiate Phase 2 trials shortly thereafter."

The Company's MoxDuo® product portfolio includes both immediate and controlled release, as well as intravenous formulations. "Our goal is to provide physicians and patients with a variety of complementary Dual-Opioids™ for managing moderate to severe pain from hospital to home," added Holaday.

Pearl Therapeutics Presents a Bronchodilator Combination Therapeutic for COPD

PRNewswire: May 5, 2010 – REDWOOD CITY, CA – Pearl Therapeutics Inc., a company developing clinically differentiated double- and triple-combination therapies for the treatment of highly prevalent chronic respiratory diseases, presented four posters at the 2010 Annual Meeting of the American Thoracic Society (ATS) in New Orleans. Results from Pearl's Phase I safety and pharmacokinetics study of PT003 were presented. In addition, data were presented that demonstrated the safety, pharmacokinetic, efficacy and drug delivery characteristics from Phase IIa trials of glycopyrrolate (PT001) and formoterol fumarate (PT005), the components of PT003, when delivered via Pearl's proprietary porous particle suspension technology.

PT003 is an inhaled combination of glycopyrrolate, a long-acting muscarinic antagonist (LAMA), and formoterol, a well-known, established, long-acting B2-agonist (LABA), delivered by metered dose inhalers (MDI), the most widely used inhalation drug delivery format. PT003 is the first and only dual long-acting rapid bronchodilator LAMA-LABA combination product in development as a pressurized hydrofluoroalkane MDI (HFA-MDI) formulation and is currently being investigated in a Phase IIb study. Full abstracts of the ATS presentations are now available on the ATS website at http://conference.thoracic.org.

SIOGEN Biotech and Veeda Clinical Research Announce a Strategic Partnership to Develop a New Nanoparticle Formulation of Doxorubicin to Treat Cancer

Business Wire: May 4, 2010 – CHICAGO, IL – SIOGEN Biotech (Kuala Lumpur, Malaysia), an innovative leader in the field of silicon-based nanoparticle drug delivery and targeting, and Veeda Clinical Research (Ahmedabad, India), a global clinical research organization, signed a strategic partnership agreement at the BIO conference in Chicago to develop a new nanoparticle formulation of doxorubicin to treat cancer.

"Following extensive Government investment in our growing biotech sector, this agreement is a showcase of the enormous talent found in Malaysian companies and underlines the growing importance of the Malaysian Biotechnology industry in the global arena," stated the Minister of Science, Technology and Innovation of Malaysia Datuk Seri. Dr. Maximus Johniti Ongkili was present to witness the signing of the deal, which is highly significant in the progression of the Malaysian biotechnology sector.

Under the terms of the agreement, SIOGEN will use its patented Siosomes® drug delivery and targeting technology to encapsulate doxorubicin, a drug used for cancer treatment, and Veeda will undertake Phase I/II clinical trials of this formulation. Doxorubicin is an established drug that is used in chemotherapy for the treatment of leukemias, lymphomas, and other cancers. In the past, pegylated liposome formulations of doxorubicin presented with adverse side effects that limited their dosage and efficacy. Encapsulation of doxorubicin in Siosomes® is designed to increase the efficacy of the drug through targeted delivery to the site of disease and decrease adverse effects by lowering the exposure of the drug to the tissues and cells.

Otonomy Presents Data on Breakthrough Ear Treatment

PRNewswire: May 3, 2010 – SAN DIEGO, CA – Otonomy, Inc. has announced the presentation of preclinical experimental results for OTO-104, the company's sustained-release dexamethasone gel for the treatment of hearing and balance disorders. The studies demonstrate that OTO-104 can effectively deliver a prolonged and dose-proportional exposure of dexamethasone to the inner ear when administered by direct injection into the ear. The data were presented on May 1 at the 2010 Combined Otolaryngology Spring Meeting (COSM) in Las Vegas.

At the highest single dose of OTO-104, therapeutic levels of dexamethasone could be sustained for over 4 weeks in both animal species evaluated (guinea pigs and sheep). The studies also provide the first demonstration of dose proportionality, whereby inner ear concentrations of dexamethasone are related to the dose of OTO-104 administered. OTO-104 was well tolerated in a broad set of safety evaluations.

"We are pleased to be the first to demonstrate sustained release drug delivery to the inner ear as this has been a goal of the otolaryngology research community for many years," said Jay Lichter, Ph.D., CEO and co-founder of Otonomy. "We are also excited to see how this optimized drug delivery profile will translate into patient benefit in our ongoing clinical trial with Meniere's disease patients."

OTO-104 is a patent-protected, sustained-release dexamethasone gel designed for direct injection into the ear (an intratympanic or IT injection) as a potential treatment for hearing loss and balance disorders. Otonomy has initiated a prospective, randomized, placebo-controlled, multicenter, Phase Ib study of OTO-104 given as a single IT injection in subjects with unilateral Meniere's disease. While the primary endpoint of the study is safety and tolerability, a number of efficacy endpoints will be monitored, including the frequency of vertigo attacks experienced by patients pre- and post-treatment.

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Spring Creek Capital Corp. Signs Strategic Licensing Agreement for Patented Oral Drug Delivery System

Business Wire: May 3, 2010 – NEW YORK, NY – Spring Creek Capital Corporation (OTCBB: SCRK), a healthcare solutions company whose business plan is distributing cutting-edge solutions for the medical, pharmaceutical, and healthcare markets, has signed a strategic licensing agreement for an innovative, patented oral spray drug delivery system via the inner lining of the cheek.

The licensing agreement between Spring Creek Capital Corp and McCoy Enterprise, LLC/Vectoris Pharma LLC gives Spring Creek the exclusive rights to produce, market, distribute, and sell products based on an innovative method of delivering medicine via the mouth, more specifically the inner lining of the cheek, known medically as the buccal mucosa. This patented oral spray process compares favorably with the foremost technologies in nasal inhalation and injection and has the advantage of being socially non-intrusive and convenient. Utilizing this pain-, needle-, and inhalation-free delivery system can provide better stability and may reduce the side effects seen with certain nasal delivery and inhalation methods.

"We are excited to announce this new licensing agreement, which brings a patented process and an innovative drug delivery method to Spring Creek's portfolio," said Kelly T. Hickel, chair and CEO of Spring Creek Capital. "We will utilize this oral drug delivery system to improve the administration of drugs including chemical entities, proteins, and peptides without the use of more invasive forms of drug delivery systems such as needles."

Landec Corporation Acquires Lifecore Biomedical

Business Wire: May 3, 2010 – MENLO PARK, CA – Landec Corporation (Nasdaq: LNDC), a materials science company that develops and markets patented polymer products for food, agriculture, personal care, and drug delivery applications, has acquired Lifecore Biomedical, Inc. from Warburg Pincus Private Equity IX, LP. When acquired by Warburg Pincus in March 2008, Lifecore had two divisions: the Dental Division and Hyaluronan Division. The Dental Division was merged into a Warburg Pincus portfolio company. The Hyaluronan Division, now Lifecore, based in Chaska, MN, is a leading supplier of premium hyaluronan-based biomaterials for the medical and veterinary markets. Lifecore hyaluronan biopolymers are used in a wide and ever-growing range of therapeutic treatments, including cataract surgery, degenerative joint disease, spinal defect filling, medical device coatings, cosmetic soft tissue enhancement, and equine osteoarthritis, as well as in numerous research initiatives.

April 2010

Pre-clinical Results Show NexACT® Technology Significantly Improves Subcutaneous Delivery and Anti-metastatic Activity of Angstrom's A6 Cancer Compound

Business Wire: April 28, 2010 – SAN DIEGO, CA – NexMed, Inc. (Nasdaq: NEXM), a specialty CRO with a pipeline of products based on the NexACT® technology, has announced that results from a pre-clinical study showed significant improvement in the delivery and half life of Å6, a proprietary peptide treatment for ovarian cancer currently in Phase II development by Angstrom Pharmaceuticals. Specifically, the incorporation of NexACT® enabled the dose of Å6 to be cut by half, or from twice per day to once per day delivered subcutaneously, while achieving the same level of efficacy in the mouse lung metastasis model.

Bassam Damaj, Ph.D., president and chief executive officer of NexMed, stated, "These new findings, incorporating the NexACT-Å6 peptide formulation, correlate with the half life and delivery profile of the Å6 compound from Angstrom's previous studies using the higher dose. The positive results offer Angstrom the potential to clinically test the NexACT-Å6 peptide at much higher doses while maintaining continuous coverage of the intended therapeutic target in human patients." Dr. Damaj further added, "This study was NexMed's first entry into the subcutaneous delivery of peptide drugs, and the results further confirmed the depot-like effect of the NexACT® technology which we had seen in our subcutaneous delivery studies with insulin and taxol." Malcolm Finlayson, Ph.D., president and chief executive officer of Ångstrom, noted, "Our relationship with NexMed continues to evolve in a fast and promising way. This new data is very exciting and warrants further investigation to support the opportunity to license the NexACT® technology for human clinical trials."

Alnylam Biotherapeutics Presents New Results on Use of RNAi Technologies for Biotherapeutics Manufacturing

Business Wire: April 28, 2010 – CAMBRIDGE, MA – Alnylam Biotherapeutics, a division of Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), a leading RNAi therapeutics company, has announced the presentation of new data at the Cell Culture Engineering XII Conference held in Alberta, Canada, in April 2010. Alnylam Biotherapeutics was formed by Alnylam to develop RNAi technologies for application in manufacturing processes for biotherapeutic products, including recombinant proteins and monoclonal antibodies. The new data presented demonstrate the ability to achieve efficient delivery of siRNAs into Chinese hamster ovary (CHO) cells grown in 1-L suspension culture and to achieve potent silencing of CHO host gene targets involved in both cellular apoptotic and metabolic pathways.

The new research employed siRNAs designed to target key genes involved in the survival and optimal growth of CHO cells: Bax and Bak, which are apoptotic regulators, and lactate dehydrogenase (LDH), a key metabolic enzyme. siRNAs were

delivered to CHO cells grown in 1-L suspension culture using proprietary delivery lipids. Specifically, siRNA-treated cells showed: silencing of Bax, Bak, and LDH mRNA levels by approx. 80%; a >65% decrease in LDH enzyme activity; an approx. 90% decrease in caspase 3 activity, a well-characterized downstream mediator of apoptotic cell death; and, a >90% increase in viable cell density.

Alnylam Biotherapeutics expects to continue to advance RNAi technologies for biologics manufacturing and plans to form partnerships with established biologics manufacturers, selling licenses, products, and services.

Antares Pharma and Uman Pharma Enter Collaboration for VIBEX™ MTX Novel Injectable Methotrexate Product Opportunity Incorporating Proprietary AutoInjector Technology

Business Wire: April 27, 2010 – EWING, NJ, and MONTREAL, QC, CANADA – Antares Pharma, Inc. (NYSE Amex: AIS), a leader in self-injection drug delivery technology, and Uman Pharma, a manufacturer of top-quality injectable pharmaceutical products based in Quebec, Canada, have announced the formation of a strategic alliance covering Antares' VIBEX™ MTX.

Under the terms of the agreement Antares and Uman will invest jointly to develop and commercialize VIBEX™ MTX, Antares' novel pressure-assisted, injection device, containing methotrexate (MTX) for rheumatoid arthritis and related autoimmune conditions, in the United States and Canada. Antares will lead the clinical development program and FDA regulatory submissions and retains rights to commercialize the VIBEX™ MTX product outside of Canada. Uman will perform formulation development and manufacturing activities to support the registration of VIBEX™ MTX and supply MTX in prefilled syringes to Antares for the U.S. market. Uman received an exclusive license to commercialize the VIBEX™ MTX product in Canada. The companies intend to work together to commercialize the VIBEX™ MTX product in other regions.

Echo Therapeutics and Ferndale Pharma Group Initiate Clinical Trial for Prelude SkinPrep Device and 4% Lidocaine Cream

PRNewswire-FirstCall: April 27, 2010 – FRANKLIN, MA – Echo Therapeutics, Inc. (OTC Bulletin Board: ECTE), a company developing its needle-free Symphony tCGM system as a non-invasive, wireless, transdermal continuous glucose-monitoring (tCGM) system and its Prelude SkinPrep system for transdermal drug delivery, in collaboration with its strategic partner Ferndale Pharma Group, Inc., has announced that the first patients were enrolled in a clinical study of its Prelude SkinPrep system. This clinical study is designed to evaluate the ability of the Prelude SkinPrep System to ablate the skin prior to application of OTC 4% lidocaine cream for local dermal anesthesia. Upon completion of this study, Ferndale and Echo anticipate submitting a 510(k) premarket notification to the U.S. Food and Drug Administration (FDA), with subsequent commercial launch of the product after 510(k) clearance. In May 2009, Echo granted Ferndale a license to develop, market, and sell Prelude for delivery of Ferndale's topical 4% lidocaine product in North America and the United Kingdom. Echo received $750,000 up front and expects to receive $750,000 upon FDA clearance of the product, as well as $12.5 million in milestone payments and guaranteed minimum royalty payments. Echo will also receive an ongoing royalty on net sales of the product.

"This clinical study is a milestone event for Echo Therapeutics and is the final step before an FDA submission," commented Patrick T. Mooney, M.D., CEO, president, and chair of the Board of Echo Therapeutics. "We have worked hard to finalize the design of the Prelude SkinPrep System and as a result of our effort, we are now ready to commence the study. Once completed, we anticipate the submission of a 510(k) with the FDA, clearing the way for a near-term commercial launch after FDA clearance. The use of Prelude for local dermal anesthesia represents the best near-term revenue opportunity for Echo. The topical anesthetic market exceeds $200 million annually and we believe that this new product-candidate, with demonstrably faster activity, has the potential to grow it significantly. We are extremely excited to begin enrolling patients and look forward to providing updates in the near-term."

Nuvo Research Announces U.S. Availability of PENNSAID

PRNewswire-FirstCall: April 27, 2010 – MISSISSAUGA, ON, CANADA – Nuvo Research Inc. (TSX: NRI), a drug development company focused on the research and development of drug products that are delivered to and through the skin using its topical and transdermal drug delivery technologies and on the development of its immune modulating drug candidate WF10, has announced that PENNSAID (diclofenac sodium topical solution) 1.5% (wt/wt) is now available by prescription in U.S. pharmacies.

PENNSAID is a non-steroidal anti-inflammatory drug (NSAID) indicated for the treatment of the signs and symptoms of osteoarthritis of the knee(s). Nuvo's U.S. licensee, Mallinckrodt Inc., a Covidien company, has now commenced U.S. commercialization activities for PENNSAID. Nuvo will receive royalties on net U.S. sales of PENNSAID at rates that are consistent with industry standards. Nuvo will also be eligible to receive sales milestone payments totaling up to US$100 million as U.S. annual sales levels are achieved.

Nuvo develops drug products delivered to and through the skin using its topical and transdermal drug delivery technologies. Covidien is the largest supplier of controlled pain medications in the United States based on number of prescriptions. "Physicians in the United States now have a new alternative to help patients manage their signs and symptoms of osteoarthritis of the knee," said Dr. Brad Galer, president of Nuvo Research's Pain Group. "Covidien's commercial launch of PENNSAID in the U.S. is the culmination of our attainment of U.S. Food and Drug

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Administration approval, and the establishment of a strong collaboration with an exceptional sales and marketing organization in Covidien. The launch of PENNSAID in the U.S. should further strengthen Nuvo financially and support the Company's continued growth as a leader in the development of new pain medications."

Pro-Tect, Inc. Acquires Revolutionary Drug Delivery Patents

PRNewswire-FirstCall: April 26, 2010 – WEST CALDWELL, NJ – Pro-Tect Pharmaceuticals, Inc. (PRTT) has completed the acquisition of multiple patents and patents pending from Nectid, Inc. that enable three revolutionary drug delivery technologies. The acquired patents would enable Pro-Tect to provide efficient, effective drug delivery platforms for three essential yet currently unmet needs: a gastro-retentive platform for drugs that otherwise have short time windows for absorption; an abuse deterrent platform for prescription drugs that are prone to abuse, especially narcotic pain-killers; and a once-daily platform that allows two or more drugs commonly taken in combination to be delivered via a single dose with fewer side effects.

In the near term, Pro-Tect intends to proceed with a comprehensive program to develop and commercialize once-daily drugs for diabetic neuropathic pain, fibromyalgia, postherpetic neuralgia, and epilepsy. Pro-Tect also plans to develop and commercialize once-daily opioid combinations, as well as abuse-deterrent opioid combinations, for moderate to severe pain. The patents acquisition includes a pain project that is already under discussion for a potential licensing agreement with a multinational pharmaceutical manufacturer.

Covidien Launches EXALGO Extended-Release Tablets

Business Wire: April 26, 2010 – ST. LOUIS, MO – Covidien (NYSE: COV), a leading global provider of healthcare products, has introduced EXALGO (hydromorphone HCI) extended-release tablets (CII)—the only extended-release hydromorphone treatment available in the United States. This proven therapy, combined with an innovative delivery system, provides opioid-tolerant patients suffering from moderate-to-severe chronic pain with relief for 24 hr per dose.

Approved by the U.S. Food and Drug Administration (FDA) on March 1, 2010, EXALGO tablets provide a well-known therapy in hydromorphone HCl, which has been used in the treatment of chronic pain for more than 80 years. The indication for EXALGO is once-daily administration for the management of moderate-to-severe pain in opioid-tolerant patients requiring continuous, around-the-clock opioid analgesia for an extended period of time. EXALGO is available in 8-, 12-, and 16-mg tablets. For more information about EXALGO, visit www.keeppainwaiting.com.

FDA Launches Initiative to Reduce Infusion Pump Risks

PRNewswire-USNewswire: April 23, 2010 – SILVER SPRING, MD – The U.S. Food and Drug Administration has announced a new initiative to address safety problems associated with external infusion pumps, which are devices that deliver fluids, including nutrients and medications, into a patient's body in a controlled manner. As part of its initiative, the FDA is moving to establish additional premarket requirements for infusion pumps, in part through issuance of a new draft guidance and letter to infusion pump manufacturers. The FDA also has launched of a new web page devoted to infusion pump safety. The new infusion pump safety web page features basic information about infusion pumps and steps that patients and healthcare professionals can take to prevent and report safety problems, even before new or redesigned pumps are brought to market.

Intezyne Receives Intent-to-Grant Notice from the European Patent Office

Business Wire: April 22, 2010 – TAMPA, FL – Intezyne has received notification that the European Patent Office intends to grant a patent covering a key element of Intezyne's breakthrough drug delivery technology, the IVECT method. At the core of this technology is the IVECT micelle, a proprietary, polymeric nanoparticle designed to encapsulate and deliver best-in-class therapeutics, while limiting exposure to healthy tissues. The IVECT method is already covered by seven additional patents, both in the United States and worldwide. This wide-ranging European patent covers technology that allows greater flexibility and versatility of the IVECT micelle, particularly with respect to the amount of hydrophobic material that can be encapsulated in this drug delivery vehicle, further bolstering Intezyne's intellectual property portfolio.

"Historically, encapsulating highly hydrophobic drugs has proven to be a major stumbling block for the great majority of drug delivery systems," explained Kevin Sill, Ph.D., chief scientific officer of Intezyne. "The advanced technology covered by this patent protects Intezyne's ability to encapsulate hydrophobic drugs more efficiently. Further, we have shown for the first time IVECT micelles are able to encapsulate several hydrophobic compounds that were previously intractable to delivery methods at therapeutically relevant levels." For more information, please visit www.intezyne.com.

Mystic Pharmaceuticals Receives U.S. Patent for Needle-free Vaccine and Drug Delivery Technology

Business Wire: April 22, 2010 – AUSTIN, TX – Mystic Pharmaceuticals has been granted U.S. Patent 7,669,597, a key technology of its VRx2™ drug delivery platform. The VRx2™ delivery platform provides preservative-free, precision-dose delivery for ophthalmic and intranasal drugs and biologics. The issued patent covers Mystic's proprietary unit dose blister technology for packaging of drugs or biologics that have been freeze-dried to powder form to improve stability, reduce the need for cold chain management, and enable auto-reconstitution to a liquid form at the time of administration.

Dr. C. J. Peters, director for biodefense in the Center for Biodefense and Emerging Infectious Diseases at the University of Texas Medical Branch, stated, "One of the primary

applications for this technology will be to develop needle-free vaccines for pandemic and bioterror threats that are safer, easier and less costly to produce and deploy." A wide range of drugs, proteins, peptides, and biologics require an uninterrupted cold chain of refrigeration or freezing during storage, transport, and deployment to maintain stability and potency. Cold chain management adds cost and complicates the task of deploying drugs or vaccines to large populations. Freeze-drying reduces or eliminates the need for cold chain management by converting the drug or vaccine from a liquid form to a stable powder using processes such as spray-drying or lyophilization. Freeze-dried vaccines must be reconstituted prior to use, a process that requires trained medical personnel and is difficult to do under adverse field conditions often encountered in a crisis situation.

Mystic's patented unit dose blister technology enables freeze-dried drugs or biologics to be pre-packaged in novel intranasal or ophthalmic delivery systems and automatically reconstituted and self-administered by the consumer with the push of a button. For more information please visit the Mystic website at www.mysticpharmaceuticals.com.

Labopharm Introduces INTELLITAB™: A Proprietary Abuse- and Misuse-Deterrent Technology Platform

PRNewswire-FirstCall: April 21, 2010 – LAVAL, QC, CANADA – Labopharm Inc. (TSX: DDS; NASDAQ: DDSS) has introduced INTELLITAB™, the brand name for its proprietary abuse- and misuse-deterrent technology platform. The INTELLITAB™ platform, which can deliver one or more therapeutic drugs in combination over periods of up to 24 hr, has the potential to provide a patient with a controlled release medication while minimizing the risk of intentional abuse or accidental misuse.

"Intentional abuse and accidental misuse of prescription medications is a serious and growing socio-health problem and increasingly becoming the focus of patients, public advocacy groups, government agencies and the global pharmaceutical industry," said James R. Howard-Tripp, president and chief executive officer of Labopharm Inc. "The development of safer pharmaceutical formulations is a major new direction for the industry, not unlike the advent of child-proof caps was to packaging several decades ago. It just makes sense that if we, as an industry, can offer patients less abusable formulations of existing medications, we should."

Labopharm's INTELLITAB™ technology platform enables controlled release, single and combination drug medications to mitigate against "dose dumping." INTELLITAB™'s proprietary delivery mechanisms maintain the controlled release properties of a drug even if the tablet is broken, crushed, or consumed with alcohol. Additionally, INTELLITAB™'s tablets, if crushed and added to water, alcohol, or other solvents, form a solid matrix that will prevent intravenous injection or insufflation (snorting).

Alnylam Demonstrates Regression of Pathogenic Transthyretin (TTR) Amyloid Deposits Following Treatment with an RNAi Therapeutic in an Animal Model of TTR-Mediated Amyloidosis

Business Wire: April 20, 2010 – CAMBRIDGE, MA – Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), a leading RNAi therapeutics company, has presented new pre-clinical data from its ALN-TTR program at the XII International Symposium on Amyloidosis in Rome in April 2010. ALN-TTR01 is a systemically delivered RNAi therapeutic being developed for the treatment of transthyretin (TTR)-mediated amyloidosis (ATTR), including familial amyloidotic polyneuropathy (FAP) and familial amyloidotic cardiomyopathy (FAC). These new pre-clinical data demonstrate for the first time that treatment with an RNAi therapeutic can result in regression of pre-existing pathogenic TTR deposits in peripheral tissues. Additional pre-clinical data presented at the meeting demonstrate the potential application of TTR-specific siRNA for the treatment of ocular disease in ATTR.

ATTR is caused by mutations in the TTR gene, which is expressed predominantly in the liver, that result in the accumulation of pathogenic deposits of mutant and wild-type TTR protein in several tissues, including nerves, heart, and gastrointestinal tract. There are more than 100 mutations that have been identified in the TTR gene. ALN-TTR targets a conserved region of the TTR gene in wild-type and all known mutant forms of TTR and, therefore, has potential as a therapeutic for all patients with FAP and FAC. TTR is also expressed in the eye by retinal pigment epithelial (RPE) cells, and mutations in TTR can lead to ocular complications in ATTR patients, including blindness.

"We are very encouraged by these important new pre-clinical data from our ALN-TTR program which we believe point to the breakthrough potential of an RNAi therapeutic strategy in ATTR. Importantly, we have demonstrated for the first time the ability of achieving regression of pathogenic TTR deposits in tissues when ALN-TTR01 is administered in a treatment paradigm," said Rene Alvarez, Ph.D., associate director of research at Alnylam. "These new data significantly extend our previous results showing that ALN-TTR01 can prevent TTR deposition when administered in a prophylactic regimen. We are also encouraged by our initial pre-clinical data using siRNAs targeting TTR for the treatment of ocular amyloidosis. Expression of mutant TTR in retinal cells can lead to blindness in ATTR patients, and an intraocular injection approach with our TTR-specific siRNA could be advanced as a Direct RNAi therapeutic strategy."

Previous pre-clinical studies reported by Alnylam have demonstrated the ability of TTR-specific RNAi therapeutics to mediate potent and durable silencing of both wild-type and mutant forms of the TTR gene in rodents and non-human primates. In the first half of 2010, Alnylam expects to initiate a Phase I clinical trial with ALN-TTR01 in patients with ATTR.

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ALN-TTR01 is being advanced using stable nucleic acid-lipid particles (SNALP) delivery technology developed in collaboration with Tekmira Pharmaceuticals Corporation. In parallel, Alnylam is also advancing ALN-TTR02 utilizing second-generation lipid nanoparticles. For more information, please visit www.alnylam.com.

3M Drug Delivery Systems Grows Partnerships in Asia

PRNewswire-Asia: April 15, 2010 – ST. PAUL, MN – 3M Drug Delivery Systems recently advanced its participation in the Asian market with a sponsorship of the Asia Pharma R&D Leaders 2010 event, held in Shanghai, China. The event, organized by the Global Leaders Institute, the leading life science event producer in China, brings together leading pharmaceutical industry professionals, policymakers, and academics to discuss Asia's role in the manufacturing, research, and development of today's drug and biotech innovations, as well as opportunities for future growth.

3M Drug Delivery Systems is playing an active role in the growth of the pharmaceutical industry in Asia with its recent construction of a new laboratory facility at the 3M Singapore site in Yishun. The laboratory is 3M Drug Delivery Systems' first contract research and development facility in the Asia Pacific Region dedicated to pharmaceutical product development. The country's infrastructure makes it an ideal hub for 3M's Asia Pacific customers, and Singapore's scientific talent pool adds to the site's appeal. The Singapore lab will develop products in both the inhalation and transdermal drug delivery categories, bringing 3M's innovative inhalers and patches to pharmaceutical customers and patients in the Asia Pacific Region.

Research conducted at the Singapore facility will contribute to 3M Drug Delivery Systems' growing capabilities and product portfolio. Since its invention of the metered-dose inhaler (MDI) 50 years ago, the company has remained a pioneer in the technology and now offers a full suite of MDI development and manufacturing capabilities and components, including the 3M integrated dose-by-dose counter. Additional technologies are available to improve patient experience and help ensure the technical success of clients' products.

Other recent offerings in inhalation include the 3M Taper dry powder inhaler, which stores API on a microstructured carrier tape, virtually eliminating the need for lactose or complex powder formulations, as well as the 3M Conix dry powder inhaler, which uses reverse-flow cyclone technology to enable a patient's inhalation to efficiently aerosolize the drug. The company has also recently introduced two new inhaler components, the 3M face seal valve, which eliminates the need to prime an inhaler and 3M plasma coating technology, which provides protection from degradation, deposition, and corrosion. For more information, visit http://www.3M.com/dds.

LATITUDE Pharmaceuticals Initiates Four Additional Collaboration Studies for Its PG Depot

Business Wire: April 14, 2010 – SAN DIEGO, CA – LATITUDE Pharmaceuticals, Inc., a San Diego-based drug formulation developer, has initiated four additional collaborative programs for its phospholipid gel (PG) depot drug delivery technology. The programs are designed to provide sustained delivery of small and large therapeutic molecules up to 7 days following a single subcutaneous or intramuscular injection. The new studies bring the total to 11 collaborations that are applying the PG depot to deliver small molecule, peptide, and protein drugs across a broad spectrum of therapeutic applications.

"Our latest projects represent a growing recognition from startups to large pharma of the potential for LATITUDE's PG Depot technology," noted Andrew Chen, Ph.D., president of LPI. "We are very pleased that our newest collaborators have selected the value-adding PG Depot to overcome the short half-life and frequent injection issues problematic for many emerging medicines, especially proteins and peptides. By reducing the discomfort of daily injections, LATITUDE's approach offers an attractive alternative for producing better compliance and outcomes for patients."

LPI is a drug delivery company that develops new intellectual property for the biotech and pharmaceutical industries through IP-driven, leading-edge drug formulation approaches and technologies. LPI has built a solid reputation as an innovator and for its successful track record in formulating difficult and/or highly insoluble drug molecules.

Particle Sciences Announces the Acquisition of Unique PEG-based Polymer Technology

PRNewswire: April 13, 2010 – BETHLEHEM, PA – Particle Sciences Inc., a leading pharmaceutical CRO, is adding to its portfolio of drug delivery technologies through the acquisition of a versatile PEG-based technology. The technology covers a series of PEG-grafted cationic polymers that have a wide variety of applications in the pharmaceutical arena.

According to Robert Lee, VP of pharmaceutical development for Particle Sciences, "PEGylation is a recognized approach to stabilize drug suspensions, improve drug solubility and bioavailability, and reduce toxicity and reticuloendothelial system interaction. The technology we have acquired covers a set of novel, biocompatible PEGylated polymers allowing the PEGylation of particles and biological surfaces. We are confident that our clients will benefit from this acquisition and have already started several development programs utilizing them."

"Particle Sciences has been working with this technology for some time now and we are very happy with the performance and *in vivo* tolerability results obtained thus far in several different systems. To bolster the acquired technology, we have filed additional intellectual property to both broaden and extend its patent coverage," added Andrew Loxley, director of new technologies for Particle Sciences.

Celator Pharmaceuticals Receives Notice of Allowance on U.S. Patent for Its CombiPlex Technology Platform

PRNewswire: April 12, 2010 – PRINCETON, NJ – Celator Pharmaceuticals has announced that the U.S. Patent and Trademark Office has issued a Notice of Allowance for a patent covering the company's CombiPlex technology platform (U.S. patent application 10/417,631), the basis for the company's product pipeline, which includes two clinical-stage products for acute myeloid leukemia and colorectal cancer.

CombiPlex is a unique approach to the development of combination drug therapies used for treating cancer. It is the only approach using drug carriers to deliver synergistic ratios of cancer drug combinations. In contrast to conventional combination chemotherapies, Celator recognized that different ratios of the same two (or more) drugs can be synergistic, additive, and even antagonistic. CombiPlex identifies a synergistic ratio of drugs and locks this ratio in nano-scale (about 100 times smaller than a red blood cell) carriers that are able to deliver and maintain the synergistic drug ratio after injection into a patient. This extended delivery of a synergistic ratio of drugs is intended to increase the effectiveness of the combination and improve clinical outcomes.

"This broad allowance protects our ability to utilize the CombiPlex platform with a wide variety of antineoplastic agents, opening up numerous potential combinations for investigation and possible commercialization," said Dr. Lawrence Mayer, president and head of research at Celator Pharmaceuticals. Celator received similar patent protection for CombiPlex from the European Patent Office in 2006. The U.S. patent will extend until at least 2024.

"Extending patent protection of CombiPlex to the US strengthens our intellectual property portfolio as we advance our pipeline of cancer therapies and collaborative programs with other pharmaceutical companies," said Scott Jackson, chief executive officer of Celator Pharmaceuticals. "The technology has already yielded promising clinical data. In December, we reported encouraging interim data from the first of two randomized Phase 2 clinical studies in patients with acute myeloid leukemia treated with our lead drug, CPX-351, and we will report additional efficacy and safety data with CPX-351 later this year."

Cephalon Completes Acquisition of Swiss Pharmaceutical Company Mepha

PRNewswire-FirstCall: April 9, 2010 – FRAZER, PA; AESCH, SWITZERLAND; and MAISONS-ALFORT, FRANCE – Cephalon, Inc. (Nasdaq: CEPH) has completed its previously announced acquisition of Mepha, a Swiss-based pharmaceutical company. As a result of the acquisition, Mepha is now a wholly owned subsidiary of Cephalon. The purchase price paid at closing, inclusive of certain closing adjustments, was CHF 662.4 million (or approx. US$615.4 million). The purchase price is also subject to further post-closing working capital and net debt adjustments.

"We are proud to include Mepha as part of the Cephalon family. Mepha has a strong reputation for high quality products and services that deliver value to patients and healthcare professionals," said Frank Baldino, Jr., Ph.D., chair and CEO of Cephalon. "This acquisition expands our presence in Europe, and we believe Mepha will contribute to our long-term growth."

Alain Aragues, executive vice president and president of Cephalon Europe, said, "We are pleased to add Mepha's experience and expertise, which are critical to our successful development of a balanced business mix in Europe, Middle East and Africa. Cephalon intends to leverage Mepha's brand recognition as the number one generics company in Switzerland and a prominent generic pharmaceutical company in many other markets."

Transdel Pharmaceuticals Closes $1 Million Debt Financing

PRNewswire-FirstCall: April 8, 2010 – LA JOLLA, CA – Transdel Pharmaceuticals, Inc. (OTC Bulletin Board: TDLP), a specialty pharmaceutical company focused on developing topically administered products using its proprietary transdermal delivery platform, has completed a private debt financing of $1 million. The company issued a senior convertible promissory note with an annual interest rate of 7.5% to an existing shareholder. The note has a two-year term. The company has a right to prepay the note at any time upon providing written notice to the holder. At any time prior to the company's repayment of the note, the holder may convert all or any part of the outstanding principal and accrued interest on the note into shares of the company's common stock at a conversion rate of $1.00 per share.

"We are pleased by the continued support from our shareholders. This financing provides us with additional resources to continue planning the second Phase 3 clinical study for our lead topical pain drug, Ketotransdel® as well as continue our ongoing partner discussions for Ketotransdel® with U.S. and foreign based companies," said John Lomoro, acting chief executive officer and chief financial officer. "During 2010, we plan to raise additional funding through either partnership arrangements or further equity or debt financings to complete the Phase 3 clinical program for Ketotransdel®."

Pitt-led International Study Identifies Human Enzyme that Breaks Down Potentially Toxic Nanomaterials and Opens Door to Novel Drug Delivery

University of Pittsburgh: April 7, 2010 – PITTSBURGH, PA – An international study based at the University of Pittsburgh provides the first identification of a human enzyme that can biodegrade carbon nanotubes—the super-strong materials found in products from electronics to plastics—and in laboratory tests offset the potentially damaging health effects of being exposed to the tiny components, according to findings published online in *Nature Nanotechnology*.

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The results could open the door to the use of carbon nanotubes as a safe drug-delivery tool and also could lead to the development of a natural treatment for people exposed to nanotubes, either in the environment or the workplace, the team reported. The researchers found that carbon nanotubes degraded by the human enzyme myeloperoxidase (hMPO) did not produce the lung inflammation that intact nanotubes have been shown to cause. Furthermore, neutrophils, the white blood cells that contain and emit hMPO to kill invading microorganisms, can be directed to attack carbon nanotubes specifically.

"The successful medical application of carbon nanotubes [relies] on their effective breakdown in the body, but carbon nanotubes also are notoriously durable," said lead researcher Valerian Kagan, a professor and vice chair in the Department of Environmental and Occupational Health in the University of Pittsburgh Graduate School of Public Health. "The ability of hMPO to biodegrade carbon nanotubes reveals that this breakdown is part of a natural inflammatory response. The next step is to develop methods for stimulating that inflammatory response and reproducing the biodegradation process inside a living organism."

Kagan and his research group led the team of more than 20 researchers from four universities, along with the laboratory groups of Alexander Star (assistant professor of chemistry, University of Pittsburgh School of Arts and Sciences), and Judith Klein-Seethharaman (assistant professor of structural biology, University of Pittsburgh School of Medicine). Additional Pittsburgh researchers included Yulia Tyurina (assistant professor of environmental and occupational health, Graduate School of Public Health) and Donna Stolz (associate professor of cell biology and physiology, Medical School); other researchers are from Sweden's Karolinska Institute, Trinity College in Ireland, the National Institute for Occupational Safety and Health, and West Virginia University.

Carbon nanotubes are 1-atom thick rolls of graphite 100,000 times smaller than a human hair yet stronger than steel. They are used to reinforce plastics, ceramics, and concrete; are excellent conductors of electricity and heat; and are sensitive chemical sensors. However, a nanotube's surface also contains thousands of atoms that could react with the human body in unknown ways. Tests on mice have shown that nanotube inhalation results in severe lung inflammation coupled with an early onset of fibrosis. The tubes' durability raises additional concerns about proper disposal and cleanup. In 2008, Star and Kagan reported in *Nano Letters* that carbon nanotubes deteriorate when exposed to the plant enzyme horseradish peroxidase, but their research focused on cleanup after accidental spills during manufacturing or in the environment.

For the current study, the researchers focused on human MPO because it works via the release of strong acids and oxidants—similar to the chemicals used to breakdown carbon nanotubes. They first incubated short, single-walled nanotubes in an hMPO and hydrogen peroxide solution—the hydrogen peroxide sparks and sustains hMPO activity—for 24 hr, after which the structure and bulk of the tube had completely degenerated. The nanotubes degenerated even faster when sodium chloride was added to the solution to produce hypochlorite, a strong oxidizing compound known to breakdown nanotubes.

After establishing the effectiveness of hMPO in degrading carbon nanotubes, the team developed a technique to prompt neutrophils to attack nanotubes by capturing them and exposing them to the enzyme. They implanted a sample of nanotubes with antibodies known as immunoglobulin G (IgG), which made them specific neutrophil targets. After 12 hr, 100% of IgG nanotubes were degraded versus 30% of those without IgG. The researchers also tested the ability of macrophages, another white blood cell, to breakdown nanotubes, but after 2 days, only 50% of the tubes had degenerated. In subsequent laboratory tests, lung tissue exposed to the degraded nanotubes for 7 days exhibited negligible change compared with unexposed tissue. On the other hand, tissue exposed to untreated nanotubes developed severe inflammation.

March 2010

Access Pharma's Korean Partner Gains Marketing Approval for MuGard

PRNewswire-FirstCall: March 25, 2010 – DALLAS, TX – Access Pharmaceuticals, Inc. (OTC Bulletin Board: ACCP) has announced that JCOM Co., Ltd., its Korean licensee for both MuGard and ProLindac, has received approval from the Korean Food and Drug Administration (KFDA) of its registration dossier for MuGard, an oncology supportive-care treatment for the management of oral mucositis. Under the agreement, JCOM is responsible for obtaining the necessary regulatory approvals for MuGard in Korea. As soon as JCOM has completed the additional steps required to import MuGard from the United States, marketing will commence.

"JCOM is a well-regarded company with an extensive distribution network in Korea," said Jeffrey Davis, CEO of Access Pharmaceuticals. Davis continued, "JCOM receiving technical approval is a critical step in the launch of MuGard in Korea and it fits in nicely with our broad commercialization strategy of MuGard in the global market. We look forward to working with them on [the] next steps, including a potential supply arrangement, and to leveraging their expertise throughout the region."

"We are pleased with the continued progress being made to commercialize MuGard in Korea," stated Yong Seok Kang, CEO of JCOM Co., Ltd. "We remain on track and look forward to commercializing actively in the second half of the year."

As previously announced, MuGard has been launched in the United Kingdom, Germany, Italy, Sweden, Norway, and Greece through its European partner SpePharm. Additionally, Access Pharmaceuticals and its respective marketing partners continue preparing for the commercial rollout of MuGard in the United States and additional countries in Europe set for later this year.

Cornerstone Pharmaceuticals Enters into a Collaboration Agreement with the U.S. National Cancer Institute to Evaluate Cornerstone's Highly Selective Cancer Cell-targeting Nanotechnology, Emulsiphan, in Combination with Innovative NCI Anticancer Agents

PRNewswire: March 23, 2010 – CRANBURY, NJ – Cornerstone Pharmaceuticals, Inc. (http://www.cornerstonepharma.com), a private pharmaceutical company focused on therapies exploiting distinctive cancer cell metabolism, has entered into a collaboration agreement with the U.S. National Cancer Institute (NCI). This collaboration calls for Cornerstone to apply its proprietary Emulsiphan cancer-selective delivery nanotechnology platform to a class of agents developed at the NCI's Center for Cancer Research Nanobiology Program. These agents developed within the laboratory of biologist Dr. Robert Blumenthal can be turned into toxic compounds by targeted radiation and ultrasound. Cornerstone and NCI will evaluate the potential of these combined technologies in reducing tumors.

Cornerstone has been able to formulate multiple types of anti-cancer compounds in Emulsiphan, its novel lipid oil nanoemulsion. Emulsiphan is designed to maximize drug concentration into tumor cells, thereby enhancing the anti-cancer compound's selectivity and specificity, leading to a potentially safer and more effective cancer treatment. This is of particular importance for those tumors that may be located in a site not accessible to surgical intervention, e.g., tumors of the brain, liver, pancreas, and gallbladder.

Dr. Yossef Raviv in Dr. Blumenthal's laboratory at NCI discovered that a class of agents may become toxic when delivered to cancer cells and activated by an external energy source. NCI and Cornerstone have agreed to collaborate to evaluate the combination of these agents with Emulsiphan. "This is an important step forward towards achieving the dream of safe and effective cancer therapy for the most difficult to treat cancer types," remarked Dr. Robert Shorr, chief executive officer of Cornerstone Pharmaceuticals. "We are very excited to work with the NCI and look forward to progressing from studies in cell tumor models to actual human clinical studies."

Many approved drugs as well as newer cancer-selective agents in use or in development today are difficult to solubilize and rely on diffusion after intravenous or oral administration to reach tumor cells. Often drugs may be metabolized and cleared from the body prior to reaching their target, and as cells are distal from a tumor's vasculature, it is more difficult for a drug to reach a sufficient concentration to be useful. While technology continues to be evaluated for increasing the concentration of drugs in a tumor mass, some of these may actually inhibit the uptake of a drug into tumor cells. Cornerstone's Emulsiphan drug delivery technology aims to overcome these challenges so that increasing the required effective dose doesn't deliver treatment at the expense of risking a patient's safety.

Celsion Corporation Announces Presentation of ThermoDox Abstract

PRNewswire-FirstCall: March 18, 2010 – COLUMBIA, MD – Celsion Corporation (CLSN) has announced that an abstract on the Phase I/II trial of ThermoDox in recurrent chest wall cancer (RCW) has been accepted for presentation at the 2010 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago, IL. The abstract presents the background, rationale, and design of the DIGNITY study, which is ongoing and evaluating ThermoDox in combination with hyperthermia in women with recurrent breast cancer on their chest wall.

The abstract, titled "Phase I/II Study Evaluating the Maximum Tolerated Dose, Pharmacokinetics, Safety, and Efficacy of Approved Hyperthermia and Lyso-thermosensitive Liposomal Doxorubicin in Patients with Breast Cancer Recurrence at the Chest Wall," was presented by Nicholas Borys, M.D., chief medical officer of Celsion.

"We are pleased that our study was among those that were accepted, providing continued evidence of the medical community's high interest level in ThermoDox, the progress of our clinical program, and our focus on a cancer that is very difficult to treat," commented Michael H. Tardugno, president and chief executive officer of Celsion. "We are grateful for the commitment of our clinical investigators to this important work and look forward to their on-going participation in the DIGNITY trial."

Dr. Borys commented, "Our Phase I/II trial combines ThermoDox with hyperthermia, offering a unique approach to treating patients with difficult loco-regional recurrence of breast cancer at the chest wall. In a separate trial of similar design being conducted at Duke University Medical Center, researchers are reporting convincing evidence of clinical activity. I look forward to the continuation of our trial and the potential to provide an improvement in the standard of care for this devastating disease."

PEGylated Dendrimers: A Novel Mechanism of Drug Delivery

ScienceDaily: March 10, 2010 – MELBOURNE, AUSTRALIA – Monash Institute of Pharmaceutical Science (MIPS) researchers, in collaboration with the biotechnology company Starpharma Holdings Ltd. (ASX: SPL), have developed a new method to deliver medications that may benefit thousands of patients with particular types of cancer, HIV, and lymphatic conditions worldwide. The Melbourne-based research team has shown how PEGylated polylysine dendrimers, a new type of nano-sized drug delivery system, can be altered to target either the lymphatic system or the bloodstream.

Lead researcher at MIPS and Associate Dean of Research Prof. Chris Porter said the discovery has particular implications for the treatment of diseases that are spread via the lymphatics and lymph nodes. "We are excited by the possibilities that this technology may provide in the improved treatment of particular

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types of diseases, including metastatic cancer, lymphoma, HIV and metastitial tuberculosis," Prof. Porter said.

Dendrimers are precisely defined, synthetic nanomaterials that are approx. 5–10 nm in diameter. They are made up of layers of polymer surrounding a central core. The dendrimer surface contains many different sites to which drugs may be attached and also attachment sites for materials such as polyethylene glycol (PEG), which can be used to modify the way the dendrimer interacts with the body. PEG can be attached to the dendrimer to "disguise" it and prevent the body's defense mechanisms from detecting it, thereby slowing the process of breakdown. This allows the delivery system to circulate in the body for an extended time period, maximizing the opportunities for the drug to reach the relevant sites.

Prof. Porter's group and Starpharma have been investigating dendrimer-based drug delivery systems for some time, but these most recent findings appear to hold particular promise. The data, published in the *Journal of Controlled Release*, demonstrate that by increasing dendrimer size by increasing the chain length of attached PEG chains, a dramatic increase in absorption efficiency after subcutaneous injection can be achieved and transported into the lymphatic system. Conversely, a shorter PEG chain was shown to lead to rapid absorption into the blood.

"Our work suggests that careful design of the size and surface characteristics of PEGylated Polylysine dendrimers provides an opportunity to choose whether these delivery systems are absorbed and distributed via the bloodstream or the lymphatic system," Prof. Porter said. "The ability to target therapeutic treatments in this way offers the potential to maximise drug concentrations at sites of action within the lymphatic system—and importantly to minimise concentrations elsewhere, potentially reducing side effects and toxicity. It is still early days, but we're confident the potential for improved patient treatment is significant." ■

37th Annual Meeting & Exposition of the Controlled Release Society

July 10-14, 2010 • Oregon Convention Center • Portland, Oregon, U.S.A.

Personalized Medicines and Products for the Next Generation

Confirmed Plenary and Podium Sessions

Monday, July 12

Morning

Plenary: *Genetics and Genomics in Clinical Medicine*, Raju Kucherlapati, Harvard University, U.S.A.

Podium Sessions:
New Chemistries for Drug Delivery
Non-Parenteral Delivery of Biologics
Novel Materials and Release Systems
Ophthalmic Medicines
Prediction and Application of IVIVC for Veterinary Species
Transdermal

Mini-symposium:
Theranostics: Diagnosis and Treatment in One Box

Afternoon

Plenary: *Creating and Growing an Innovative Company Without VC Funding*, Ramin Najafi, NovaBay Pharmaceuticals, U.S.A.

Podium Sessions:
Nanoparticles and Fibers for Controlled Release Systems
Peptides and Proteins
Polymers in Medicine
Pulmonary Delivery
Translational Studies

Mini-symposium:
Biomarkers: The Needle in the Haystack

Tuesday, July 13

Morning

Plenary: *Role of Polymer Architecture in Tumor Drug Delivery*, Frank Szoka, University of California-San Francisco, U.S.A.

Podium Sessions:
Encapsulation for Environmental Protection
Medical Devices
Oral Delivery I
PEGylated Technologies
Vaccines

Mini-symposium:
siRNA/Micro RNA

Afternoon

Plenary: *The Enhanced Permeability and Retention Effect in Cancer and Inflammation for More Selective Drug Delivery: Past, Present, and Future Outlook*, Hiroshi Maeda, Sojo University, Japan

Podium Sessions:
DNA Delivery
Encapsulation of Cells and Microorganisms
Intracellular Trafficking
Liposomes
Oral Delivery II
Tumor Targeting

Wednesday, July 14

Morning

Plenary: *Nanotechnologies for Personalized Medicine*, Mauro Ferrari, The University of Texas-Houston, U.S.A.

Podium Sessions:
Blood Brain Barrier
Environmentally Friendly and Biodegradable Controlled Release Systems
Nanomedicines I
Hydrogels

Mini-symposia:
Biomedical Photonics: In Vivo Diagnostics of Malignancy with Targeted Delivery Tools
Stem Cells—Yes, We Can!

Afternoon

Plenary: *Controlled Release 50 Years Later: Responsive Intelligence and Delivery by Design*, Nicholas Peppas, The University of Texas-Austin, U.S.A.

Podium Sessions:
Biomaterials
Biomedical Imaging
Nanomedicines II
Tissue Engineering

Mini-symposium:
Vaginal Drug Delivery: Past, Present, and Future

Controlled Release Society
3340 Pilot Knob Road
St. Paul, MN 55121
United States of America

Calendar of Events

2010

Chemistry, Manufacturing & Control (CMC): Quality, Regulatory and Scientific Requirements and Strategies

June 21-22
Shanghai, China
www.cpa.org.cn

37th Annual Meeting & Expostion of the Controlled Release Society

July 10-14
Oregon Convention Center
Portland, Oregon, U.S.A.
www.controlledreleasesociety.org/main/meetings

31EPS Satellite Symposium on Cell Penetrating Peptides

September 10-11
Panum Institute
Copenhagen, Denmark
http://icmm.ku.dk/forskerskole_i_genmedicin/genetic_medicine/symposium

CRS-IPTS Educational Workshop on Vaccine Development (Immediately prior to 15th International Pharmaceutical Technology Symposium)

September 11-12
Kervansaray Lara Hotel
Antalya, Turkey
http://ipts-hacettepe.org

Workshop Sponsored by CRS: Recent Advances in Controlled Release and Non-Invasive Drug Delivery of Biopharmaceuticals

September 20-21
Sheraton Baltimore Inner Harbor
Baltimore, MD, U.S.A.
www.aapspharmaceutica.com/meetings/workshops/NIDD

8th International Nanomedicine and Drug Delivery Symposium (Presented by Center for Drug Delivery and Nanomedicine)

October 3-10
Hilton Omaha
Omaha, NE, U.S.A.
www.nanodds.org

CRS Satellite Workshop: Novel Methods for Developing Clinically Relevant Product Specifications

November 13
Morial Convention Center
New Orleans, LO, U.S.A.
www.controlledreleasesociety.org/main/meetings

FIP Pharmaceutical Sciences 2010 World Congress (in association with the AAPS Annual Meeting and Exposition)

November 14-18
New Orleans, Louisiana, U.S.A.
www.pswc2010.org/

2011

38th Annual Meeting & Exposition of the Controlled Release Society

July 30-August 3
Gaylord National Resort and Convention Center
National Harbor, Maryland, U.S.A.
www.controlledreleasesociety.org/main/meetings