CRS Leading Delivery Science and Technology

Newsletter

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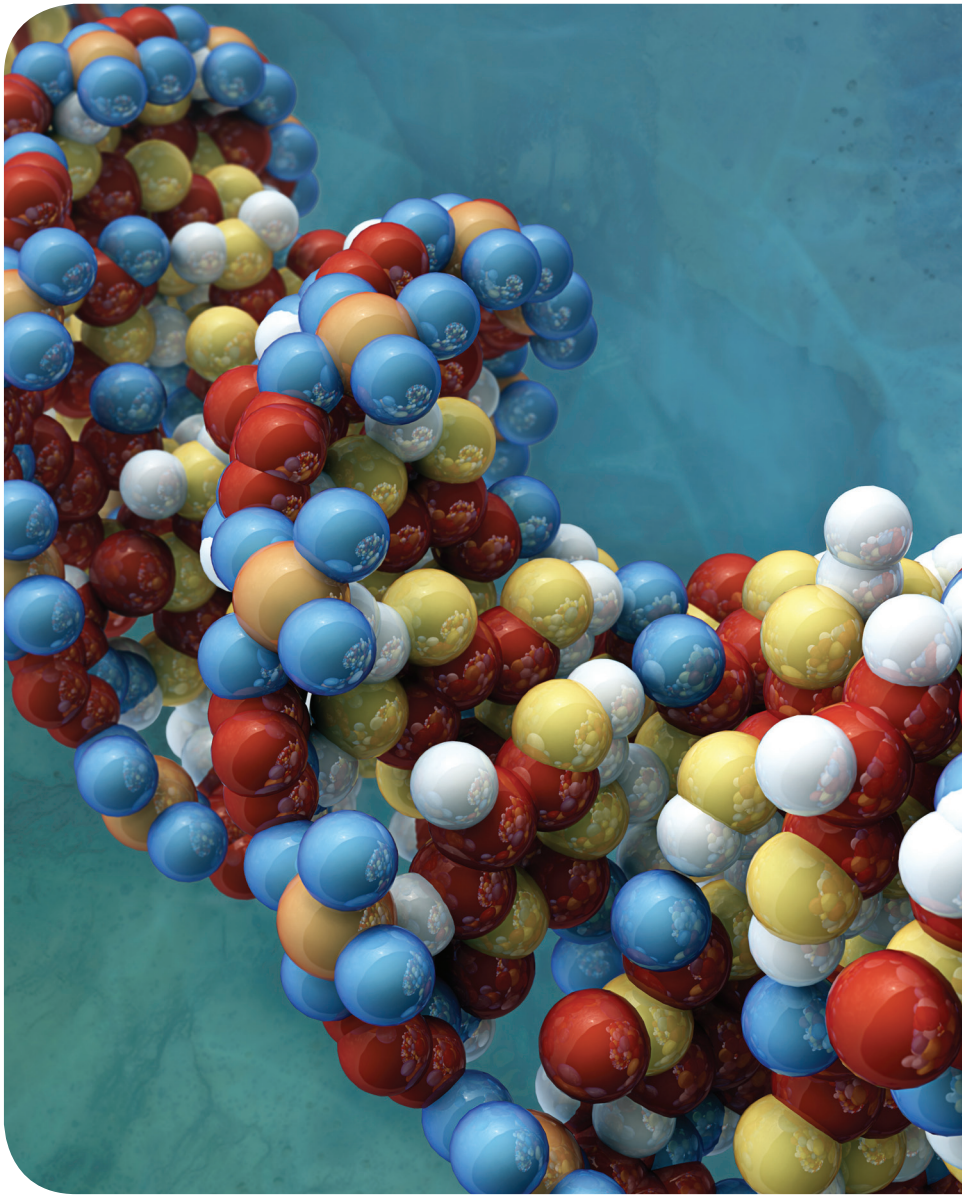
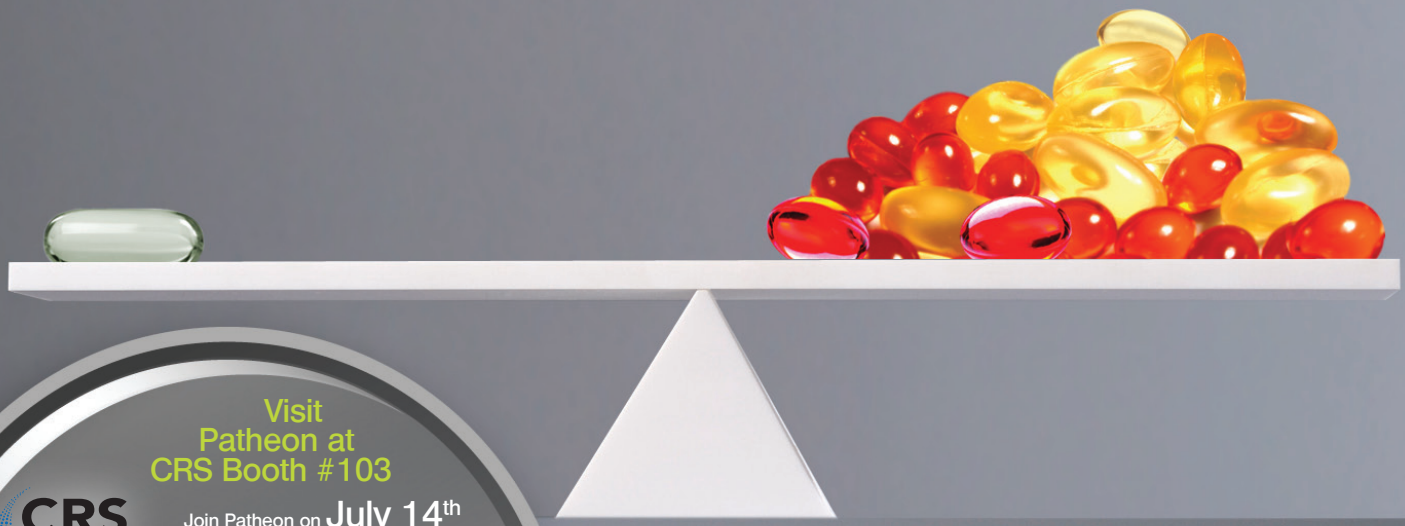
What's Inside



Does cost make you think twice about softgels?



Visit
Patheon at
CRS Booth #103

CRS Leading Delivery Science and Technology

Join Patheon on July 14th for Two Workshops:

Formulation and Process Considerations in the Development/Scale Up of Osmotic Dosage Forms. Chaired by Don Barbieri, Patheon and Karen Coppens, Dow Wolff Cellulosics.

Setting Release Specifications for *in vitro* Testing of Controlled Release Dosage Forms. Chaired by Bob Stagner, Patheon.

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CRS Newsletter

Leading Delivery Science and Technology

Vol. 29 • No. 3 • 2012

Table of Contents

Advertisers' Index

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The CRS Newsletter is the official newsletter of the Controlled Release Society. The newsletter is published six 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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Contact dwoodard@scisoc.org for information about exhibiting, advertising or other visibility opportunities.

Yvonne Perrie
Aston University, School of Life and Health Sciences
Aston Triangle, Birmingham, U.K.

Darth Vader as a Manager

Dear Reader,

Within this issue, we have an interesting line-up of articles and updates from CRS, including the schedule for our forthcoming Annual Meeting & Exposition in Québec City, Canada, which runs from Sunday, July 15, to Wednesday, July 18, with workshops preceding the meeting on Saturday, July 14. As always, there is a great selection of speakers, and you can use the CRS Annual Meeting Mobile App to ensure you get everything you want out of the meeting. It is always nice to go to a conference and get away from some of the daily grind and management that can overshadow our research. However, unfortunately, love it or hate it, there is no avoiding it; even as scientists, we all end up either managing or being managed, and generally both.

Whilst good project management can be pivotal to research programmes, management can often mean we are periodically exposed to management jargon (to put it in polite terms). To consider the impact this has on us, let's all go into breakout groups and bullet point our thoughts before feeding them back to the wider group; this will be integral to squaring the circle and passing through our gateways, blah blah blah. Need I continue? We have all been subjected to this mind-numbing terminology at some point, which generally kills time in meetings and doesn't really change outcomes but is overall quite harmless. However, there is also the less subtle and bullish type of management code that can be adopted, such as:

- *No one likes change*—use this when you want to push through an idea no one agrees with.
- *We need to work smarter*—use this to stop people complaining about workloads (as overworked people must not be smart).
- *Paradigm shift*—use this to scrap any current plans/objectives without further justification.
- *Empowerment*—use this to off-load big decisions and tasks onto other people.

Notwithstanding this issue of jargon, should scientists have more training in management? Do we have what is needed to be good managers? Perhaps the most extreme manager we could consider is Darth Vader. His particular management style allowed him to rise to the second-highest position in the largest corporate body in the galaxy, with unlimited budget and resources. His particular techniques included fear (basically "it's my way or the highway"), punishment of incompetence (normally by death), intolerance to dissent (choke anyone not in agreement with you), and identifying strong talent and asking them to join you (if they don't, kill them). This is certainly an interesting strategy, but one that may result in dwindling research teams, though unlimited resources and budget would be nice. However, perhaps instead we would be better to turn to the "People in the News" section compiled by Steven Giannos for more productive inspiration. Here Steven outlines the impressive achievements of Tejal Desai, who is being honoured with the prestigious Dawson Biotechnology Award. Steven also outlines the new appointments in ACT, Intarcia, and Hovione, each of whom has a notable track record. Steven also produces our "In the News" section for each issue of the newsletter, which is the backbone of our newsletter. If you have not read it before, it is certainly worth a read.

Best regards,
Yvonne Perrie ■

Martyn C. Davies
University of Nottingham
Nottingham, United Kingdom

Building Blocks

The past few years have been a time of growth for CRS as a society. We have sought to develop a stronger foundation for CRS—improving the governance structure and developing new and more streamlined processes. As the natural next step, with strong leadership in place, we have developed the next layer of blocks—a new strategic plan.

We have taken great care while developing this plan—it has been in development for more than a year and half, with work starting on it by the Board under the direction of Mark Tracy. We are fully aware that delivery science is a growing discipline but that we also face the challenges of economic uncertainty around the world. That is why we have scanned the horizon and worked to create a strategic plan that not only looks at present needs but also positions the organization for years to come. We have goals for 2015 and beyond. We believe this forethought will help us continue to build on the successes of the past few years.

The new strategic plan has goals for:

- Communications
- Finances
- Governance
- International development
- Maintaining leadership within delivery science and technology
- Membership
- Translational/regulatory activities
- Volunteer recruitment

You will be hearing details about all areas of the strategic plan in the upcoming months and at the CRS Annual Meeting & Exposition in July. However, there are a few areas I would like to address.

First, as part of building strong governance, the Board has taken a close look at the role of committees. In building the new strategic plan, existing committees are being recruited to help achieve the society's goals and be part of the fundamental structure of the society. Specific charges were developed for each committee, which were sent along with other details to the committees in June. Expectations and deliverables have been more clearly defined. The new strategic plan also requires the committees to work more closely with each other and with the Board, intertwining the efforts of many committees to better support the society. Finally, the reporting structure for the committees has been improved, with a cleaner way to report and shifting the timing to ensure tasks are completed to keep projects moving forward.

In addition, new committees are being developed, and some current committees are being transitioned. A visible change you will notice at the upcoming annual meeting is the transition of the Board of Scientific Advisors to the Emerging Issues and Trends Advisory Committee (EITAC). This name change was made to better reflect the core activity of the EITAC annual review and reporting of key trends and areas of future focus.

The CRS Annual Meeting & Exposition is the biggest society event held each year, and it is the primary source of income for the society. As part of the new strategic plan, how we plan for the annual meetings will be changed. We will continue to have an annual meeting program committee, which works on the programming for the current and immediately upcoming meetings. However, the new structure calls for the Annual Meeting Committee, which is charged with looking at the meeting in the long term. They are to ensure that the annual meeting provides the latest science and technology, emerging trends, networking opportunities, and exhibition in the most cost-effective manner.

CRS is committed to providing members access to the latest delivery science and technology year-round and to promoting the advancement of our field. To help meet this purpose, there are many more changes set to take place—many more building blocks—which will be discussed at this year's annual meeting and in future newsletters and other communications. We now have a strong platform to take the society forward in the years to come, and I am excited about what the future will bring for CRS! ■

C'est Presque Ici—It's Almost Here!

The 39th Annual Meeting & Exposition of the Controlled Release Society

July 15–18, 2012 • Centre des congrès de Québec • Québec City, Canada

Smart Materials—From Innovation to Translation

The 39th Annual Meeting & Exposition of the Controlled Release Society will be held in just a few weeks. This is the premier event for delivery science and technology. The CRS Annual Meeting & Exposition brings together top delivery scientists from around the world, giving attendees access to the latest research and the brightest minds in the field. Use the following pages to plan your time at the annual meeting. *If you're not registered yet, now is the time*! Online registration closes July 9. Register now to join the leaders in delivery science in beautiful Québec City!

Daily Schedule

For a complete schedule, visit www.controlledreleasesociety.org/meetings.

Saturday, July 14

08:00 – 12:00	**Educational Workshop:** Formulation and Process Considerations in the Development/ Scale Up of Osmotic Dosage Forms*
08:00 – 17:00	**Educational Workshop:** Critical Appraisal of EPR Effect and Intratumoral Distribution of Nanomedicine*
08:00 – 17:00	**Young Scientist Workshop:** Mucosal Drug and Gene Delivery: Barriers and Opportunities
13:00 – 17:00	**Educational Workshop:** Setting Release Specifications for *In Vitro* Testing of Controlled Release Dosage Forms*

Sunday, July 15

08:00 – 12:00	**Young Scientist Workshop:** Professional and Self Development for Young Scientists and Protégés—Time Management
09:00 – 12:30	**Releasing Technology Workshops**
11:30 – 12:30	First Timers' Meeting
12:30 – 14:00	**Young Scientist Roundtable:** Entrepreneurship: A Journey from Conception to Commercialization
12:30 – 17:30	**Educational Workshop:** Preserving and Enhancing Vision via Ophthalmic Drug Delivery*
13:00 – 15:10	**Soapbox Sessions**
13:00 – 17:30	CRS Central Open
15:30 – 17:30	**Industry Roundtable:** Game-Changing Innovation
17:30 – 19:30	**Exposition Grand Opening and Welcome Reception**
17:30 – 19:30	Poster Viewing Hours

Monday, July 16

07:00 – 08:00	Get Up! Get Educated! Interface of Biomaterials Elucidated
08:00 – 09:30	**CRS Opening Session**
09:30 – 10:30	Poster Session 1 (*authors present*)
09:30 – 10:30	Exposition Open
09:30 – 17:00	CRS Central Open
09:30 – 17:30	Poster Viewing Hours
10:30 – 12:00	**Scientific Sessions** • Bioactive Materials: Biomaterials • Bioactive Materials/C&DP: Imaging Diagnostics for Material Characterization • C&DP: Fragrances and Flavors • Mini-Symposium: Active Targeting vs. Passive Targeting • Veterinary: Protein and Peptide Therapeutics for Animal Patients
11:30 – 13:30	Mentor-Protégé Meet and Greet
12:00 – 13:30	Exposition Open
13:30 – 14:45	**Plenary Session:** Donald A. Tomalia
15:00 – 16:30	**Scientific Sessions** • Bioactive Materials: Nanomedicines • Bioactive Materials: Oral Controlled Release • Bioactive Materials/Veterinary: Protein and Vaccine Delivery • C&DP: Hydrogel Delivery Systems in Consumer Products • Mini-Symposium: Recombinant Polymers—Macromolecules from Microbes
16:30 – 17:30	Poster Viewing and Exposition Happy Hour
17:30 – 18:30	Preclinical Sciences & Animal Health Get-Together
21:00 – 22:30	Young Scientist Networking Evening*

**Additional fee applies*

Tuesday, July 17

07:00 – 08:00 Get Up! Get Educated! How to Get Published in *JCR*—Editor's and Publisher's Views
07:00 – 16:00 Poster Viewing Hours
08:00 – 09:30 **Plenary Session:** Molly Shoichet
09:30 – 10:30 Poster Session 2 (*authors present*)
09:30 – 10:30 Exposition Open
09:30 – 15:30 CRS Central Open
10:30 – 12:00 **Scientific Sessions**
- Bioactive Materials: Intracellular Processes
- Bioactive Materials: DNA and RNAi Delivery
- Bioactive Materials: Drug Delivery to the Brain
- C&DP: Consumer and Industrial Applications of Nanoparticle Technology
- Mini-Symposium: Morphologies and Cell Responses

12:00 – 13:30 Women in Science Luncheon*
12:00 – 13:30 C&DP Division Luncheon*
12:00 – 16:00 Exposition Open
13:30 – 15:00 **Scientific Sessions**
- Bioactive Materials: Inorganic Nanosystems
- Bioactive Materials: Oncology and Tumor Targeting
- Bioactive Materials: Transdermal Drug Delivery
- C&DP: Nutraceuticals and Functional Foods
- Mini-Symposium: Smart Textiles

15:00 – 16:00 Poster Session 3 (*authors present*)
16:00 – 17:30 **Roundtables and Focus Groups**
- Nanomedicine
- Ocular Drug Delivery
- Oral Drug Delivery

18:30 – 22:00 **CRS President's Banquet***

Wednesday, July 18

08:00 – 11:30 CRS Central Open
07:30 – 12:00 CRS Registration Open
08:00 – 09:30 **Scientific Sessions**
- Bioactive Materials: Stem Cell and Regenerative Medicines
- Bioactive Materials: Theranostics and Cancer Nanotechnologies
- Bioactive Materials: Translational Nanomedicine
- Bioactive Materials/C&DP: Nanofibers/ Nanoparticles
- Mini-Symposium: New Chemistries—Click It, Fit It, Test It

09:45 – 11:00 **Plenary Session:** Vladimir P. Torchilin
12:00 – 16:00 **Educational Workshop:** Considerations for Future Regulatory Submissions of Transdermal Products *
Cosponsored by AVEVA Drug Delivery Systems

Build Your Networks for Success: CRS Innovation Sunday

Sunday, July 15

Cosponsored by Pfizer

Science • Connections • Development • Commercialization

Build your networks for success during the third annual CRS Innovation Sunday! Designed to connect you with people, research, companies, and novel technologies that address challenges in delivery, come to Sunday's interactive program open to asking questions and finding answers.

Releasing Technology Workshops

Are you interested in learning more about a company's research and products? Interested in a new technology from the company that developed it? The Releasing Technology Workshops (RTWs) give you the opportunity to gain in-depth information presented by the hosting company. Participants as of press time:

Agilent Technologies
Ashland
Catalent Pharma Solutions
EMD Millipore
Gattefossé SAS
Grünenthal GmbH
MedinCell SA
OctoPlus and Mirna Therapeutics
SOTAX Corporation
Team Consulting Ltd.

Soapbox Sessions

What's new in delivery science? Come to the program where presenters "get up on their soapbox" to give you a quick glimpse of some of the most innovative technologies and products in development today. Linger to network and exchange business cards with the presenters as you enjoy refreshments sponsored by Catalent Pharma Solutions.

Industry Roundtable: Game-Changing Innovation

Moderator: *Baruch Harris, Enlight Biosciences, U.S.A.*

Speakers: *Julia Rashba-Step, Pfizer, U.S.A., and Ronald L. Smith, Merck & Co., Inc., U.S.A.*

Game Changer

Definition: A visionary. A person or idea that transforms the accepted rules, processes, strategies, and management of business functions.

From Incremental to Exponential Innovation: Game Changing!

If most innovation is incremental and game changers spark exponential innovation, how do you find a game changer? How do you identify one, or a dozen, game changers for your organization? Who has the skills to put the new rules into play? How do you recognize, integrate, and fully benefit from a game changer arriving from an entirely different discipline? Through panels, presentations, and audience participation, gain insight for *game-changing* strategies, nontraditional partners, and relationships.

CRS Annual Meeting continued

Exposition Grand Opening and Welcome Reception

Sunday culminates in the Exposition Hall, where thousands of products, services, and still-to-be-developed innovations can be discussed one-on-one while enjoying a glass of wine or beer and some of Québec City's finest hors d'oeuvres.

Leading Experts to Deliver Plenary Addresses

This year's plenary speakers offer their insights on a variety of innovative and thought-provoking subjects in delivery science and technology.

Molly Shoichet
University of Toronto, Canada

Dr. Shoichet is an expert on the study of polymers for drug delivery and regeneration, which are materials that promote healing in the body. She has published close to 400 papers, patents, and abstracts, has given over 250 lectures worldwide, and currently leads a laboratory of 25 researchers and has graduated 75 researchers over the past 15 years.

Dr. Shoichet will present **"Drug and Cell Delivery Strategies to the Central Nervous System" on Tuesday, July 17**. Her presentation will describe three regenerative medicine strategies for treatment of spinal cord injury, stroke, and blindness. In each strategy, delivery to the tissue is key to success, necessitating a local delivery strategy.

Donald A. Tomalia
NanoSynthons LLC, U.S.A.

Dr. Tomalia is the pioneering scientist and inventor associated with the discovery of dendrimers and polyoxazolines. In addition to being the CEO and founder of NanoSynthons, Dr. Tomalia currently serves as an associate editor, *Nanomedicine* (Elsevier); editorial advisory board member, *Bioconjugate Chemistry*; faculty member, *Faculty 1000 Biology*; director, National Dendrimer and Nanotechnology Center; distinguished visiting professor, Columbia University; and external faculty, University of Wisconsin–Madison (School of Pharmacy).

Join Dr. Tomalia on **Monday, July 16, for "Dendrimer-Based Nanomedicine—The Present and Future."** Dr. Tomalia will overview the current use of abiotic dendrimers in a variety of nanomedical applications, including nanodiagnostics, drug delivery, imaging, and nanopharmaceuticals, and look at important dendrimer properties such as polyvalency, nanoscaffolding, and nanocontainer properties that have underpinned the development of many current commercial products.

Vladimir P. Torchilin
Northeastern University, U.S.A.

Professor Torchilin has published more than 350 original papers and more than 150 reviews and book chapters, written and edited 10 books, and holds more than 40 patents. He is editor-in-chief of *Current Drug Discovery Technologies* and of *Drug Delivery* and is on the editorial boards of many journals, including *Journal of Controlled Release* (review editor). In 2005, he was president of the CRS.

Professor Torchilin will discuss **"Targeting Cell Organelles" on Wednesday, July 18**. He will discuss coupling of cell-penetrating peptides (CPP) to various molecules, including peptides and proteins, or even to nanoparticles, to dramatically facilitate their intracellular delivery. The combination of targeted delivery of drug-loaded nanocarriers to target cells and their subsequent delivery inside cells might significantly improve the efficiency of therapy.

Hear Professor Torchilin introduce his plenary at www.controlledreleasesociety.org/meetings/annual/program/Pages/PlenarySpeakers.aspx.

Have You Planned Your Stay?

The CRS hotel reservation deadline was June 15; however, all CRS-contracted hotels are still accepting reservations on an availability/rate basis. Visit www.controlledreleasesociety.org/meetings/annual/hotel/ for updates and booking instructions for each of the annual meeting hotels. Book your hotel room now to ensure availability!

Easy Networking at the CRS Annual Meeting with CRS Connect

You come to the meeting to get the latest in delivery science and to make targeted connections with scientists and companies in the field. This year, CRS is making it easier than ever to reach those individuals with the new CRS Connect.

How Does It Work?

As a CRS Annual Meeting & Exposition attendee, you are able to access CRS Connect, available in mid-June, via the CRS Annual Meeting Mobile App or the internet. If you are looking to contact a specific meeting attendee, simply search for their name through the CRS Connect program. If you wish to make contact with a specific company, simply search for the company and see who is representing that organization at the meeting. You can also search specific field of interest information for attendees that have the same research interests as you or your company.

Once you identify the individual you wish to contact, click on their name to send them a private message to which they can respond. In addition to private messages, you can also send appointment requests. All of this takes place through CRS Connect while maintaining full privacy, as personal contact information is never shared.

Once contact has been made, you are then able to set up professional, one-on-one meetings that best fit your schedule during the annual meeting. CRS has designated an area in the Exposition Hall in which CRS Connect meetings can take place, although utilizing this space is not a requirement.

Once CRS Connect is available to attendees, specific instructions will be sent out to assist you with this easy-to-use networking tool. Please feel free to contact Megan Pagel, CRS Program Manager, at mpagel@scisoc.org with any questions or comments regarding CRS Connect.

Young Scientist Events at the 2012 CRS Annual Meeting & Exposition

Are you a student, postdoc, early-career scientist, or new professional in delivery science? If so, take part in this year's Young Scientist events and benefit from programming created specifically for you!

The following events are organized by the CRS Young Scientist Committee and the CRS Mentor-Protégé Subcommittee. The events are programmed specifically to uphold the mission of the CRS Young Scientist Committee—to stimulate educational opportunities, provide career development and training, and offer inexpensive and innovative networking events.

Get Up! Get Educated!

Interface of Biomaterials Elucidated

Monday, July 16

Are protein adsorption, cellular adhesions, immune responses, or inflammatory reactions fogging the surface of your biomaterials? Wake up to this session illuminating the interactions of biomaterial surfaces with the complex biological milieu. This session will cover interactions and forces at the interface of materials with proteins, cellular membranes, organelles, and DNA. Learn how these interactions can determine the fate of biomaterials and about novel approaches to circumvent or advantageously utilize these interactions.

Young Scientist Workshops

Young Scientist Workshop #1: Mucosal Drug and Gene Delivery: Barriers and Opportunities

Saturday, July 14

This is a workshop not to be missed by young scientists. Local drug and gene delivery offers various advantages; however, many local administration routes involve delivery to the dynamic and complex mucosa. The mucosal layer and underlying membrane are involved in the absorption and secretion of molecules and are important targets for vaccine development and treatment of diseases. In this workshop, all relevant barriers will be discussed, and successful approaches for various administration routes will be presented.

Young Scientist Workshop #2: Professional and Self Development for Young Scientists and Protégés—Time Management

Sunday, July 15

Effectively managing time is extremely important for young scientists. This workshop will cover time-management skills essential for coping with busy schedules, planning and executing projects, and meeting deadlines. Special emphasis will be on time-management techniques and on utilization of those techniques to function effectively under intense pressure. Applying the skills learned in this workshop will ensure optimal effectiveness when undertaking tasks. Above all, young scientists will gain a clearer understanding of the value of time.

How to Get Published in *JCR*—Editor's and Publisher's Views

Tuesday, July 17

Speakers: **Kinam Park,** Purdue University, U.S.A., and **Jaap van Harten,** Elsevier, The Netherlands

Getting your work published in any highly ranked journal is a matter of presenting good research. Each manuscript needs to be tailor-made for a specific journal. In this workshop, the editor-in-chief and publisher of *JCR* will explain and give opportunity for discussion on the editorial decision-making process of *JCR*, including main reasons for acceptance and author–editor–reviewer communication. Get up! Get educated! Get more successfully published!

Roundtable

Entrepreneurship: A Journey from Conception to Commercialization

Sunday, July 15

Discover a new way to use your lab skills and make a change for your organization or yourself! Every great company starts with a novel idea that was recognized and developed at the right time. You might have an innovative and exciting idea, but then what? This roundtable discussion will bring together thought leaders from academia, industry, legal, and finance to discuss the whirlwind journey from conception to commercialization and how scientists can recognize and seize opportunities for starting a business.

Networking and Social Events

Young Scientist Mentor-Protégé Meet and Greet

Monday, July 16

This is a must-attend session for anyone enrolling in the 2012–2013 CRS Young Scientist Mentor-Protégé Program. You will be introduced to your mentor and be given the opportunity to meet face-to-face to discuss how you are going to interact with your mentor over the next 12 months, what your career ambitions are, and what you want out of the program. Attend this meeting for your first CRS mentorship experience.

Young Scientist Networking Evening

Monday, July 16

Enjoy an evening of interacting with colleagues when you attend the Young Scientist Networking Evening and dessert reception at the only revolving rooftop restaurant in Québec City, L'Astral Restaurant at Loews Hôtel Le Concorde. Enjoy French Canadian desserts, crepes, coffee, and tea. Loews Hôtel Le Concorde will be offering a dinner special for those who wish to dine at L'Astral Restaurant before the networking event. *Advance registration and payment required. Ticket price is $50.* For more information on CRS Young Scientist events, visit the CRS Annual Meeting & Exposition website.

Not to Be Missed!

Here is a list of great opportunities to hear world-renowned speakers, meet with colleagues, and enjoy Québec City's famous cuisine.

Exposition Grand Opening and Welcome Reception

Sunday, July 15

Preclinical Sciences & Animal Health Get-Together

Monday, July 16
Sponsored by Pfizer Animal Health

Poster Viewing and Exposition Happy Hour

Monday, July 16
Cash bar only.

Young Scientist Networking Evening

Monday, July 16
Organized by the Young Scientist Committee
Sponsored by Upsher-Smith Labs

C&DP Division Luncheon

Tuesday, July 17
Sponsored by Coating Place, Inc., Fleet Laboratories, and Ronald T. Dodge Co.

Women in Science Luncheon

Tuesday, July 17
Sponsored by *Gattefossé*
Moderator: Diane Burgess, University of Connecticut
This popular event provides an insightful and informative presentation relevant to women in science and includes ample networking time to meet with your fellow women scientists in Québec City.

CRS President's Banquet

Tuesday, July 17

Kinam Park

The President's Banquet is a premier opportunity to meet and dine with your colleagues from around the world. Our featured speaker will be the ever-popular Dr. Kinam Park, Showalter Distinguished Professor of Biomedical Engineering and Professor of Pharmaceutics, Purdue University, U.S.A. His areas of expertise include nano- and microparticles, polymer micelles, drug-eluting stents, extracellular matrix, fast-dissolving tablets, and smart hydrogels. Don't miss this rare opportunity to be entertained and educated by one of CRS's most distinguished members. Join us for an elegant evening showcasing French Canadian cuisine and culture at the Hilton Québec.

Register to attend the C&DP Division Luncheon, Young Scientist Networking Evening, Women in Science Luncheon, and President's Banquet when you register for the meeting. Already registered? Simply log in to your registration and add an event.

So Much Science—So Little Time!

There are so many great scientific sessions packed into this year's annual meeting that it may be difficult to attend every session you want to attend. Note that many of the sessions will be recorded and available after the meeting as online webcasts, which are free for CRS members to access. Watch for webcasts to be posted throughout 2012.

Registration Is Still Open!

Online registration will close July 9; after that time, you can register onsite in Québec City.

www.controlledreleasesociety.org/meeting

Come to the CRS Exhibition

Focused. Effective. Unique.

The CRS Exposition Hall is the venue for the targeted business of delivery science and profitable collaboration. As an attendee or an exhibitor, the CRS Exposition Hall presents you with new opportunities to discover. Kicking off with the Sunday evening Exposition Opening and Welcome Reception, the Exposition/Poster Hall will also be open Monday and Tuesday as the central hub for poster viewing, program breaks, and refreshments. Many thanks to the CRS Café Sponsors (*) for providing complimentary beverages.

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American Pharmaceutical Review
Apricus Bio/NexMed U.S.A.*
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Investigating Cationic Vector-RNA Complexation by All-Atomic Molecular Dynamics Simulations

Defang Ouyang,[1,2] Harendra S. Parekh,[3] and Sean C. Smith[4]

Introduction

Gene therapy is a promising and rapidly developing medical approach, aiming to cure diseases of genetic origin by correcting the over- or underexpression of biologically relevant genes. Although significant progress has been made toward realizing this medical approach, it is hampered by a fundamental lack of safe and effective vectors. To address this shortfall, it is first important to appreciate the obstacles that stand in the way of effective delivery. For a gene to efficiently transfect a host cell population *in vivo*, it must first overcome five major barriers: extracellular physical and biochemical degradation, the cell membrane, endosomal-lysosomal degradation, the dissociation of the gene from its vector, and the nuclear membrane (nuclear delivery applies to plasmid DNA [pDNA] only).[1] In the case of RNA interference (gene silencing using siRNA), however, the cytosol is the target site for delivery; hence, passage across the nuclear membrane is not necessary. Given that the association of carrier-RNA is a prerequisite of any gene delivery system, understanding the molecular mechanisms of the interaction is expected to facilitate the rational design of vectors.

Molecular modeling is a specialized form of computer modeling, which is used to model or mimic the behavior of molecules. Molecular modeling is based on molecular mechanics, which uses Newtonian mechanics to model molecular systems.[2] A distinguishing feature of the technique is to describe molecular systems at the atomistic level. In the recent past, molecular modeling was widely used in computational biology, computational chemistry, material sciences, and rational drug design.[2] From a theoretical aspect, molecular modeling techniques also offer considerable potential to study the drug/gene delivery mechanism on a molecular level. Thus, we employed molecular dynamics (MD) simulations to shed light on this phenomenon—the complexation of siRNA with vector.

Conformational Fluctuation of Short-Strand Duplex RNA Molecule in Water

Before we embarked on studying the intricate mechanics leading to RNA-vector complexation, we first used molecular dynamics simulations to study the conformational structure and dynamics of a 21-base pair RNA sequence (as shown in Figure 1A) in the presence of counterions and explicit water.[3] This study added a dynamical perspective to the solid-state structural information that has been derived from X-ray data for RNA molecules. After the analysis of the three main structural descriptors (major groove width, inclination, and the number of base pairs in a helical twist), over 30 ns simulation times we revealed a flexible structure in aqueous solution with fluctuations in the values of these structural parameters. The apparent structural flexibility observed in our simulations is likely to bear ramifications for the interactions of RNA with biological molecules (e.g., proteins) and nonbiological molecules (e.g., nonviral gene delivery vectors).

Single Polymer-RNA Complexation in a Neutral pH Environment

Next, we investigated the complexation of RNA with a single cationic polymer in a neutral (pH) environment.[4] The simulations revealed detailed molecular-level pictures of the structures and dynamics of the RNA-polycation complexes, as shown in Figure 1B. Estimates for the binding free energy indicated that electrostatic contributions were clearly dominant, followed by van der Waals interactions. The binding free energy between the 8^+ polymers and RNA was found to be greater than that of the 4^+ polymers, a finding that was in general agreement with previously published data. The binding free energies provide an effective index of the ability of the polycationic carrier to bind the nucleic acid and also carry implications for the process of gene release within the cytosol.

The Effect of pH on PAMAM Dendrimer-RNA Complexation: Endosomal Considerations

Endo-lysosomal degradation is considered as a significant bottleneck to (nonviral) gene delivery *in vivo*.[1] Previous reports claimed that carriers possessing a mixture of primary, secondary, and tertiary amines are able to buffer the acidic environment within the endosome, allowing for timely release of their contents, leading to higher transfection rates.[5] To mimic conformational changes of RNA-vector complexation in the degradative environment within maturing "late-endosomes," we compared the complexation of RNA with low-generation

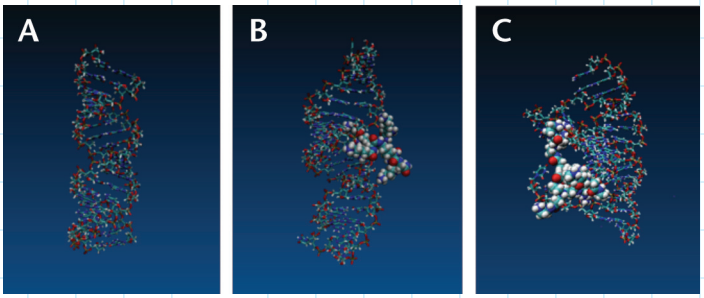

Figure 1. *(A) Snapshot of A-RNA. (B) Snapshot of 8^+ G1 PAMAM dendrimer–RNA complex at neutral pH after 18 ns. (C) Snapshot of 14+ G1 PAMAM dendrimer–RNA complex at low pH after 18 ns (water molecules and counterions are omitted for clarity).*

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polyamidoamine (PAMAM) dendrimers (G0 and G1) at both neutral and acidic pH.[6] Our simulations revealed that the time taken for the dendrimer–gene complex (dendriplex) to reach equilibrium was appreciably longer at low pH, and this was accompanied by more compact packaging of the dendriplex (as shown in Figure 1C), as compared with simulations performed at neutral pH (as shown in Figure 1B). Larger absolute values of calculated binding free energies of the dendriplex at low pH indicated a higher dendrimer–nucleic acid affinity in comparison with neutral pH. These novel simulations mimicked the endosomal environment and provided crucial input of direct relevance to the well-accepted "proton sponge theory."[5]

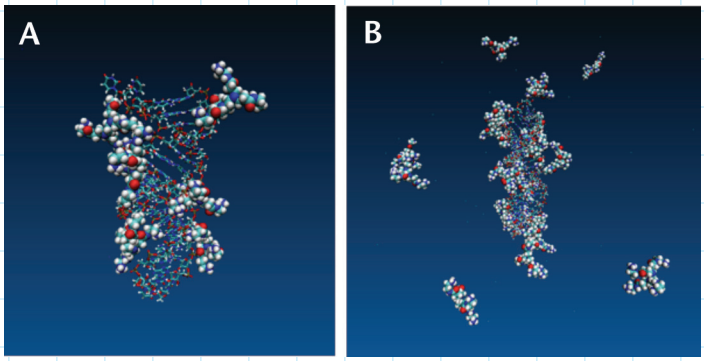

Figure 2. *(A) Snapshot of 4+ polymer-siRNA complex at 10 ns at charge ratio of 0.6/1 (molecular ratio 6/1). (B) Snapshot of 4+ polymer-siRNA complex at 10 ns at charge ratio of 2/1 (molecular ratio 20/1). Water molecules and counterions are omitted for clarity.*

Multiple Cationic Vectors-siRNA Complexation

To closely model the biological environment where differing charge ratios between the carrier and RNA would exist, we next studied the complexation of RNA with cationic carrier systems at different charge ratios by all-atomic molecular dynamics (MD) simulation.[7] At lower charge ratios, polymers bind quite effectively to RNA, whereas at high charge ratios, the complexes are saturated, and there are free polymers distant to and unable to associate with RNA, as shown in Figure 2. We also observed reduced fluctuations in RNA structures when complexed with multiple polymers in solution as compared with both free RNA in water and the single polymer complexes described previously.

Conclusion

From our extensive MD simulations and discussions, we clearly demonstrate that our novel simulations provide a much better understanding of key mechanistic aspects in RNA-polycation complexation, and thereby we expect this knowledge to advance progress toward the rational design of nonviral gene delivery systems.

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Texture Technologies Demonstrates TA.XT*Plus* Capability to Quantify Characteristics of Microspheres and Orally Disintegrating Tablets

Marc Johnson, President, Texture Technologies Corp.

Texture Technologies Corp. is the exclusive North American distributor of Stable Micro Systems's family of texture analyzers, including the TA.XT*Plus*, TA.HD*Plus*, and TA.XT*Express*. Texture Technologies has been developing methods and test techniques that quantify controlled release attributes for approximately twenty years. Among the fields that use our instruments to quantify controlled release behaviors are gels, capsules, films, tablets, powders, transdermals, bioadhesives, and granules. Each of our thousands of customers has had unique concerns, which we have solved with our instrument, software, training, custom fixtures, test methods, and applications support.

This spotlight article illustrates test techniques that use the same instrument and same software on two different products that are of interest to the controlled release industry. The first is to quantify critical parameters of gel beads and microspheres. The second is the disintegration and swelling characteristics of orally disintegrating tablets (ODTs).

Gel Beads and Microspheres

Gel beads and microspheres are used as a drug release vehicle in a variety of locations within the body. Beads and microspheres must (1) survive manufacture; (2) remain stable while stored for long periods in solution without swelling or disintegrating; (3) survive delivery, which typically involves being injected through a syringe into location; (4) adhere long enough to properly deliver their drug profiles; and (5) remain firm and adequately cross-linked to dissolve at targeted rates. The physical properties of these products that are critical to their objectives are firmness, resilience, springback, relaxation, adhesion, swelling, disintegration, and cyclic stability. Although most gel bead manufacturers measure the force to compress beads a certain percentage, many other parameters are equally relevant to product performance. Our TA.XT*Plus* texture analyzer is used by

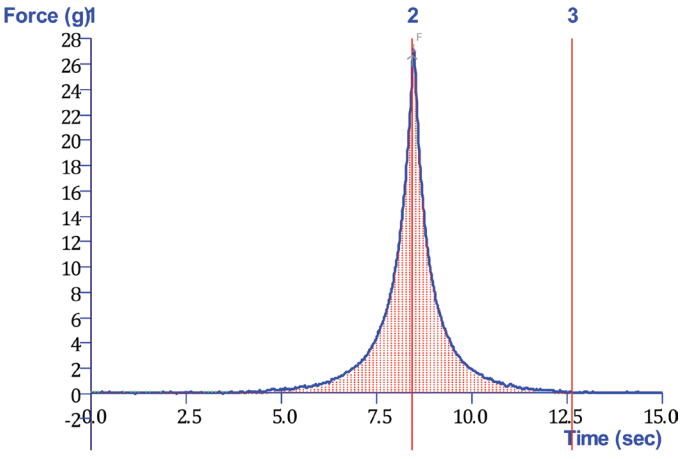

Figure 1. *This graph illustrates how microspheres react to compression and decompression. The firmness of the microsphere is measured by the initial slope of the plot and the peak force. The ratios of work and distance before and after anchor 2 are used to quantify microsphere resilience and instant springiness.*

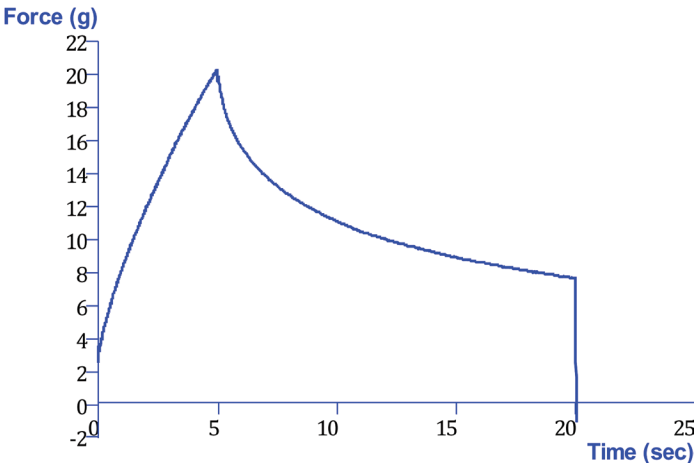

Figure 2. *This graph illustrates how microspheres relax and is an excellent metric to measure bead stability under moderate pressure.*

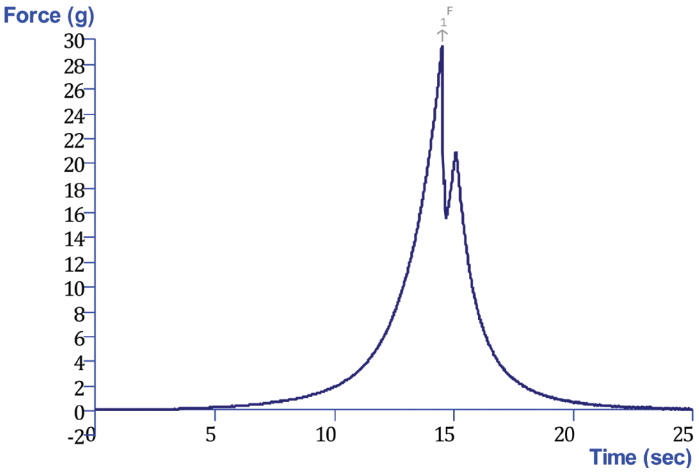

Figure 3. *This graph illustrates how microspheres burst under compression, which is an undesirable attribute since beads that have ruptured are difficult to deliver* in situ *and will underperform their design specs.*

the pharmaceutical industry to quantify the all of these critical product attributes.

Since gel beads can be extremely soft and delicate, instrument and test protocols for testing them must be very sensitive at low force levels to obtain clear, repeatable test results. In a typical configuration, an individual microsphere is isolated on a calibrated platform, and the bead is then subjected to a moderate compression. Other tests involve beads that are (1) compressed with a hold-time cycle to measure relaxation, (2) compressed under a maintained applied force for a fixed time to measure adhesive forces, and (3) subjected to repeated cyclic compressions.

Examples of the tests that can be conducted on gel beads and microspheres are shown in Figures 1–5. These tests were all conducted on microspheres that were between 350 and 500 microns in diameter.

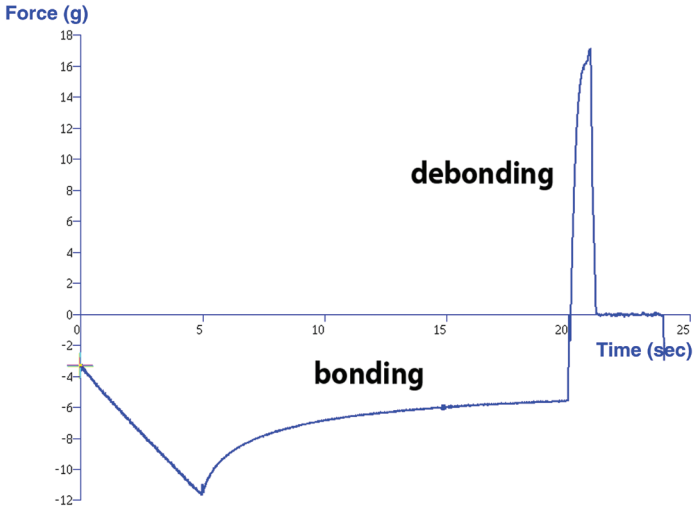

Figure 4. *This plot illustrates how the adhesiveness of microspheres can be quantified by applying a defined bond and then debonding. The Exponent software automatically calculates the area of adhesive work, the peak adhesive force, and the microsphere's relative cohesion.*

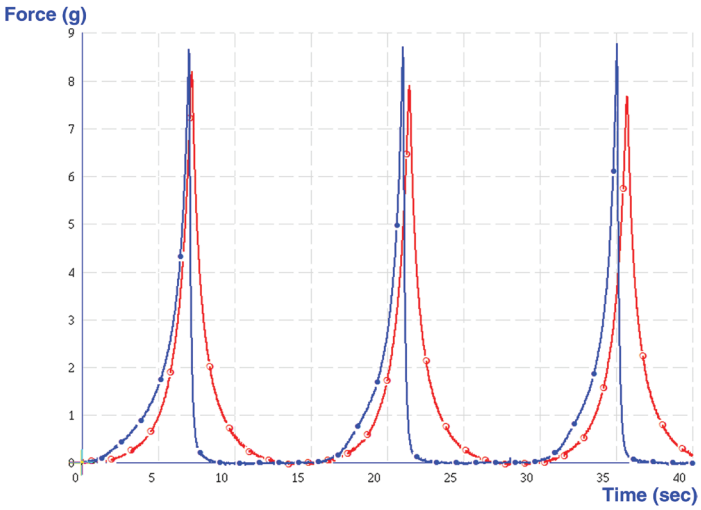

Figure 5. *This graph illustrates how cycling onto microspheres can quantify their strength and whether they fatigue under repeated stresses.*

Because these test methods generate very repeatable results, bead and microsphere manufacturers are able to quantify the performance impact of very impact-subtle formulation and storage differences.

Disintegration of Tablets

ODTs must be strong enough to survive manufacturing and shipping, yet friable enough to instantly dissolve and release their active ingredients once placed in the mouth. Some ODT formulations swell before eventually dissolving, and others simply start dissolving. Traditional U.S. Pharmacopeia disintegration tests generate a single time value for disintegration in the submerged basket and are not always sensitive enough to discern disintegration rates of the new types of ODTs on the market. Our ODT test methods using the TA.XT*Plus* texture analyzer quantify many critical product attributes: onset time of swelling; rate, magnitude, and duration of swelling; onset time of disintegration; disintegration rate; and magnitude and duration of disintegration. These attributes are all marked on a typical disintegration plot in Figure 6.

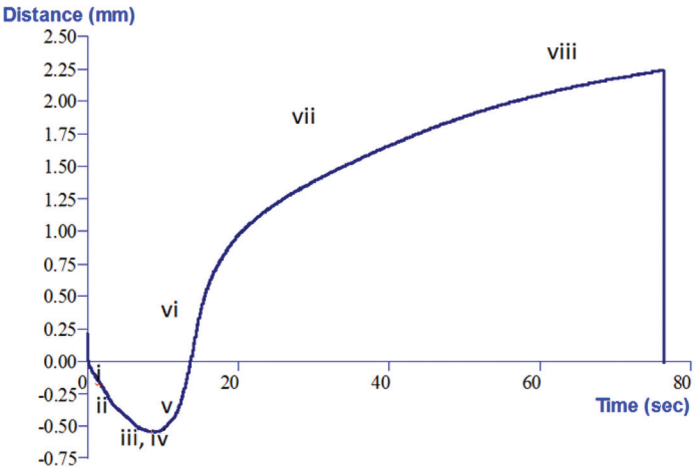

Figure 6. *This annotated graph illustrates the (i) onset time it takes for an ODT to swell, (ii) rate of swelling, (iii) magnitude of swelling, (iv) duration of swelling, (v) onset time to disintegration, (vi) disintegration rate, (vii) magnitude of disintegration, and (viii) duration of disintegration. All of these attributes are quantifiable from a single test.*

The TA.XT*Plus*'s ODT methods can be programed to conduct the tests at different pressure levels, using different amounts of aqueous solutions, with different product geometries, and at different temperatures. The flexibility of our instrument and the degree of customization enabled by the software's programmability allow ODT manufacturers to quantify subtle formulation and processing differences.

An example of the TA.XT*Plus*'s ability to provide detailed information on critical product attributes is shown in Figure 7, which compares several ODTs. One of the products started disintegrating immediately at a fast rate. Several other formulations started disintegrating immediately, but did so at different disintegration rates and to different total magnitudes. The magnitudes are dif-

Spotlight continued on page 14

Spotlight continued from page 13

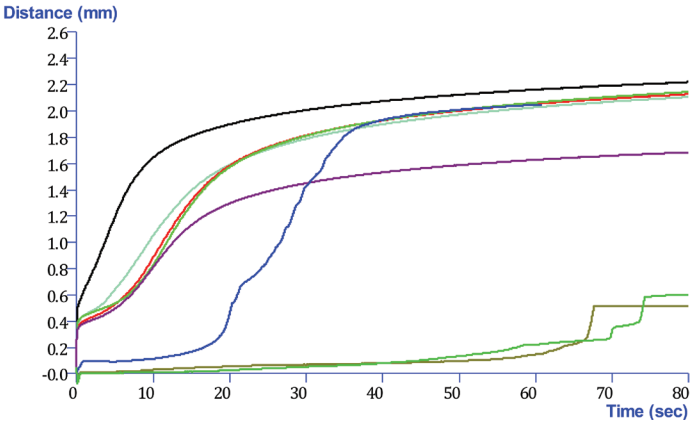

Figure 7. *This plot is an overlay of similarly sized tablets that disintegrate at different rates and magnitudes.*

ferent because the test picked up that some of the ODT excipients did not disintegrate in this time scale. One sample began to disintegrate after 10 seconds but at a slow rate until 18 seconds. Two ODT formulations disintegrated slowly over 30–60 seconds, then accelerated until 75 seconds, and finally stabilized by 80 seconds. In those final two instances, the probe ended up slightly compressing a pile of undissolved excipients. None of these formulations swelled before they started disintegrating. All of the observable differences were quantified by our Exponent software package. In comparison, traditional U.S. Pharmacopeia disintegration tests would instead give similar values for each of these ODTs.

These two types of tests, which were conducted on the TA.XT*Plus* texture analyzer, illustrate the instrument's flexibility in measuring physical properties important to the pharmaceutical industry. The instrument provides more information than traditional methods and offers extremely repeatable test results on critical performance attributes. The same instrument and software can be used to quantify critical physical parameters for granules, powders, tablets, gels, creams, lotions, bioadhesives, patches, films, and capsules. In all instances, scientists can quantify more attributes than with traditional methods and thus can truly see the subtle differences between their formulations.

For more information please, contact Marc Johnson, President, Texture Technologies Corp., 978-468-9969, marcj@texturetechnologies.com, or visit our website at www.texturetechnologies.com. ■

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Tram Dang Chosen as Sung Wan Kim Postdoctoral Fellowship Winner

Tram Dang of the Massachusetts Institute of Technology, U.S.A., was chosen as the 2012 Sung Wan Kim Postdoctoral Fellowship winner and will be receiving the $30,000 award from the award's namesake, Sung Wan Kim, during the 39th CRS Annual Meeting & Exposition. Tram will also present a poster during the annual meeting and will serve as an invited speaker at the 2013 annual meeting to present outcomes of her research.

Chosen from an applicant pool of extraordinary young scientists, Tram Dang currently studies in the Department of Chemical Engineering at MIT as a graduate student in the laboratories of Robert Langer and Daniel G. Anderson. Tram will be completing her Ph.D. by July 2012 with a minor in business management. For her thesis research, Tram developed new noninvasive imaging techniques to assess and understand the effects of controlled release anti-inflammatory drugs on the immunological response to biomaterials in rodent models. Her research has important applications in enhancing the efficacy of encapsulated pancreatic islets for diabetes therapy. In addition, Tram also pioneered the development of new glucose-responsive biomaterials as well as innovative microfabrication methods for tissue engineering and controlled drug delivery. Tram's work has been published in established journals such as *Biomaterials, Small,* and *Plos One* and has resulted in one patent application.

Tram aims to pursue postdoctoral research at the interface of engineering and immunology, with a focus on solving critical medical problems with clinical impacts. She writes, "I'm extremely grateful for the recognition that the fellowship selection committee has given to my graduate work and their trust in my scientific potential. I'm very honored to receive the 2012 Sung Wan Kim postdoctoral fellowship from the CRS Foundation. This is such a wonderful opportunity for me to pursue my next scientific challenge!"

About the Fellowship

Sung Wan Kim

The CRS Foundation's fellowship for 2012 honors Sung Wan Kim, University of Utah, for his leadership in delivery science. As a pioneer in drug delivery research, Professor Kim has focused on hydrogels, biodegradable drug conjugates, self-regulating drug delivery, and stimuli-sensitive polymers. He has worked extensively in medical polymers, especially blood-compatible polymers. Professor Kim is highly recognized throughout the field with multiple honors, including the CRS College of Fellows and Founders Award. ■

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Monday, July 16
13:30 Plenary and Awards • Room 303 A/B

Sung Wan Kim Postdoctoral Fellowship 2012 Award Presentation

Tram Dang

Professor Kim will award the fellowship to Tram Dang, whose work at MIT led to the postdoctoral fellowship in which she will pursue research at the interface of engineering and immunology. This award honors Professor Kim for his CRS leadership and pioneering research in delivery science.

Tsuneji Nagai Postdoctoral Fellowship 2011 A Year in Review

Soo Hyeon Lee

Soo Hyeon Lee will share research on the design of new delivery systems for gastrointestinal disease therapy with nucleic acid drug, conducted in the laboratory of Prof. Jean-Christophe Leroux at ETH Zurich in Switzerland, made possible by the fellowship honoring Professor Nagai for his CRS leadership and lifetime achievements in delivery science.

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The CRS Foundation thanks past and future donors.

In 2007 CRS established the CRS Foundation, a 501(c)(3) educational endowment to honor individuals who have made notable contributions to the Society and its technologies, and to support the scientific training of its future leadership.

Young Scientist Mentor-Protégé Corner

Padma V. Devarajan & Pirthi Pal Singh
Cochairs, CRS Young Scientist Mentor–Protégé Subcommittee

Friends and colleagues of CRS, the Young Scientist Mentor-Protégé (YSMP) Subcommittee welcomes all of you to proactively participate in the Mentor-Protégé Program. The program offers a great platform to network, a great opportunity to share experiences, and, for protégés in particular, a chance to interact and learn from global leaders in delivery science.

The CRS Annual Meeting & Exposition in Québec City, Canada, will feature a professional and self-development workshop for young scientists and protégés with a topic of time management to help attendees effectively hone skills in managing their time, and a Mentor-Protégé Meet and Greet session that will facilitate face-to-face meeting of mentors and protégés. Join us to benefit from this important platform that CRS has created for young scientists and protégés.

Read below for a response from a current CRS protégé about his experience in the CRS Mentor-Protégé Program. All mentors and protégés are invited to share their experiences. Let us all get together and grow together.

Protégé's Perspective

I am Aniket Magarkar, a Ph.D. student from University of Helsinki, Finland. A year and a half ago, I joined the faculty of pharmacy in the computational drug delivery group with Dr. Alex Bunker. With my background, including a master's in bioinformatics and experience in chemoinformatics and drug design in India, I entered into the field of pharmacy for my graduate studies.

As excited as I was to start my projects, I also was a bit skeptical, as I was entering a field in which many of my colleagues and friends were not involved. I became aware that not many pharmacy projects in the drug delivery area are focused on a computational paradigm. Thrilled with the project of investigating the role of polymers in nanotechnology with the targeting ligands for specific delivery, I began my journey to the thesis. In the project, we used the molecular dynamics to reach the conclusion that the hydrophobic nature of the polymer is responsible for the failing nanoparticle *in vivo* and *in vitro*. With the joy of my first glimpse of contribution to the field of drug delivery, I was advised to participate in the 2011 CRS Annual Meeting & Exposition in National Harbor, MD, U.S.A., by presenting my project.

Face to Face: Aniket and Padma

The CRS Annual Meeting was the first meeting I attended in the area of delivery science. I was expecting to see a wide variety of approaches that have been researched over time in the area of drug delivery. As the conference held separate activities listed for graduate students, I decided to participate in them. One was the CRS Mentor-Protégé Program. After attending the program, I must say it was a very wise decision that I made in my career. After a matching of research interests, I was accepted as a protégé by Prof. Padma Devarajan, Head of Pharmacy from the Institute of Chemical Technology, India. I was glad to be her protégé and considered myself very lucky because, being from India, I understand how difficult it is to get into the ICT, and it is almost every 12th grader's dream institute. This program gave me the opportunity to interact with her, which would not have been possible otherwise.

In talks with Prof. Devarajan at the annual meeting, she guided me through the specific doubts in my mind dealing with the scope of *in silico* experiments in the field of pharmacy. She also told me about untapped areas that can be explored with the strength of computing power, which will lessen the *in vitro* and *in vivo* efforts to test a hypothesis and accelerate the process development of drug delivery methods. Prof. Devarajan also advised me concerning a future career in industry and academia, put me in contact with personnel from Piramal Healthcare R&D division, and brought my attention to the fantastic research opportunities opening up in India.

During my holidays, I visited India this winter, and I was hoping for a meeting with Prof. Devarajan. Even after a break in conversation, upon meeting we resumed where we left off with the same enthusiasm. Prof. Devarajan provided me the opportunity to interact with the graduate students in her lab, which was very important for me as I could ask them stupid questions, which we often hesitate to ask professors. The time that I have already spent interacting with Prof. Devarajan has not only been informative but also joyful. Thank you, CRS, for providing me such a wonderful opportunity, and I am sure the mentor-protégé relationship will continue.

Lunch with Prof. Devarajan in India.

Aniket is enjoying this new experience. In case you wish to share your thoughts and experiences, please write to us at pvdevarajan@gmail.com or pirthi@gmail.com.

Register now for the 2012 CRS Annual Meeting & Exposition. We look forward to meeting you in Québec! ■

CRS Election Results

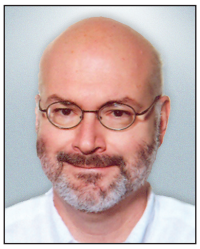
The votes have been tallied, and the results are in for this year's CRS election. This was a landmark year, as we changed to the new Board structure, approved in 2011, and the new nominating process. This new structure expands the Board from eight members to 11, allowing a nimble board that can represent the many interests of our membership. The new nominating process, led by the Nominating Committee headed by Mark Tracy, allowed more opportunities for members to participate in the process, with an open nomination period and the chance to write in a candidate. The new members, listed below, will join the Board of Directors and the Board of Scientific Advisors after the 2012 CRS Annual Meeting & Exposition in July.

Congratulations to our newly elected CRS Board

Treasurer
Tom E. Redelmeier
Northern Lipids Inc., U.S.A.

Secretary
Ruth B. Schmid
SINTEF Materials and Chemistry, Norway

Director-at-Large, 2012–2015
Christine J. Allen
University of Toronto, Canada



Director-at-Large, 2012–2014
Marcus E. Brewster
Johnson & Johnson Pharmaceutical Sciences, Belgium

Director-at-Large, 2012–2013
Andrew L. Lewis
Critical Pharmaceuticals, United Kingdom

Director-at-Large, 2012–2014
Tamara Minko
Rutgers University, U.S.A.

Director-at-Large, 2012–2015
Yvonne Perrie
Aston University, United Kingdom

Board of Scientific Advisors, 2012–2015

Theresa M. Allen
University of Alberta, Canada

María José Alonso
Universidade Santiago de Compostela, Spain

Justin S. Hanes
Johns Hopkins University, U.S.A.

Leaf Huang
University of North Carolina, U.S.A.

Edith Mathiowitz
Brown University, U.S.A.

Gert Storm
Utrecht University, The Netherlands

Ernst Wagner
Ludwig Maximilians University, Germany

Please note that given the new structure of the CRS Board, more than the usual number of Directors-at-Large were voted in to fill the new requirements. These directors have varying terms, based on a percentage of votes received, to ensure that the new proper rotation will occur in the coming years. The term going forward of Directors-at-Large will be three years.

Thank you to all the impressive candidates who participated in the election. Thank you to all the members who voted this year, helping to decide the future of our society.

Controlled Release and Delivery Technologies

Charles Frey
Coating Place, Inc., Verona, WI, U.S.A.

The following is a brief summary of selected patents from the U.S. patent database that were granted between July 1 and December 31, 2011, and involve aspects of controlled release or controlled delivery. They are presented without categorization in a somewhat random order.

Dendritic Polymers with Enhanced Amplification and Interior Functionality; U.S. Patent 7,985,424

This patent discloses dendritic polymers with enhanced amplification and interior functionality. Fast, reactive ring-opening chemistry (or other chemistries) and branch cell reagents are used to rapidly and precisely build structures with benefits including cleaner chemistry, often single products, lower excess reagents, lower dilution, higher capacity, easier scale up, new material ranges, and lower cost. Compositions with novel internal functionality and greater stability are claimed. Many examples are described. Surface and interior properties can potentially be applied in drug delivery, transfection, and diagnostic applications.

Delivery System for Low-Calorie Bulking Agents; U.S. Patent 7,981,453

A coating system to delay and control water uptake by low-calorie bulking agents such as cellulose, starch, bran, glucans, hydrocolloids, and the like is disclosed. The system involves a lipid base coat and a hydrophilic edible protein top coat. Protein coat selections include soy isolate, milk protein, and whey protein. Water absorption in the bulking agent and associated swelling can effectively be delayed until the agent reaches the stomach.

Gastric Retentive Oral Dosage Form with Restricted Drug Release in the Lower Gastrointestinal Tract; U.S. Patent 7,976,870

This patent discloses a gastro-retentive tablet for agent delivery to the upper gastrointestinal tract. The system uses any of a variety of biocompatible, hydrophilic polymers that swell in the presence of water and erode over time to release the agent. Many therapeutic agents with decreasing solubility at increasing pH levels including various antibiotics are mentioned.

Controlled Release Bioactive Agent Delivery Device; U.S. Patents 7,976,862 and 8,021,680

An implantable sustained release bioactive agent delivery device is described. The device employs a coil-shaped body member coated with the agent in a two-polymer matrix layer of polyalkyl(meth)acrylate and poly(ethylene-co-vinyl acetate) to sustain release of the agent for up to three years and longer. Use of the device in the eye is used as an example in the disclosure.

Controlled Release CGRP Delivery Composition for Cardiovascular and Renal Indications; U.S. Patent 7,976,847

A system for controlled delivery of calcitonin gene-related peptide (CGRP) for treatment of heart failure and improving renal function is disclosed. The system involves introduction of a biodegradable polymer and CGRP solution into a bodily tissue or fluid. Subsequent formation of the CGRP-polymer matrix sustains CGRP release for up to 180 days.

Method for Control of the Volume Flux of a Liquid in an Osmotic Micropump and Osmotic Micropump; U.S. Patent 7,976,535

The invention discloses methods for control of volume flows within and from osmotic micropumps. Semipermeable membranes are employed in several configurations to control fluid output through manipulation of internal solution concentrations using electrophoretic, mechanical, or selective membrane permeability mechanisms. The invention is capable of moving volumes that are large in comparison to the combined volume of the source chamber and the dilution chamber. The invention is useful for microfluidic, microanalytic, or liquid administration and sampling applications.

Aroma-Producing Compositions for Foods; U.S. Patent 7,972,646

An improved, shelf-stable, controlled release aroma composition is disclosed. This homogeneous one-phase composition includes the aroma-producing material, a medium-chain fatty acid triglyceride fat-containing composition, and a fat or lipid with a melting point greater than the medium-chain fatty acid triglyceride. The composition becomes fluid at temperatures greater than ≈35°C and releases aroma upon microwave heating, baking, or other heating processes. The composition can be applied to foods by spraying at temperatures of 40–80°C.

Pharmaceutical Dosage Forms Having Immediate Release and/or Controlled Release Properties; U.S. Patent 8,007,827

This invention discloses use of a two-enteric layer coat system for extended enteric delivery to the small intestinal region. The coat system is configured such that the dissolution onset pH is higher for the base (inner) enteric coat than the top (outer) enteric coat. The system provides targeted delivery for drugs requiring delivery to the small intestine such as baclofen, gabapentin, levodopa, α-methyldopa, and valacyclovir.

Patent Watch continued on page 22

Patent Watch continued from page 21

Microporous Articles Comprising Biodegradable Medical Polymers, Method of Preparation Thereof and Method of Use Thereof; U.S. Patent 8,007,823

This patent discloses a means to create a biocompatible polymer article with controlled porosity for tissue engineering or controlled release applications. Two immiscible or partially immiscible polymers with or without a compatibilizer are melted together to create a homogenous, continuous morphology. After cooling, a solvent is used to dissolve and remove one polymer and compatibilizer, leaving a microporous formation of the other polymer.

Delivery System for Biological Component; U.S. Patent 8,007,777

The invention discloses a means of delivering lactic acid bacteria enterically through the use of hydrophilic polymers and electrolytic pH control agents such as salts of carbonate and phosphate.

Biocompatible Hydrogels Made with Small Molecule Precursors; U.S. Patent 8,003,705

Biocompatible cross-linked polymers and methods for their *in situ* preparation and use are disclosed. The polymers are formed from water-soluble precursors, one with at least two electrophilic groups and another with at least two nucleophilic functional groups, capable of reacting and cross-linking *in situ*. Cross-linking reactions may be carried out *in situ* on organs or tissues or outside the body. Applications include controlled delivery of drugs, prevention of postoperative adhesions, coating of medical devices such as vascular grafts, wound dressings, and surgical sealants.

Lumen-Traveling Delivery Device; U.S. Patent 7,998,060

Fantastic Voyage realized. Devices designed to travel the vascular systems of the body are described. The devices include a propelling mechanism, sensors, material release and sampling capabilities, and control circuitry. They provide a means to treat and/or sample target sites within the lumen.

Tablet Composition for the *In Situ* Generation of Chlorine Dioxide for Use in Antimicrobial Applications; U.S. Patents 7,993,545 and 8,017,032

A tablet system for controlled release of chlorine dioxide as a biocide treatment for aqueous systems such as cooling towers is disclosed. The system uses sodium chlorite encapsulated in polyvinyl alcohol and trichloroisocyanuric acid with an organic acid pH control agent and a boron donor to provide a shelf-stable product that releases chlorine dioxide upon exposure to water.

Hydrogel Compositions, Devices, and Microscale Components; U.S. Patent 7,988,685

An implantable, hydrogel-actuated microvalve is described. The device uses the glucose-moderated volume increase and decrease of 3-methacrylamidophenylboronic acid or 3-acrylamido-4-nitrobenzeneboronic acid, respectively, to close and open the valve. Porous rigid plates and a deformable substrate make up the physical closure. The devices provide a means for controlled delivery of drug or agent in response to glucose levels such as for diabetes treatment, hormonal treatments, fermentation systems, and the like.

Method of Cell Storage in a Delivery System Comprising a Fibrous Matrix; U.S. Patent 8,021,869

A system of electrospun fibers of biodegradable and/or bioabsorbable material containing viable cells and nutrients for controlled delivery of tissue precursor or stem cells to mammals is disclosed.

Nitric Oxide–Releasing Biodegradable Polymers Useful as Medical Devices and Coatings Therefor; U.S. Patent 8,021,679

This invention discloses use of biodegradable, biocompatible polymers derived from [1,4]oxazepan-7-one as coatings on vascular stents for controlled delivery of nitric oxide to treat and prevent conditions such as restenosis, aneurysms, and plaque.

Controlled Release Polymeric Compositions of Bone Growth Promoting Compounds; U.S. Patent 8,017,144

This invention provides an injectable composition of bone growth promoter, biodegradable polylactide-co-glycolide polymers, and *N*-methyl-2-pyrrolidone for controlled release of the promoter to bone tissues.

Process for the Preparation of Extruded Delivery Systems; U.S. Patent 8,017,060

The invention discloses an extrusion process for the preparation of a granular delivery system for the controlled release of flavoring or perfuming ingredients. The extrusion involves the blend of a viscous emulsion of the active with hydrophilic polymers and eliminates the need for a dehydration step.

Gastric Retention Controlled Drug Delivery System; U.S. Patent 8,012,496

This invention provides a gastroretentive system for controlled delivery of baclofen. The system uses hydrophilic polymers and a super-disintegrant with a gas-generating salt to form a matrix that rapidly swells and floats in gastrointestinal fluids for once-per-day dosing.

Slow-Release Inhibitor for Corrosion Control of Metals; U.S. Patent 8,012,374

This invention provides for a slow-release corrosion inhibitor in paints or primers for metal surfaces. The system involves use of cesium and vanadium salts and an azole. Salts are coated with a hydrophobic polymer to sustain release.

Shell-and-Core Dosage Form Approaching Zero-Order Drug Release; U.S. Patent 8,043,630

This invention involves the use of a swellable, hydrophilic coating to create a gastroretentive tablet that approaches zero-order release.

Algae-Resistant Roofing Granules with Controlled Algaecide Leaching Rates, Algae Resistant Shingles and Process for Producing Same; U.S. Patent 8,039,048

Algae-resistant roof granules are created by coating granules with formulations containing binder, copper or zinc algicides, and a pore-forming agent. Subsequent heat treatment vaporizes the pore former to create a controlled release structure.

Microencapsulation Product and Process; U.S. Patent 8,039,015

This patent discloses a means for controlled release of an insect repellent. The water-immiscible repellent is first emulsified with a Lewis base surfactant material (such as an amine or quaternary ammonium compound). Subsequently, a Lewis base polymeric material (such as a polyacrylic acid) is added to form an insoluble ion-paired shell with the base material around the repellent droplets.

Sustained Release Systems of Ascorbic Acid Phosphate; U.S. Patent 8,034,363

Ascorbic acid phosphate is dried and melt-blended with absorbable aliphatic polyester polymers such as poly(lactide-glycolide) to form a controlled release ascorbic acid phosphate system for tissue repair.

N-hydroxylsulfonamide Derivatives as New Physiologically Useful Nitroxyl Donors; U.S. Patent 8,030,356

Novel *N*-hydroxysulfonamide derivatives that release NHO at a controlled rate under physiological conditions are described for treatment of diseases or conditions that are responsive to nitroxyl therapy. Release is modulated by varying the nature and location of functional groups.

Rupturing Controlled Release Device Having a Preformed Passageway; U.S. Patent 8,029,822

This invention incorporates multiple preformed passageways into an osmotic delivery device designed to open successively during *in situ* application. The added passageways provide more complete release of the payload. In one embodiment, a swellable polymer is incorporated to help expel final actives from the device.

Controlled Release Composition and Method of Producing the Same; U.S. Patent 8,067,030

A controlled release injectable peptide therapy system incorporating the peptide, a naphthoic acid or salt, and poly(lactic acid) is disclosed.

Extended Release Compositions Comprising as Active Compound Venlafaxine Hydrochloride; U.S. Patent 8,062,666

Venlafaxine hydrochloride and binder are coated on a nonpareil core, which is then coated with an ethylcellulose-based sustained release coating for sustained 24-hour delivery.

Particulate Flavoring Composition; U.S. Patent 8,057,784

A sustained release flavoring composition for toothpaste and confectionaries such as chewing gum is disclosed. The gelatin:fat ratio and gelatin Bloom strength provide release rate control.

Delivery System; U.S. Patent 8,057,433

A sustained system for delivery of antifungal agents to the vaginal cavity for up to one month is disclosed.

Solid Oral Dosage Form Containing an Enhancer; U.S. Patent 8,053,429

This patent describes various tablet and capsule systems for enteric delivery of active material combinations such as heparin and enhancer.

Acoustically Controlled Substance Delivery Device; U.S. Patent 8,083,710

This patent discloses remote means of controlled fluid delivery including acoustic controls. Embodiments include delivery within the body of an organism, a body of water, or in an enclosed volume of fluid.

Fragrance Precursor; U.S. Patent 8,080,690

This patent claims a sustained release means for fragrances in fiber conditioning compositions such as fabric softeners and hair conditioners.

Time-Release Dental Adhesive; U.S. Patent 8,080,594

This patent discloses a dental adhesive with sustained adhesive strength that declines in the presence of water. The time before release is controlled by the amount of sugar or sugar-based sweetener in the adhesive.

Preparation of Biodegradable Polyesters with Low-Burst Properties by Supercritical Fluid Extraction; U.S. Patent 8,076,448

This method discloses the use of supercritical fluid extraction to isolate a purified poly(lactide-glycolide) fraction with reduced initial burst effect in controlled release applications such as injected implants.

Controlled Release of Biopharmaceutical Growth Factors from Hydroxyapatite Coating on Bioresorbable Interference Screws Used in Cruciate Ligament Reconstruction Surgery; U.S. Patent 8,075,562

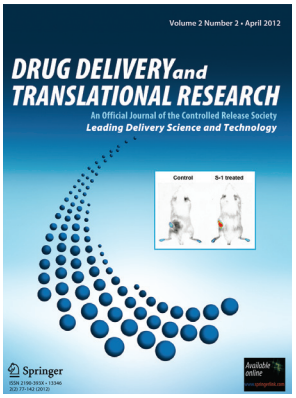
This patent discloses the application of bone growth factors to implants to enhance bone healing.

Controlled Release Implantable Dispensing Device and Method; U.S. Patent 8,071,119

This patent describes the use of "hyper compression" of therapeutic agent and a biocompatible polymer to form sustained release micro- or nanoparticles. ■

Drug Delivery and Translational Research (*DDTR*) Updates

Vinod Labhasetwar, Ph.D., Editor-in-Chief



Thanks to Reviewers

The editorial team of *Drug Delivery and Translational Research* (*DDTR*) is thankful to the journal's reviewers, whose efforts and timely responses allowed the journal not only to maintain its high quality of published papers but also to provide rapid feedback to authors. *DDTR*'s average response time to a first submission is only three weeks.

DDTR is an official member journal of CRS, providing a unique forum for publication of high-quality research that focuses exclusively on translational aspects of science and technology of delivery of bioactives. Join the leading scientists who are publishing their work in *DDTR*. It is available online to CRS members as a benefit.

Consider submitting your best translational drug delivery research to compete for the outstanding paper award for 2013, which will be selected from the research articles published in *DDTR* during 2012. The award winner for 2012 has been selected from the research articles published in *DDTR* during 2011, and the award will be given during the 2012 CRS Annual Meeting & Exposition to be held in Québec City, Canada.

Editor's Pick (Vol. 2, Issue 2)

Sampling of disease biomarkers from skin for theranostic applications

Makoto Ogura, Sumit Paliwal, and Samir Mitragotri

In this paper, the authors have demonstrated the use of an ultrasonic sampling technique that can recover a wide variety of biomolecules from skin in a minimally invasive manner. This technique could be useful in diagnosis of dermatological diseases including psoriasis, eczema, infections, and cancer, collectively constituting a large category of human conditions. The large area and ease of access of skin open excellent opportunities for theranostic applications, that is, diagnosis as well as therapy of the disease. Such applications can be based on evaluation of skin's molecular composition in terms of proteins, nucleic acids, and small molecules. Using different mouse models of dermatological conditions, the authors have shown regulation of several established biomarkers in the skin.

Upcoming Special Issues

DDTR has published two well-received theme issues: "Advances in Vaginal Drug Delivery," edited by David R. Friend of CONRAD, Arlington, VA, U.S.A., and "Advances in Image-Guided Drug Delivery," edited by Profs. Arash Hatefi and Tamara Minko from Rutgers, The State University of New Jersey, U.S.A. We are developing several theme issues on delivery science and technology with a translational focus. The primary focus of *DDTR* is to advance delivery science and technology and to provide a unique forum for publication of high-quality translational drug delivery research. If you are interested in developing a theme issue, please contact me with a brief summary and list of potential contributors (labhasv@ccf.org). Also, contact me if you are interested in writing an editorial on topics relevant to translational aspects of drug delivery research and technology.

A *DDTR* Special Focus Issue on "Biomimetic and Biofunctional Materials in Regenerative Medicine," with V. Prasad Shastri, University of Freiburg, as Guest Editor

The main objective of this themed issue is to highlight the evolution of concepts in materials engineering for inducing autologous regeneration and the challenges associated with clinical translation. In this context, material design that incorporates principles of directed self-assembly, surface engineering, metabolic engineering, extracellular matrix mimicry, and synthetic biology for driving functional cellular organization and recapitulation of signaling environments in embryonic and fetal development will be highlighted.

A *DDTR* Special Focus Issue on "CNS Drug Delivery of Biologics," with Pericles Calias, Shire Human Genetic Therapies, as Guest Editor

Strategies for treating the Central Nervous System (CNS) manifestations of diseases have evolved well beyond the traditional size/lipophilicity paradigm. This special issue describes the challenges of developing therapies targeted to the CNS, from bench to clinical development. A review of the biological hurdles and current strategies for overcoming them will set the stage for discussions on the assessment of the product's pharmacologic effect within the CNS and regulatory considerations for the incorporation of biomarkers into product development programs.

CRS members receive a subscription to *DDTR* as part of membership. Learn more and get access to special focus issues and all the important research published by visiting www.controlledreleasesociety.org/publications/Pages/DDTR.aspx. ■

Journal of Controlled Release's Most Wanted

An official journal of the Controlled Release Society, the *Journal of Controlled Release* (*JCR*) publishes innovative, original research involving the controlled release and delivery of drugs and other biologically active agents. The terms "controlled release" and "delivery" are used in their broadest sense to include mechanisms such as diffusion, chemical and enzymatic reactions, dissolution, osmosis, targeting, and the utilization and manipulation of biological processes.

Below are the top ten most cited articles published in *JCR* since 2007 (extracted from SciVerse Scopus, April 25, 2012).

A review of stimuli-responsive nanocarriers for drug and gene delivery
126(3): 187-204, March 2008
Ganta, S, Devalapally, H, Shahiwala, A, Amiji, M

Nano/micro technologies for delivering macromolecular therapeutics using poly(D,L-lactide-co-glycolide) and its derivatives
125(3): 193-209, February 2008
Mundargi, RC, Babu, VR, Rangaswamy, V, Patel, P, Aminabhavi, TM

***In situ* gelling stimuli-sensitive block copolymer hydrogels for drug delivery**
127(3): 189-207, May 2008
He, C, Kim, SW, Lee, DS

Albumin as a drug carrier: Design of prodrugs, drug conjugates and nanoparticles
132(3): 171-183, December 2008
Kratz, F

Pluronic block copolymers: Evolution of drug delivery concept from inert nanocarriers to biological response modifiers
130(2): 98-106, September 2008
Batrakova, EV, Kabanov, AV

Polymer-based siRNA delivery: Perspectives on the fundamental and phenomenological distinctions from polymer-based DNA delivery
121(1-2): 64-73, August 2007
Gary, DJ, Puri, N, Won, Y-Y

Polysaccharide hydrogels for modified release formulations
119(1): 5-24, May 2007
Coviello, T, Matricardi, P, Marianecci, C, Alhaique, F

Triggered destabilisation of polymeric micelles and vesicles by changing polymers polarity: An attractive tool for drug delivery
120(3): 131-148, July 2007
Rijcken, CJF, Soga, O, Hennink, WE, van Nostrum, CF

Biodegradable polymers as non-viral carriers for plasmid DNA delivery
126(2): 97-110, March 2008
Luten, J, van Nostrum, CF, De Smedt, SC, Hennink, WE

Cationic lipids and polymers mediated vectors for delivery of siRNA
123(1): 1-10, October 2007
Zhang, S, Zhao, B, Jiang, H, Wang, B, Ma, B ■

"Drug Delivery Through the Ages": UKICRS 2012 Annual Meeting, May 1–2, 2012

Jitinder Singh Wilkhu and Yvonne Perrie, Aston University

The United Kingdom and Ireland Local Chapter of the Controlled Release Society (UKICRS) was proud to announce that the venue for the 2012 meeting was Aston University. It had been seven years since the UKICRS symposium had last been to Britain's dynamic second city, Birmingham. London may well have the 2012 Olympics, but Birmingham got the UKICRS conference—far more interesting.

Interactive Workshop—A First for UKICRS

As an innovation, this year UKICRS ran a half-day workshop prior to the conference. This was funded via sponsorship and was designed to give both hands-on experience and technical background into a range of techniques that is available for application in controlled release and drug delivery. We asked a range of technical experts to give a 15 minute overview of the principles in equipment available, followed by a 15 minute "hands-on" use of equipment, where workshop attendees could try out the equipment for themselves using their own samples, which they were invited to bring along for testing. The day kick-started with a warm welcome to this year's meeting from the UKICRS Chairman, Prof. Yvonne Perrie, followed by presentations and hands-on demonstrations from companies including Agilent Technologies, Biolin Scientific, Surface Measurement Systems, Sympatec, and Mettler Toledo. This was a dynamic session, as there was much delegate participation and interaction, which was welcomed by the companies, as they were able to clear out any issues regarding technologies and uses of their equipment. This session was followed by a well-deserved coffee and retro classic Coca Cola break, where bottles were provided in a bucket full of ice! After a thirst-quenching break, the presentations continued with talks and interactions from companies including Stable Microsystems, Capsugel, Presearch, and Ceram. Following the second session of the day, the floor was open for delegates to have their samples analysed before the workshop ended.

After ending a successful workshop event, the day was rounded up by an evening dinner at Jee Jee's Punjabi cuisine, where the exhibitors and delegates were treated to a delightful symposium dinner that proved to be an excellent networking opportunity. The exhibitors and delegates were wowed by the quality of food, pleased at the running of the day, and grateful for the hospitality.

Symposium Day

After an intense workshop day and a filling evening dinner, the delegates and exhibitors were ready to start the main symposium day, which hosted over 100 delegates. After an opening speech by Prof. Yvonne Perrie (Aston University), Dr. Woei Ping Cheng (University of Hertfordshire) chaired the first session of the symposium. Opening the meeting, Prof. Theresa Allen from University of Alberta, Canada, presented a talk on "Controlled Release Delivery Systems: From Coated Aspirin to Personalized Nanomedicines." Terry is a world-leading researcher with 30 years' experience in the drug delivery field and a vast array of publications in this field. Her talk focussed on the use of multifunctional pharmaceutical nanomedicines, mainly liposomes and the product Doxil. Following on from Prof. Allen's opening talk, the next speaker of the day, Lauren Shurety from Q Chip Cardiff, U.K., presented her talk on "Q-Sphera: From Proof of Principle Microfluidic Chips to Full Scale Aseptic Manufacturing Platform." This presentation provided an insight into the scale-up of microsphere production to clinical aseptic processes for parenteral peptide therapeutics. This is an important procedure from laboratory research to commercially producing the parenteral formulations, as parenteral drug delivery products account for nearly 30% of total global pharmaceutical sales and were valued at $27 billion in 2011, with figures rising to a predicted $51 billion in 2015.

Straight after the coffee break, it was time for the session of postdoctoral speakers chaired by Jitinder Singh Wilkhu (UKICRS Graduate Chairman, Aston University). The first speaker of this session was Dr. Randip Kaur (Aston University); the emphasis of her talk was based on PEGylation of DDA:TDB liposomal adjuvants reducing the depot effect and altering the TH1 and TH2 immune responses. Results reported within this study demonstrated that higher levels of PEG (i.e., 25%) were able to significantly inhibit the formation of a liposome depot at the injection site and also severely limit the retention of antigen at the site, therefore resulting in a faster drainage of the liposomes from the site of injection. The presentation showed that that the depot formation is due to electrostatic forces between the net negatively charged proteins found at the injection site and the positively charged liposomes. The *in vivo* theme continued from the second speaker, Dr. Viraj Mane (University of Maryland, U.S.A.), who considered drug delivery via the oral route with a presentation on ICAM-1 mediated targeting and endocytosis in the gastrointestinal tract in mice. The presentation showed that fluorescence imaging of anti-ICAM nanocarriers demonstrated attachment to gastrointestinal epithelium, and transmission electron microscopy further showed the internalisation and accumulation of anti-ICAM nanocarriers into endocytic vesicles of epithelium.

The workshop presenters and organisers.

Some of the technical talks and hands-on sessions.

Keynote speakers (Prof. Terry Allen and Prof. Molly Stevens) and poster award winners (Rhys Jones of Aston University and Hiteshri Makwana of Nottingham University).

Chapter News continued on page 28

Chapter News continued from page 27

The third speaker, Dr. Timothy Doody (University College Cork), finished off the session with the development of a murine pulmonary model for assessment of nanoparticle delivery *in vivo*. By fluorescently labelling nanoparticles, the study was able to demonstrate that the Aerogen nebulising device system was effective in delivering nanoparticles to the mouse lung. The morning sessions provided insight into current developments in the delivery of drugs via various routes, and this prepared us nicely for the poster session and lunch!

Peer-Reviewed Posters: Who Wins? The Audience Decides

During the poster session, we had 64 posters presented, and the judging of the posters for the poster awards was by peer review. Each delegate had a "bright yellow star" that they were asked to place beside the poster they felt was the best—the winners of the poster session were the two posters with the most stars by the end of the second poster session.

After returning from lunch fully energised, the session chair, Dr. Vitaly Khutoryanskiy (University of Reading), began the third session of the day, where the postgraduate students featured. Nicola Irwin (Queen's University, Belfast) opened with considering the kinetic and thermodynamic control of antibiotic release from infections and pH-responsive hydrogels. Results from the study showed that it is possible for nalidixic acid in hydrogels to respond to pH trigger, and it is inherently responsible for its own release. This represents a novel approach toward achieving rapid, infection-responsive drug delivery. Following this talk, Michael Cook (University of Reading) presented another hydrogel system for the oral delivery of probiotic bacteria. From the presentation, hydrogel matrices may offer a desirable environment for entrapment of cells and can be produced in ways that are "gentle" enough to not harm the cells, so they are of interest in this field of research. Moving on from hydrogels, the next speaker, Amy Judd (Keele University), provided an insight into the use of nanomaterials for the prevention of infectious diseases. The U.K. Department of Health stated that each infection acquired in hospital costs between £4,000 and £10,000, totalling £1 billion each year for the NHS as a result. The research has shown the positive use of dendrimers for drug delivery and providing many biomedical applications. Before the second poster session, the second keynote invited speaker, Prof. Molly Stevens (Imperial College, London), provided an intriguing outlook on biomaterial-based strategies for regenerative medicine and biosensing. The talk focussed on Molly's primary research on bone regeneration, and her research includes the directed differentiation of stem cells and the design of novel bioactive scaffolds toward tissue regeneration. The third session was then closed, ready for the second poster session and afternoon tea break.

The final session of the symposium proceeded with the session chair, Dr. Katie Ryan (University College Cork), introducing the first speaker of the fourth session, Wilson Oguejiofor (Aston University). The presentation provided insight into the spray-dried combinations of lactoferrin with antibiotics and how they appear to be more superior to monotherapy for reducing biofilm formation by *Pseudomonas aeruginosa*. Rosalind Chong (Cardiff

Posters and networking.

University) then took to the stage with her presentation on the delivery of siRNA to skin using microneedle devices, an *in vitro* and *in vivo* proof of concept. As mentioned by Rosalind, there are significant challenges in this field; hence, current studies are therefore characterising microneedle delivery of fluorescently labelled siRNA to human skin explants, alongside keratinocyte cultures, to determine correlation between siRNA delivery, uptake, and subsequent gene expression reduction. The final talk of the symposium, on the *in vitro* evaluation of the mechanism of action of a novel absorption enhancer (CriticalSorb®), was presented by Saif Shubber (University of Nottingham). Transport studies using FITC-insulin showed significant differences in insulin transport across the Calu-3 cell monolayer in the presence and absence of CriticalSorb® at 37°C, indicating its permeability-enhancing properties.

After a day of exceptional presentations by all speakers and a significant contribution from the delegates during the Q&A, the session was brought to a close by Yvonne Perrie announcing the two poster prize winners. Voted by the attendees, the winners were Hiteshri Makwana from Nottingham University, with a poster on "Responsive Protein Polymer Conjugate Therapeutics," and Rhys Jones from Aston University, with a poster on "A DOE Study Evaluating the Properties of Freeze-Dried Orally Disintegrating Tablet Formulations." They were the happy recipients of the UKICRS 2012 poster prizes, and congratulations to all who participated in the poster presentations. Overall, Aston University proved to be a great place to host the 2012 annual conference, with a splendid atmosphere and the vast selection of presentations throughout both days. The delegates and exhibitors were all left smiling and left Aston University with a positive feeling, eagerly anticipating what the 2013 conference will hold. We thank all exhibitors and delegates for the level of expertise and research that was presented within the symposium and workshop.

For more information on UKICRS, please visit www.ukicrs.org or follow us on Facebook (http://www.facebook.com/groups/UKICRS/). ■

CRS Connecticut Student Chapter

Jill Steinbach, President, CRS-CT

The Connecticut Student Chapter of the Controlled Release Society (CRS-CT), U.S.A., is a consortium comprising members from the University of Connecticut (UConn, Storrs), Yale University, and the University of Connecticut Health Center (UCHC). To date, the chapter consists of 56 members with approximately 14% undergraduate students, 61% graduate students, 18% postdoctoral affiliates, 4% faculty, and 3% industry members. Because we are a student chapter committed to promoting collaboration and networking opportunities, all three institutions are represented on our leadership team: Dr. Jill Steinbach (Yale, President), Keshia Ashe (UCHC, Vice President), Michail Kastellorizios (UConn, Secretary), and Dr. Ragy Ragheb (Yale, Treasurer). Dr. Sangamesh Kumbar, joint professor of chemical, materials, and biomolecular engineering at UCHC, serves as the chapter faculty advisor.

As a local chapter of the larger CRS, a primary goal is to contribute to advancements in the field of drug delivery. To achieve this, the chapter provides a comfortable atmosphere in which scientists and engineers can share information on drug delivery, controlled release, and the broader science related to pharmaceuticals. The chapter has a multidisciplinary focus that encompasses drug delivery, chemistry, chemical engineering, biomedical engineering, pharmaceutics, materials science, and the biological sciences.

To promote an understanding of the current research on both a local and an international level, the chapter has now held two annual research symposia, interim workshops, an industry site tour, multicampus seminars, integrated social events, and quarterly meetings. By organizing these scientific meetings and events, the chapter garners the participation of scientists and engineers from academia and industry alike. Lab tours were provided at each campus during these meetings to encourage collaborations and networking between the chapter's members.

We are excited to share a detailed description of the organized events we held during the 2011–2012 academic year.

Committee members: Keshia Ashe (Vice President), Ragy Ragheb (Treasurer), Michail Kastellorizios (Secretary), and Jill Steinbach (President).

Despite the intrusion of Storm Albert, the worst winter storm Connecticut has ever seen in the month of October, members of the CRS-CT Student Chapter braved the elements to joyfully gather for a "History Happy Hour" on November 3, 2011. The social event took place at the Butler-McCook house and garden, a historic Connecticut landmark that, over 189 years, was home to four generations of a family who participated in, witnessed, and recorded events of the American Revolution. A free history tour and walk in a hidden garden, combined with delicious finger foods and delightful wines, fostered a warm and friendly environment as members learned American Revolution history and connected with others from the year before. While Jill Steinbach, newly elected president, reminded members from Yale, UConn, and UCHC of successful events from the organization's inaugural year, she expressed her excitement and anticipation of events ahead—particularly the 2nd annual symposium to be held January 28, 2012, at Yale University.

The next event was the symposium, graciously sponsored by Covidien. The symposium theme was "Emerging Technologies in Therapeutic Delivery." We were thrilled to host six highly esteemed speakers. Dr. W. Mark Saltzman (Yale) gave an opening talk, followed by chapter president Dr. Jill Steinbach's opening thank you to the approximately 70 attendees. Of the invited guest speakers, Dr. Thomas Webster (Brown University) started the day with his presentation, "Novel Self-Assembled

Event at the historic Butler-McCook House, November 2011.

Chapter News continued on page 30

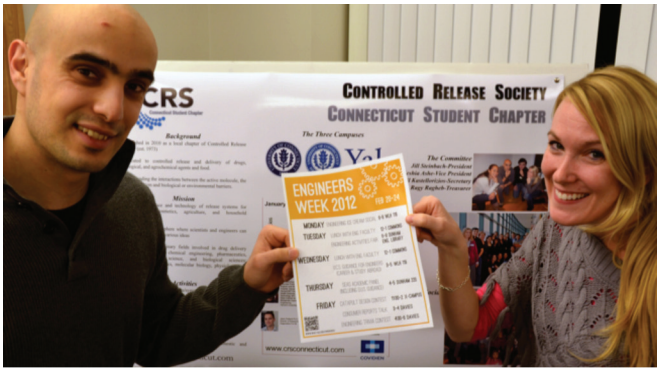
Chapter News continued from page 29

Nanostructures for Regenerative Medicine: Carriers Can Be Proactive," followed by Dr. Deborah Palliser (Albert Einstein College) with her presentation titled "Optimizing Cell-Targeted siRNA Delivery." Dr. Ali Khademhosseini (MIT/Harvard) presented his talk, "Microengineered Hydrogels for Stem Cell Bioengineering and Tissue Regeneration." After lunch, we reconvened with Dr. Kathryn Uhrich (Rutgers), "Polymers with a Purpose: Biocompatible Polymers That Degrade into Bioactives," followed by Dr. Jason Rolland (Diagnostics for All), "Paper Microfluidics as an Enabling Platform for Low-Cost Diagnostics." The last speaker of the day, Dr. Xiuling Lu (UConn), presented her work on "Delivery of Theranostic and Radiotherapeutic Cancer Nanomedicines."

The day-long symposium culminated with a student poster/awards session and a closing statement by Dr. Ragy Ragheb at the Malone Engineering Center at Yale University. The three top student poster presentation awards, chosen anonymously by symposium participants, were presented to Dr. Chris Cheng (Yale), Dr. Xiaoming Xu (UConn), and Jenny Saucier-Sawyer (Yale). The three winners each received a prize in acknowledgement of their contribution.

Shortly thereafter, the CRS-CT Student Chapter had the privilege of cosponsoring National Engineers Week through the School of Engineering and Applied Science at Yale University, February 20–24, 2012. A series of events, Monday through Friday, showcased what engineering at Yale had to offer. CRS-CT had the opportunity to present their motivations and numerous accomplishments as a chapter over the last couple of years at Tuesday's Engineering Activities Fair. It was a great chance to interact and engage budding and creative minds across several engineering disciplines.

Covidien site tour, April 2012.



Engineers Week at Yale University, February 2012.

In an effort to integrate industry and academia, for the next event the CRS-CT chapter took to the road to visit Covidien's Polymer Development and Braid Manufacturing Facility (PDBMF) and Needles Buildings at the North Haven site on April 17, 2012. Covidien is a leading manufacturer of medical devices and supplies, diagnostic imaging agents, and pharmaceuticals. They have 41,000 employees in more than 65 countries with approximately 2,000 employees at the North Haven site. We had the pleasure of meeting up with Jessica Gould, project manager at Covidien who, along with others, enlightened us as to Covidien's manufacturing, some of which included polymer synthesis and processing along with high-throughput braid manufacturing. We also had the pleasure of observing highly efficient and precise manufacturing processes for surgical needles. It was an inspiring event that led CRS members from Yale, UConn, and UCHC to reflect on the methodology and organization of their own research and bench work, prompting discussions of research optimization at the academic level.

In addition to these events, we look forward to having our final event of the 2011–2012 year at the University of Connecticut–Storrs. We are thrilled to be hosting our seminar speaker, Dr. Vince Rotello from the University of Massachusetts Amherst. He will be presenting a talk titled "Tuning Nanoparticles for Therapeutics and Diagnostics."

Since its establishment in 2010–2011, the CRS-CT Student Chapter has been promoting student participation by encouraging new students to join the executive committee. The chapter will conclude this year's proposed activities with the chapter elections in August 2012.

For more information about the CRS-CT Student Chapter, including a list of activities and pictures, please visit www.CRSConnecticut.com. ■

AUS-CRS 2011: 5th Annual Meeting of the Australian Local Chapter of the Controlled Release Society, October 21–22, 2011

Ben Boyd, President, AUS-CRS

AUS-CRS 2011 was the 5th annual meeting of the Australian Local Chapter of the Controlled Release Society held at Hamilton Island, a tropical island off the coast of northern Queensland, Australia. The meeting included invited and contributed talks and posters from a range of fields within delivery research, including peptide and protein delivery, lipid-based drug delivery, pulmonary delivery, anticancer drug delivery, and drug development from a range of academic and industry speakers.

The conference commenced with plenary speaker Prof. Martin Malmsten from the University of Uppsala, Sweden, giving his presentation "Peptides and Proteins in Polyelectrolyte Microgels," which highlighted the issues associated with charge association of peptides and proteins with hydrogels, the influence of microgel structure, and consequent potential for shell formation as opposed to uniform particle loading.

There were three papers presented on the interaction of peptides and proteins with solid inorganic materials and consequent release behavior. Michael (Chengzhong) Yu from University of Queensland described his research using temperature-controlled vacuum-assisted vapour deposition to control the pore size in mesoporous materials. Applications in both enrichment and detection of peptides in serum, and in the controlled loading and release of camptothecin, were demonstrated. Continuing the theme of inorganic drug delivery matrices, Ramin Rohanizadeh (University of Sydney) discussed the differential adsorption of proteins onto crystalline hydroxyapatite and amorphous calcium phosphate and rationalized differences in protein release rate from the materials. A novel approach to reveal subtle changes in protein conformation at the surface of porous silicon using TOF-SIMS was described by Tim Barnes (University of South Australia). Differences in the complex amino acid fragmentation patterns provided discrimination between native and denatured human serum albumin, insulin, and papain as model compounds.[1]

To complete the protein and peptide delivery session, there were two presenters from New Zealand. The preparation of injectable implants using β-glucan was the topic presented by Ilva Rupenthal (University of Auckland). Rheological behavior was correlated with drug-release profiles, and the optimal matrix was found to comprise a β-glucan and polyethylene glycol mixture. Thomas Rades (University of Otago, New Zealand) gave an account of the preparation, release, and efficacy of a GnRH analog from polyalkylcyanoacrylate (PACA) nanoparticles. The potential for copolymerization of the peptide with PACA during particle preparation was highlighted as a possible limitation in translation to human treatments, but the particles were shown to provide effective oral sterilization of brushtail possums, a devastating agricultural pest in New Zealand—the main target of the delivery system.

Plenary speaker Prof. Martin Malmsten

The lipid-based drug delivery session had a focus on self-assembled lipid systems that form micelles and exotic mesophase structures such as bicontinuous cubic phases and cubosomes. Martina Stenzel (Centre for Advanced Macromolecular Design, The University of New South Wales, Sydney) presented her exciting work on designing RAFT polymers to form block copolymer micelles in which drug is either solubilized into the micelle via hydrophobic interactions[2] or grafted covalently to the polymer. Impressive delivery results for platinum drugs were exemplified and attributed to enhanced stability of the micellar structures through design with very low critical micelle concentrations, but which disassemble upon cellular uptake. Three highly complementary talks followed that expounded the virtues of self-assembled cubic phases as drug delivery and bioimaging systems.

Patrick Hartley (CSIRO) presented recent studies investigating the influence of fusogenic lipids on the biological interactions of cubic phase particles, cubosomes, with biological surfaces. Using primarily surface-sensitive techniques, it was shown that introduction of phosphatidylserine residues into phytantriol-based cubosomes increases their cellular association and uptake but also their cytotoxicity.[3] The results have implications for the use of these particles as drug delivery systems for siRNA and other therapeutics. Xavier Mulet (Monash Institute of Pharmaceutical Sciences and CSIRO) described his recent efforts toward constructing multifunctional cubosomes that possess targeting capability toward specific tissues. Addressing the colloidal stability and stealth capability of the particles is an important first stage for this work, and he presented recent work aimed at discovering novel stabilisers using high-throughput technologies. The incorporation of quantum dots into the particles to impart an imaging functionality and future plans to control drug release through investigations of alternative novel self-assembled structures were highlighted.

The final speaker of the session was Ben Boyd (Monash Institute of Pharmaceutical Sciences), who illustrated his group's efforts toward the development of light-activated drug-release systems, taking advantage of the thermodynamic stability and reversibility of self-assembled systems to design systems for "on-demand"

Chapter News continued on page 32

Chapter News continued from page 31

release. Reversible control over drug release resulting from changes in light responsiveness has been demonstrated by his group—in this presentation, he focused on the use of photothermal and photochromic approaches to achieve remote activation of drug release for more convenient and effective treatment of, for example, macular degeneration.

An emerging formulation approach for poorly water-soluble drugs, "silica-lipid hybrid" capsules, similar to Pickering emulsions, was presented by Clive Prestidge (University of South Australia). The silica enables preparation of a dry powder that contains a high proportion of lipid, enabling the benefits of both lipid formulations and solid dose forms manufacture. The particles modify the rates of lipolysis and drug release and inhibit drug precipitation, leading to improved bioavailability.[4]

With increasing interest on controlling local availability of drugs in the lung after pulmonary administration,[5] a fantastic perspective on the appropriateness of pharmacopoeial methods for studying drug dissolution to predict *in vivo* dissolution and release behavior of drug particles in the lung was provided by Daniela Traini (Faculty of Pharmacy, University of Sydney). Dissolution studies with sodium cromoglycate showed that the standard USP2 dissolution apparatus is a poor predictor of likely *in vivo* dissolution profiles, failing to discriminate between different formulations. However, Franz diffusion cells, essentially being a "wetted surface model," are more representative of the *in vivo* lung surface and provided much greater discrimination between the performance of formulations. David Cipolla from Aradigm Corp. (U.S.A.) followed with discussion of an atypical formulation behavior *in vivo*. A formulation expected to provide rapid dissolution and absorption of a drug because of deep lung penetration actually provided slower uptake than a formulation that demonstrated less effective deep-lung delivery. Reasons for the difference were speculated upon, and discussion around preferential sites of drug absorption from the lung ensued.

A number of presentations centred on the discovery and delivery of anticancer compounds. Mary Bebawy (Pharmacy, University of Technology Sydney) has discovered a novel "nongenetic" pathway of multidrug resistance acquisition by cancer cells in which microparticles provide the vehicle for intercellular transfer of functional permeability glycoprotein (P-gp) from resistant (MDR^+) donor cells to drug sensitive (MDR^-) recipient cells.[6]

Two new types of anticancer candidates were described at the meeting. Targeting anticancer drugs based on α-tocopherol succinate using a triphenylphosphine lipophilic cationic group provided a highly effective compound inhibiting mitochondrial aspiration and showing efficacy against human breast cancer xenografts (Steve Ralph, Griffith University).[7] Jackie Wilce (Monash University) has been investigating a cell-permeable nonphosphorylated cyclic peptide (G7-18NATE) that specifically inhibits the SH2 domain in Grb7b protein, which plays a role in tyrosine kinase signaling—leading to inhibiting cancer cell proliferation and migration.[8]

Two novel approaches to delivery of anticancer compounds were also described. Lee-Yong Lim (University of Western Australia) described the interactions between wheat germ agglutinin–functionalised poly(lactic-co-glycolic acid) (PLGA) nanoparticles loaded with paclitaxel. Greater cytotoxicity against LS174T mucin-secreting colon cancer cells was attributable to slow diffusion and retention in the mucous layer, prolonging particle residence time in the vicinity of the cells compared with controls. Yan Yan from Frank Caruso's group at University of Melbourne described the intracellular release of doxorubicin from layer-by-layer capsules, which correlated to cytotoxicity of paclitaxel-loaded capsules against LIM 1899 human colorectal cancer cells. Binding of the capsules to cell surfaces was a key step facilitated by exofacial thiols on the cell membrane.

Michael Kassiou (University of Sydney) presented a fascinating account of his research on using *in vivo* positron emission tomography (PET) imaging in primates to detect overexpression of translocator protein (TSPO), an indicator of microglial activation leading to neurodegenera-

Delegates enjoy a predinner drink and boat cruise onboard the Denison Star.

tive diseases.[9] The administration of neuroprotective agents was shown to mitigate microgliosis, and the technique provides a new path to discovery of neuroprotective compounds that target TSPO. The central nervous system (CNS) delivery theme was continued by Pavla Simerska (University of Queensland), an expert in lipopolysaccharide synthesis for facilitating the delivery of vaccines. The lipid moiety increases the partition of compounds across biological barriers, while the polysaccharide units provide the targeting function and solubility. Her presentation described a new library of compounds designed for delivery and targeting of Enk pentapeptide, a pain regulator, which binds to opioid receptors in the CNS.

Martina Stenzel

Novel drug-polymer conjugates under development by PolyActiva (Australia) for the treatment of ocular diseases were described by Andrew Donohue. Release of ciprofloxacin for postsurgical prophylaxis against infection was at therapeutic levels (>MIC in the vitreous chamber) for over 120 days. A glaucoma treatment is also under development using the same technology.

The conference dinner was held onboard the *Denison Star*, and a short twilight cruise around the harbour in the Great Barrier Reef's Whitsunday Islands was followed by an excellent meal onboard. The keenly sought after bottle of Grange Hermitage, generously donated by Davies Collison Cave, was presented to the winner, Erica (Ying) Chen (University of Auckland, New Zealand) by Michael Caine, representing Davies Collison Cave.

Student poster prizes were awarded to Stephanie Phan from Monash Institute of Pharmaceutical Sciences ("Investigating the Evolution of Nanostructure During Digestion of Lipid-Based Drug Delivery Systems") and Warren Truong from University of New South Wales ("The Release of Therapeutics from Self-Assembling Hydrogels") to support travel to the 2012 CRS Annual Meeting & Exposition in Québec City, Canada.

Xavier Mulet checks out the beach between sessions.

The election of office bearers was held at the chapter's annual general meeting, and Ben Boyd and Leab Sek were voted to continue as president and treasurer, respectively. Dani Traini was voted in as secretary, Paul Young was voted in as scientific secretary, and Pavla Simerska was elected as vice president.

The meeting was strongly supported by our continuing sponsors: ATA Scientific, Davies Collison Cave, Monash Institute of Pharmaceutical Sciences, and new sponsors TrendBio, Avanti Lipids, and University of Technology Sydney–School of Pharmacy. Their generous and continued support is much appreciated.

In summary, this highly informative and efficient two-day meeting was a great success, with a number of collaborations arising from discussions and networking, as well as great exposure for the students involved. The quality of the meeting was again a testament to the growing significance of drug delivery research across Australia. Plans for the next meeting in Melbourne in November 2012 are already underway.

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People in the News

Compiled by Steven Giannos, Chrono Therapeutics Inc.
Industrial Editor

UCSF Professor to Receive Prestigious Dawson Biotechnology Award

Business Wire: April 12, 2012 – ALEXANDRIA, VA, U.S.A. – The American Association of Colleges of Pharmacy will recognize a pharmacy educator from the University of California, San Francisco for her contributions to contemporary teaching and scholarship in biotechnology. Tejal Desai, Ph.D., will receive the prestigious Paul R. Dawson Biotechnology Award during the AACP Annual Meeting, Pharmacy Education 2012, in Kissimmee, Florida, July 14–18.

Since receiving her Ph.D. in 1998, Desai has achieved prolific success in just a short time. She began her academic career at the University of Illinois at Chicago as the school's first faculty hire in bioengineering. In that role she was instrumental in starting a new bioengineering department and guiding the development of new curricular and laboratory approaches to bioengineering education.

Desai joined Boston University as an associate professor in 2001, where she led a new center in bionanotechnology and bioMEMS, as well as developed new courses in bionanotechnology, drug delivery, and tissue engineering. In 2005, she came to UCSF as a full professor in the Department of Bioengineering and Therapeutic Sciences (BTS), a joint department of the UCSF Schools of Pharmacy and Medicine.

"I am deeply honored to receive this award, which recognizes both research and teaching," said Desai. "This recognition would not be possible without the creative and committed students and colleagues I have had the opportunity to work with over the last 10 years."

Desai's scientific achievements are changing the way others in her field are thinking about drug delivery. She has developed new ideas to design particles with nanostructured surfaces to render both bioadhesive and biomimetic properties. Her groundbreaking work is supported by many patents as well as work with large companies such as Genentech, Kimberly Clarke, and Johnson & Johnson. Desai has a strong track record of attracting extramural support from NIH, NSF, and the pharmaceutical industry. Despite today's competitive funding environment, she has received more than $1 million in annual direct funding.

"As her research productivity and ability to attract research funding have shown, Tejal is a brilliant scientist," commented Mary Anne Koda-Kimble, Pharm.D., dean of the UCSF School of Pharmacy. "As well she is an extraordinary, prize-winning teacher. She brings to both the lab and classroom the kinds of fresh ideas and follow-through that so clearly predict even greater success in the years to come."

Desai has balanced her research productivity with excellence in both teaching and service. In collaboration with Frank C. Szoka, Ph.D., a former Dawson Award recipient and BTS department colleague, she has extensively redesigned the UCSF School of Pharmacy's drug delivery course for the Pharm.D. professional program, incorporating modern dosage formulations and principles of engineering. The revised course is now among the most highly evaluated by UCSF student pharmacists. She has supervised nearly 30 Ph.D. science students and has been recognized by the NSF New Century Scholar awards and recently received a teaching excellence recognition from UCSF School of Pharmacy Dean Koda-Kimble.

"Seeing that a young scientist can achieve so much in both teaching innovation and scholarly productivity should inspire others," said Lucinda L. Maine, Ph.D., R.Ph., AACP executive vice president and CEO. "That is why this year's recipient is so extraordinary."

The award is named in honor of Amgen former vice president of marketing and sales, Paul R. Dawson, a staunch supporter of education in biotechnology. Desai will receive a double helix glass sculpture and monetary award during the Examining Excellence Awards Plenary on July 17 at the 2012 AACP Annual Meeting.

The 2012 AACP Annual Meeting will be held July 14–18 at the Gaylord Palms Resort and Convention Center in Kissimmee, Florida. The conference offers educational programming, exhibits, networking events, and award presentations. Registration fees are waived for credentialed journalists. Visit the AACP website or contact our media relations representative for more information.

ACT Appoints Michael Heffernan to Board of Directors

Business Wire: April 9, 2012 – MARLBOROUGH, MA, U.S.A. – Advanced Cell Technology, Inc. ("ACT"; OTCBB: ACTC), a leader in the field of regenerative medicine, announced that Michael T. Heffernan, R.Ph., has been appointed to the company's board of directors, effective today.

Heffernan, 47, has 25 years of pharmaceutical industry experience. He is cofounder, president, and CEO of Collegium Pharmaceutical, a specialty pharmaceutical company developing proprietary, late-stage pharmaceutical products, and building a portfolio of products for the treatment of chronic pain that use its patented DETERx® tamper-resistant, extended-release drug delivery platform.

"Michael's expertise in pharmaceutical product development, as well as experience in capital markets and deal-making, will be invaluable to the company as we continue our forward momentum with our clinical programs, and we are excited to welcome him to our board of directors," said Gary Rabin, chairman and CEO of ACT.

While at Collegium, Heffernan also founded Onset Therapeutics, which he spun out of Collegium to form PreCision Dermatology, a dermatology-focused specialty pharmaceutical company. Prior to cofounding Collegium Pharmaceutical, he was president, CEO, and chairman of PhyMatrix (later renamed Innovative Clinical Solutions), a publicly traded, diversified healthcare management company, where he was responsible for restructuring and refinancing the company. Prior to being named president of PhyMatrix, he served as president of the clinical research division of the company. Prior to that, he was president and CEO of Clinical Studies, Ltd. and led the successful sale of the company to PhyMatrix. He was previously with Eli Lilly & Company in a number of sales and marketing roles.

Heffernan said, "I am thrilled to join ACT's board of directors at this exciting time, and I am looking forward to working with the rest of the board and ACT's management team as we continue to progress quickly with the clinical trials for dry AMD and Stargardt's disease."

Heffernan serves on the board of Collegium Pharmaceutical, PreCision Dermatology, Cornerstone Therapeutics, Inc. (traded on the Nasdaq stock exchange under ticker symbol CRTX), and TyRx Pharma, Inc. Heffernan is a registered pharmacist.

Intarcia Appoints Michelle Baron, M.D., FACE, Vice President and Chief Medical Officer

PRNewswire: March 27, 2012 – HAYWARD, CA, U.S.A. – Intarcia Therapeutics, Inc. today announced the appointment of Michelle Baron, M.D., FACE, to the position of Vice President Clinical Research and Chief Medical Officer. Dr. Baron will lead clinical development and medical affairs for the company, including the global phase 3 development of ITCA 650 (once or twice yearly subcutaneous continuous delivery of exenatide) for the treatment of type 2 diabetes.

"Michelle is an accomplished leader who brings a wealth of scientific and clinical expertise with a proven track record of building high-performing teams that get innovative therapies developed optimally and to market," said Kurt Graves, Executive Chairman and Acting CEO of Intarcia. "Attracting someone with Michelle's proven ability to shape some of the most important medicines in the diabetes field is a key appointment as we initiate our global phase 3 program for ITCA 650."

Dr. Baron is well recognized throughout the industry as an accomplished physician in clinical drug development and medical affairs, with deep expertise in cardiovascular, endocrine, and metabolic diseases. Prior to joining Intarcia, Dr. Baron was Vice President, Diabetes U.S. at Sanofi-Aventis, where her responsibilities included the design and commercialization of a U.S. diabetes patient solutions platform. Michelle also assessed business development opportunities and strategic partnerships for the U.S. Diabetes Division. Prior to her work at Sanofi-Aventis, Dr. Baron spent ten years at Novartis, most recently serving as Senior Medical Director, Diabetes Section of the Cardiovascular and Metabolism U.S. Clinical Development and Medical Affairs group. Michelle was a key member of the leadership team responsible for designing and executing the clinical development, registration, and commercialization strategies for Novartis' diabetes portfolio in the U.S. She previously served as program director of the Endocrinology and Metabolism Fellowship Program, the director of the Osteoporosis Diagnostic Center, and fellow at the SUNY Health Science Center at Brooklyn, and as an attending physician in the Department of Medicine at Kings County Medical Center. She continues to serve as an assistant professor in the Department of Medicine's Division of Endocrinology and Metabolism at SUNY. Dr. Baron received her M.D. from Howard University College of Medicine, her B.A. from The Johns Hopkins University, and did her postgraduate training in Internal Medicine at Emory University.

"GLP-1 analogue therapies are among the most efficacious and fastest growing treatments available for patients with type 2 diabetes. However, the need for regular administration by injection and bothersome side effects has limited patient acceptance and adherence to therapy," commented Dr. Baron. Sub-optimal glucose reductions and poor patient adherence to therapy continue to be two of the greatest challenges to achieving glycemic goals and optimizing diabetes care over time. The goal of the ITCA 650 program is to enhance both the important clinical properties of GLP-1 analogue therapy in a manner that will benefit a broader patient population and also by delivering a full year of exenatide treatment in just one or two administrations per year. "Once or twice yearly ITCA 650 holds the exciting potential to break away from regular self-injections and help physicians, patients and payers meet their common objectives to reach glucose-lowering goals and ensure patient adherence. It is exciting to join a team that is working to transform the way in which we care for patients with type 2 diabetes."

In December 2011, Intarcia announced the selection of Quintiles as a worldwide development partner in what will shortly become a three-party collaboration between Intarcia, Quintiles, and a Global Pharmaceutical Partner. Quintiles is ramping up to initiate the global phase 3 development program for ITCA 650, which consists of six phase 3 studies, four of which are intended to evaluate the potential of ITCA 650 to demonstrate superiority against the most commonly used oral antidiabetic medicines. Quintiles has also made strategic investments in Intarcia and the ITCA 650 program to help accelerate ITCA 650 to market.

People in the News continued on page 36

People in the News continued from page 35

Hovione Announces the Appointment of Colin Minchom, Ph.D., MRPharmS as Vice President, Particle Design Business Unit

PRNewswire: March 12, 2012 – LOURES, PORTUGAL – Hovione today announced the appointment of Dr. Colin Minchom as Vice President of its Particle Design Business Unit. Dr. Minchom was most recently with Patheon, where he held the position of Vice President, Pharmaceutical Development Services for North America. Based in East Windsor, New Jersey, Dr. Minchom will report to Guy Villax, Hovione's chief executive officer.

"We are very pleased to welcome Dr. Minchom to Hovione. He is an excellent addition to our management team in an area of critical importance to our customers. Dr. Minchom is responsible for innovating Hovione's pharmaceutical particle design offerings to meet the development and commercial supply needs of the formulator with poorly bioavailable or otherwise challenging molecules," said Mr. Guy Villax.

"I look forward to building on what has been achieved by Hovione to date in its creation of solutions for customers needing particle design for improved bioavailability and also specialist delivery by non-oral routes," said Dr. Minchom.

Dr. Minchom's 29-year career includes extensive experience in the process, science, and global regulation of drug development with emphasis on dosage forms and drug delivery. Prior to this role at Patheon, Dr. Minchom was Head of Pharmaceutical Sciences at Cerebrus Ltd., a U.K. privately held pharmaceutical company, and has also held positions of increasing scientific and management responsibility at Eli Lilly and E. R. Squibb in formulation and product development, project management and product management.

Dr. Minchom is chair of the American Association of Pharmaceutical Scientists (AAPS) 2012 Annual Meeting Planning Committee for Chicago. He also serves as a volunteer at the United States Pharmacopoeia (USP) as a member of an expert committee addressing small molecules. Dr. Minchom was until recently an advisor at the Medical and Related Sciences Discovery District (MaRS) incubator in Toronto, Canada.

Trained as a pharmacist at the Leicester School of Pharmacy in the U.K., he holds a Ph.D. in industrial pharmacy from the University of Wales College of Cardiff.

Hovione is a global company with over 50 years' experience in active pharmaceutical ingredient and intermediate drug product development and compliant manufacture. With four FDA-inspected sites in the U.S., China, Ireland, and Portugal, the company focuses on the most demanding customers, in the most regulated markets. Hovione offers integrated API, particle design, and formulation development and manufacturing. In the inhalation area, Hovione is the only independent company offering such a broad range of services. ■

In the News

Compiled by Steven Giannos, Chrono Therapeutics Inc.
Industrial Editor

April 2012

Strength of Aptalis Pharmaceutical Technologies Patents Confirmed by AMRIX® Verdict

Aptalis Pharmaceutical Technologies: April 25, 2012 – Bridgewater, NJ, U.S.A. – Aptalis Pharmatech, Inc. (previously known as Eurand, Inc.) and Cephalon, Inc. a wholly owned subsidiary of Teva Pharmaceuticals Industries Ltd., and Anesta AG prevailed in their appeal to the U.S. Court of Appeals for the Federal Circuit, which reversed a lower court's determination and held that two patents covering the AMRIX® muscle relaxant (Cyclobenzaprine Hydrochloride Extended-Release Capsules) are valid. The full text of the court's decision can be found at: http://www.cafc.uscourts.gov/images/stories/opinions-orders/11-1399-1409.pdf

The two patents, owned by Aptalis Pharmatech, Inc. and licensed to Cephalon, expire in 2023 and 2025. The patents, along with other additional patents that protect AMRIX®, are all listed on the FDA's "Orange Book" and will be enforced to the fullest extent possible.

AMRIX® is a convenient extended-release (once-daily administration) dosage form of cyclobenzaprine that is indicated for short-term relief of muscle spasm as an adjunct to rest and physical therapy. Prior to the approval of AMRIX® in 2007, only immediate-release formulations of cyclobenzaprine were available. Such formulations often required repeated administration of two to three times daily. According to recent IMS data, cyclobenzaprine is the most frequently prescribed drug for muscle relaxation in the United States.

The use of Aptalis Pharmaceutical Technologies DIFFUCAPS® Technology in AMRIX® satisfies an unmet medical need by providing a modified-release formulation, once-daily dosing of cyclobenzaprine, thereby allowing for increased patient compliance.

"Aptalis Pharmaceutical Technologies endeavors to offer to our partners the most effective patent protection possible of our broad and diversified portfolio, and this court decision confirms the strength of these formulation patents," said John Fraher, president of Aptalis Pharma.

The Aptalis portfolio is composed of numerous patents with broad claims directed to its formulation technologies and related materials, processes, equipment, and methods of manufacture. Aptalis also has many product-related patents, which contain more specific claims directed to particular drugs or classes of drugs in combination with our formulation technologies. Aptalis's owned and in-licensed patent portfolio consists of over 900 granted patents and pending applications.

Aptalis Pharmaceutical Technologies offers a broad portfolio of oral drug delivery technology platforms: customized drug release, bioavailability enhancement, and taste masking for ODTs (orally disintegrating tablets) and other dosage forms. Together, these technology platforms combined with licensing, manufacturing, and R&D capabilities enable Aptalis Pharmaceutical Technologies to produce customized drug formulation solutions for partners across a range of dosage forms and therapies. Aptalis Pharmaceutical Technologies develops and manufactures products for its partners and supports the drug development process for the Aptalis Pharma pipeline and portfolio of products. For more information about Aptalis Pharmaceutical Technologies, visit www.AptalisPharmaTech.com.

Grace and Formac Pharmaceuticals Announce Successful Clinical Trial Demonstrating the Novel Use of Silica for Drug Delivery

Business Wire: April 23, 2102 – COLUMBIA, MD, U.S.A. – W. R. Grace & Co. (NYSE: GRA), in partnership with Formac Pharmaceuticals NV, a research and development pharmaceutical company, announced today positive data from initial human studies enabled by the companies' unique mesoporous silica-based drug delivery technology. This novel technology opens up a viable new avenue for the development of poorly soluble compounds.

This was the first-ever clinical study to demonstrate the bioavailability-enhancing properties of silica in humans. Improved bioavailability enables active pharmaceutical ingredients (APIs) to more effectively absorb into the body. In this study, the bioavailability profile of fenofibrate formulated with silica was compared to the marketed micronized formulation (Lipanthyl®). The study results show a 54 percent higher bioavailability for the silica formulation than the marketed formulation.

The study confirmed the numerous promising findings obtained in preclinical models and exemplifies that the Grace and Formac Pharmaceuticals partnership can provide a fully integrated, cost effective, and innovative solution, from early phases to commercial production, for the development of poorly soluble compounds.

"We are excited about the study results proving the effectiveness of the silica-based drug delivery technology in humans," said George Young, Vice President of New Business Development at Grace. "The successful completion of this study marks an important milestone for our strategic partnership with Formac as we embark on the development and commercialization of this novel approach for improved drug delivery."

In the News continued on page 38

In the News continued from page 37

Grace and Formac partnered in 2011 to optimize and commercialize the silica-based technology that Formac created. Grace is leveraging its silica R&D and manufacturing expertise to develop a portfolio of silicas that can give pharmaceutical companies an optimized and tailored drug delivery solution for their drug. For more information, please visit www.SilicaDrugDelivery.com.

$130 Million USTAR Interdisciplinary Research Facility Dedicated at the University of Utah

Business Wire: April 19, 2012 – SALT LAKE CITY, UT, U.S.A. – The University of Utah (UofU) and the USTAR Governing Authority today cut the ribbon on a $130 million, sustainably designed interdisciplinary research facility, aimed at attracting some of the world's most internationally recognized faculty and fueling Utah's economic development activity. The James L. Sorenson Molecular Biotechnology Building—A USTAR Innovation Center, was funded through a $100 million commitment from the state of Utah along with private gifts, among them $15 million from the Sorenson Legacy Foundation and $1.25 million from the Micron Technology Foundation. "We are pleased that the building bears the name of one of Utah's most innovative and successful biomedical pioneers, James LeVoy Sorenson," said David W. Pershing, University of Utah president.

State funding comes from the USTAR (Utah Science Technology and Research) Initiative, a long-term economic development initiative that promotes world-class research facilities and research teams. USTAR is helping to create new technologies that can be commercialized, generating more technology-based start-up firms, higher-paying jobs, and additional business activity all aimed at expanding Utah's tax base.

The James L. Sorenson Molecular Biotechnology Building—A USTAR Innovation Center, which was designed to achieve LEED Gold certification from the U.S. Green Building Council, has been designed by architecture firm Lord, Aeck & Sargent's Atlanta office in association with Prescott Muir Architects in Salt Lake City.

"The building site both physically and academically unites the health sciences with main campus. Through the USTAR initiative, we are crossing traditional boundaries to accelerate research at the interfaces of medicine, pharmacy, engineering, computer science, and life sciences," said Dinesh Patel, managing director at vSpring Capital and chairman of the USTAR Governing Authority.

The 208,000-square-foot building houses senior faculty researchers, plus junior faculty and administrative and laboratory personnel. The building contains both flexible, open-bench research laboratories and specialty core research facilities for biomedical microscopy, engineering microscopy, and nano-fabrication. Open lab space has adjacent closed equipment rooms and nearby office space for the principal investigators. The flexible laboratories and their core support labs are designed to support the collaboration of scientists in many disciplines with the most sophisticated scientific tools and equipment. The energy-efficient facility is setting a high standard for sustainable design that will reduce both energy use and energy costs from current laboratory code requirements by a minimum of 40 percent.

To date, the University of Utah has successfully recruited 33 high-profile researchers through the USTAR initiative, from universities such as Harvard, UCLA, and Brown, in clusters ranging from nanomaterials, nanomedicine, and drug delivery to genetics, bioimage analysis, and the neurobiology of developmental disorders.

USTAR's full impact will be realized when new research teams commercialize innovative technologies and products. From inception through the end of FY11, the University of Utah's USTAR faculty leaders have generated nearly $76 million in grants, with more than $80 million in research proposals pending. Through FY11, USTAR teams have had 146 invention disclosures and patent filings.

USTAR is a long-term, state-funded investment to strengthen Utah's "knowledge economy" and generate high-paying jobs. Funded in March 2006 by the State Legislature, USTAR is based on three program areas. The first area involves funding for strategic investments at the University of Utah and Utah State University to recruit world-class researchers. The second area is to build state-of-the-art interdisciplinary facilities at these institutions for the innovation teams. The third program area involves teams that work with companies and entrepreneurs across the state to promote science, innovation, and commercialization activities. For more information, go to www.innovationutah.com or follow http://twitter.com/Innovationutah.

EffRx and Mission Bring New Osteoporosis Medication to the United States and Canada

Business Wire: April 18, 2012 – FREIENBACH, Switzerland – EffRx Pharmaceuticals SA announced today that Mission Pharmacal, San Antonio, Texas, has entered into a patent and technology licensing agreement with EffRx Pharmaceuticals SA, Freienbach, Switzerland, for the manufacturing and commercialization of BINOSTO™ (alendronate sodium) effervescent tablets in the United States and Canada. The U.S. Food and Drug Administration recently approved BINOSTO™ to treat osteoporosis in postmenopausal women and to increase bone mass in men with osteoporosis.

Utilizing EffRx's formulation technology, BINOSTO™ is the first and only buffered effervescent therapeutic to deliver the gold standard in osteoporosis treatment and fracture prevention of alendronate sodium—in an easy-to-swallow, buffered solution. A Harris Interactive Poll concluded that up to 40 percent of American adults have difficulties with swallowing tablets. That difficulty often results in patients having to choose between enduring painful injections or forgoing treatment for this chronic disease.

Dr. Robert Recker, President of the National Osteoporosis Foundation, notes, "BINOSTO provides an important new innovation for patients suffering with osteoporosis. BINOSTO offers those patients that struggle with taking tablets the opportunity to obtain the proven fracture prevention of alendronate in an easy-to-take, buffered solution."

"We are very excited about our partnership with EffRx and look forward to helping deliver BINOSTO to women with osteoporosis who have difficulty with pills or shots and to men who also struggle with this disease. Men's bone health has previously been overlooked," says Neil Walsdorf Jr., President of Mission Pharmacal.

EffRx CEO Christer Rosén adds, "We believe Mission is the logical choice for bringing BINOSTO to the United States and Canadian markets. Mission is focused on quality first and foremost, and they have a long history of educating patients and physicians in bone health. They also have a well-established women's health sales force where they have proven that they can launch a product and drive it to a market leadership position. We are extremely happy to have Mission as a partner."

Osteoporosis is a serious and often debilitating disease affecting more than 200 million people worldwide. According to the National Osteoporosis Foundation, the leading health organization dedicated to the prevention of osteoporosis and broken bones, more than 10 million people in the United States have osteoporosis and another 34 million are estimated to have osteopenia, or low bone density, which is often the precursor to osteoporosis.

Although it is commonly thought of as a "woman's disease," the problem of osteoporosis in men has recently been recognized as an important public health issue. It is true that women suffer relatively rapid bone loss in the first few years after menopause. However, by about age 65 men and women lose bone mass at the same rate.

"With the commercialization rights to BINOSTO, we can further our investment in promoting and treating bone health with a world-class product that addresses both osteoporosis and pill-swallowing difficulty," notes Terry Herring, President of Mission Pharmacal Consumer Operations. "We look forward to building strategic partnerships that will ensure BINOSTO is widely promoted and available throughout the United States and Canada."

CytRx Announces Issuance of Key U.S. Patent Covering INNO-206 Linker Technology

Business Wire: April 12, 2012 – LOS ANGELES, CA, U.S.A. – CytRx Corporation (Nasdaq: CYTR), a biopharmaceutical company specializing in oncology, today announced that the U.S. Patent and Trademark Office (USPTO) has issued a key patent covering the tumor-targeting conjugate INNO-206 linker platform technology and INNO-206 pharmaceutical compositions.

"We now have broad patent protection for the linker platform technology, which is exclusively licensed to CytRx from the Tumor Biology Institute in Freiburg, Germany. This technology is in essence its own pipeline with blockbuster drug potential and for which we hold exclusive worldwide rights. It has proven affinity to couple with multiple chemotherapeutic agents beyond doxorubicin, which is the formulation we are currently evaluating. We now have patent protection covering the linker technology with epirubicin, daunorubicin, and idarubicin, any of which could be incorporated into our future clinical development plans," said CytRx President and CEO Steven A. Kriegsman.

This linker technology consists of a single molecule that, when attached to a chemotherapeutic agent, binds within minutes to albumin in the bloodstream and delivers the agent to the tumor site, thus allowing for greater drug concentration within the tumor. The company believes that greater drug delivery to the tumor site could improve effectiveness while avoiding the side effects associated with the broader systemic delivery of most toxic agents.

The patent, U.S. Patent No. 8,153,581, titled "Process for Producing an Injectable Medicament Preparation," claims pharmaceutical compositions comprising a class of pro-drugs characterized by having an active agent, such as anthracyclines or other cytostatic agents, linked through a cleavable spacer to a protein-binding molecular residue, such as albumin. Certain claims of the patent also specifically cover pharmaceutical compositions of INNO-206.

CytRx has completed enrollment of a phase 1b/2 clinical trial with the doxorubicin conjugate formulation of INNO-206 in patients with advanced solid tumors (primarily soft tissue sarcomas), and has initiated an international phase 2b clinical trial in patients with soft tissue sarcomas, comparing the efficacy and safety of INNO-206 to doxorubicin, a standard treatment for soft tissue sarcomas. The phase 1b/2 clinical trial results will be presented by a premier soft tissue sarcoma expert at the American Society of Clinical Oncology (ASCO) meeting in early June. The company also has announced plans in the second quarter of 2012 to begin a phase 2 trial with INNO-206 in an undisclosed solid tumor indication. INNO-206 has been shown to have increased efficacy compared to either placebo or native doxorubicin in breast, ovarian, pancreatic, renal, and lung cancers, as well as in multiple myeloma human tumor xenograft models in mice.

CytRx Corporation is a biopharmaceutical research and development company specializing in oncology. The CytRx oncology pipeline includes three programs in clinical development for cancer indications: INNO-206, tamibarotene, and bafetinib. With its tumor-targeted doxorubicin conjugate INNO-206, CytRx has initiated an international phase 2b clinical trial as a treatment for soft tissue sarcomas, is completing its ongoing phase 1b/2 clinical trial primarily in the same indication, and plans to initiate a phase 2 trial for an undisclosed

In the News continued on page 40

In the News continued from page 39

solid tumor indication in the first half of 2012. CytRx's pipeline also includes tamibarotene, which it is testing in a double-blind, placebo-controlled, international phase 2b clinical trial in patients with non-small-cell lung cancer, and which is in a clinical trial as a treatment for acute promyelocytic leukemia (APL). The company is evaluating bafetinib in the ENABLE phase 2 clinical trial in high-risk B-cell chronic lymphocytic leukemia (B-CLL) and plans to seek a partner for further development of bafetinib. For more information about the company, visit www.cytrx.com.

Alitair Announces Notice of Patent Allowance for Its Platform Drug Delivery Technology, REA™

Business Wire: April 12, 2012 – MORRISTOWN, NJ, U.S.A. – Alitair Pharmaceuticals, Inc., a mid-stage pharmaceutical company with multiple respiratory product candidates in development, today announced that it has received a Notice of Allowance from the United States Patent and Trademark Office (USPTO) for its ion-exchange resin platform drug delivery technology, REA™. Alitair has out-licensed two product candidates utilizing its REA™ platform technology, and additional product candidates are available for out-licensing.

"Our propriety ion-exchange resin delivery platform can be utilized across a range of therapeutic classes and with many different molecules," stated Alitair President and CEO William W. Howard, Ph.D. "The REA™ platform technology allows us to improve upon currently available therapies and create new oral-solid formulations with less frequent dosing schedules, both of which have been shown to improve patient adherence."

"Receiving this Notice of Allowance is an important milestone in our product development strategy and the growth of Alitair," continued Howard. "We will continue to pursue additional patent protection in the U.S. and in key markets around the world. This Notice of Allowance from the PTO and our equally strong International Preliminary Examination Report (IPER) means that we will have a truly global patent portfolio in a short time. We are also actively seeking funding and development partners to build on the momentum we've created and advance our product development programs."

Alitair Pharmaceuticals, Inc. discovers, invents, and develops medicines for the treatment of respiratory illnesses. Alitair has out-licensed two prescription cough candidates that use its proprietary ion-exchange resin technology, REA™, and other product candidates are available for out-licensing. Additional information about Alitair is available on the Alitair website at www.alitair.com.

University of Kansas Researchers Win Co-Inventorship Dispute over Cancer Drug Formulation Patents

Business Wire: April 6, 2012 – MCLEAN, VA, U.S.A. – Pillsbury today announced that its clients, the University of Kansas (KU) and the University of Kansas Center for Research, Inc. (KUCR), a nonprofit corporation affiliated with KU, prevailed in a closely watched legal battle over cancer drug formulation patents after an arbitration panel ruled in KUCR's favor following years of litigation against the National Institutes of Health (NIH). The favorable arbitration outcome for KU and KUCR means that KU's University Distinguished Professor, Dr. Valentino Stella, and his laboratory assistant, Ms. Wanda Waugh, will receive inventorship credit on patents the NIH owns covering Velcade®, a highly successful medication for treating blood cancers. Dr. Stella and Ms. Waugh, while working under contract to NIH, co-invented crucial formulations that give Velcade® long-term shelf-life and stability, but they were never credited as co-inventors on the patents at issue (U.S. Patent Nos. 6,713,446 and 6,958,319), depriving them of recognition and legal entitlements under U.S. patent laws.

"We are extremely pleased with this outcome for our clients, KU and KUCR, and two very deserving co-inventors who—after helping create a breakthrough cancer drug formulation—were denied credit for years following their integral, essential contributions," said Pillsbury Intellectual Property partner William P. Atkins, who led a team of Pillsbury IP attorneys including associate Christopher K. Dorsey, senior associate Benjamin L. Kiersz, partner George M. Sirilla, and partner Dr. John R. Wetherell representing KU and KUCR.

"KU, KUCR, Dr. Stella, and Ms. Waugh will finally receive the co-inventorship credit they are entitled to under the law," Atkins said. "This protracted dispute with the NIH serves as a cautionary tale for organizations pursuing breakthroughs in cutting-edge research under government contracts, whether in health care, defense, or other science and technology fields."

Atkins explained that, although certain provisions of the U.S. Federal Acquisition Regulation (FAR) governing federal contracts address IP rights and ownership, the FAR does not clearly address scenarios where both federal and contractor employees work together on a project and are co-inventors of a resulting invention. He noted that universities performing much of the government's research could find themselves in such scenarios and have much to lose if they are unaware of the regulations' nuances.

"Universities may not even realize they have been deprived of inventorship credit until after a patent at issue has been licensed to industry by the government, as in KUCR's case," Atkins added. "Given the complexity of multi-party research contracts in fields like pharmaceutical development, the lesson this case offers for contractors and academia is to be proactively aware of how your contributions are utilized, document your inventions for the agency before their patent applications are underway, and prepare to challenge mistakes."

Under a research agreement with the NIH's National Cancer Institute (NCI), Dr. Stella was asked to study innovative drug delivery methods for cancer patients. Dr. Stella, a tenured professor listed as an inventor on more than 33 patents covering treatments for AIDS, epilepsy, and others, led KUCR's work on NCI's challenging assignment—formulating an effective anti-cancer treatment from a promising, but unstable, chemical

compound. Dr. Stella and Ms. Waugh, who each had twenty-plus years working on such complex drug formulation problems, devised a method that made the new medication stable—and therefore effective. Their breakthroughs led to NIH's 2001 patent application, which recited Dr. Stella and Ms. Waugh's formulation but listed the NCI's project officer as the sole inventor.

In 2002, the NIH exclusively licensed the patents to Millennium Pharmaceuticals, which developed and branded Velcade®. The drug brought in $83.5 million in the first quarter of 2008 alone. In May of 2008, Millennium was acquired for $8.8 billion by Takeda Pharmaceutical Co. Ltd. Realizing its inventors had been omitted, KUCR turned to Pillsbury. When the NIH denied KUCR's appeal for credit, Atkins' team filed a lawsuit against the NIH in November 2008 in the U.S. District Court for the District of Kansas seeking co-inventorship credit for Dr. Stella and Ms. Waugh. Millennium later intervened in the case on the side of NIH, along with Johnson & Johnson subsidiary Centocor Ortho Biotech Products LP (COBI), the company Millennium licensed to market Velcade® overseas. In 2010, the parties agreed to submit the case to binding arbitration.

Pillsbury has handled patent and trademark litigation since 1893. Now, with more than 90 IP practitioners firmwide, Pillsbury advises clients on developing successful and comprehensive IP strategies by protecting, managing, asserting, defending, and leveraging their IP assets. The IP team spans a number of offices and countries, with team members in Northern Virginia, San Francisco, Silicon Valley, Los Angeles, Houston, Washington, DC, New York, San Diego, Sacramento, Tokyo, and London. Domestically, Pillsbury has advocated for clients in 77 of the 94 U.S. district courts, as well as before the ITC in Section 337 cases, the International Chamber of Commerce, and the World Intellectual Property Organization. Pillsbury's IP lawyers have a wide range of advanced scientific and technical degrees in areas including electrical and mechanical engineering, chemistry, biology, physics, and a number of other technical disciplines.

Medical Marijuana Inc. Signs Final Term-Sheet to Purchase Cannabinoid (Cannabis) Delivery Method for Deployment into Pharmaceutical Market

PRNewswire: April 4, 2012 – SAN DIEGO, CA, U.S.A. – Medical Marijuana Inc. (OTC: MJNA) is pleased to announce it has signed contracts with a European-based pharmaceutical company for the purchase and development of a patented cannabinoid drug delivery product. The delivery method, in the form of a non-smoked product, will be able to provide benefits of cannabinoid-based healthcare research to medical professionals and patients seeking such innovative products. The product can be formulated in different dosage levels to be used for the majority of illnesses that cannabis has been shown to be effective with.

This cannabinoid delivery method will greatly expand MJNA's portfolio as the firm seeks to develop the company's presence into the medical delivery system marketplace. Many European and Middle Eastern countries have decriminalized and approved marijuana for medicinal purposes. The future of the cannabinoid industry lies in developing delivery methods that are socially and medically acceptable. Delivery methods include oral administration (tablets, liquids), intravenous therapy, topical gel-type application, lozenge, and many others. Products will be available in the U.S. in the coming months as MJNA establishes a licensing and manufacturing base with state-licensed companies.

CannaBank has agreed to provide the financing for this transaction as part of their initial $4 million financing agreement (see MJNA Press Release from Feb. 28, 2012). CannaBank shall maintain a 20% interest in Medical Marijuana Inc.'s ownership of the company, which represents an overall 10% interest. Medical Marijuana Inc. will assume 50% ownership in the European pharmaceutical company.

This is a very significant event for the company and the future of cannabis-based healthcare, as medical and consumer acceptance of cannabis and their derived extracts/compounds will have to take the form of non-smoked delivery methods. Products will have to meet "medical grade" criteria, and dosing will have to be part of the eventual overall acceptance. Today's acquisition represents the first step toward that eventual future clinical acceptance.

Doctors and patients equally will need certain levels of comfort knowing that the products are uniform, consistent in their effect, and have shown proven, verifiable results. Although the research has been mostly in overseas countries, including Europe, the United States will take a leap forward with the introduction of these products into the research and development arena.

"This is a significant step in the production of medical-grade cannabis-based products. This acquisition will significantly expand not only our portfolio of patented products that are socially and medically acceptable, but solidifies the company's future in the cannabinoid medicinal arena. We will be retaining a very experienced research, development, and critically important patent team. We expect to close on this transaction in April. We appreciate the continued support of our shareholders and look forward to updating them on our other pending transactions shortly," stated Michael Llamas, president of Medical Marijuana Inc.

Novel Prostate Nanomedicine Delivers High Drug Concentration Directly and Safely to Tumors in Phase I Trials

Business Wire: April 4, 2012 – SANTA MONICA, CA, U.S.A. – Nanomedicine research at the David H. Koch Institute for Integrative Cancer Research at MIT funded by a $5 million grant from the Prostate Cancer Foundation (PCF) has delivered the first nanomedicine shown to successfully target prostate cancer cells and deliver docetaxel chemotherapy in high concentrations in phase I clinical trials. Docetaxel is used in

In the News continued on page 42

In the News continued from page 41

prostate cancer patients who have failed hormone therapy and is currently delivered via infusion, which floods the body and affects both cancerous and healthy cells. By using targeted nanoparticles to deliver the therapeutic, healthy cells are widely spared from undesired side effects of treatment.

Results from phase I clinical trials of BIND-014 were published today in *Science Translational Medicine*. BIND Biosciences, the biopharmaceutical company that developed BIND-014, also presented the trials data today at the 2012 American Association of Cancer Research meeting in Chicago.

BIND-014 is a programmable nanomedicine that combines a targeting ligand and a therapeutic nanoparticle. BIND-014 contains docetaxel, a proven cancer drug that is approved in major cancer indications including breast, prostate, and lung, encapsulated in FDA-approved biocompatible and biodegradable polymers. BIND-014 is targeted to prostate-specific membrane antigen (PSMA), a cell surface antigen abundantly expressed on the surface of cancer cells and on new blood vessels that feed a wide array of solid tumors. In preclinical cancer models, BIND-014 was shown to deliver ten-fold more docetaxel to tumors than an equivalent dose of conventional docetaxel. The increased accumulation of docetaxel at the site of disease translated to marked improvements in antitumor activity and tolerability.

PCF has funded research on PSMA, the attractor antigen or "sticky tape" that is targeted by BIND-014 nanoparticles since 1996. This research further discovered that PSMA is also found on the surfaces of neovasculature (new blood vessels) in the tumors of other cancers.

"The development of BIND-014 represents a unique public, private, and philanthropic funding effort to fast-forward and realize the potential of nanomedicines for the benefit of cancer patients," said Jonathan W. Simons, M.D., president and CEO of the Prostate Cancer Foundation, which provided $5 million to the collaborative research project in 2007. "This is a tour de force of transdisciplinary collaboration—bioengineers, chemical engineers, nanotechnologists, oncologists, and prostate cancer biologists all came together to advance multiple components and concepts to the clinic. PCF's funding leveraged an early and significant NCI nanotechnology investment in this prostate cancer therapeutics research. With this exemplary new work across institutional boundaries, BIND-014 represents an entirely new, programmable platform for targeted cancer drug delivery—and it moved to the clinic in a strikingly short period of time."

The idea to develop aptamer-targeted nanoparticles was first conceived in 2002 and forwarded by the David H. Koch Institute for Integrative Cancer Research at MIT, Brigham and Women's Hospital, the Dana-Farber Cancer Institute, Harvard Medical School, and Weill Cornell Medical College. Funding for the research and development program was provided by both public and private sources including the MIT Institute for Integrative Center for Cancer Research, the National Institute for Biomedical Imaging and Bioengineering, a prostate cancer SPORE Grant awarded to Dana-Farber Cancer Institute, the National Cancer Institute, the NCI Alliance in Nanotechnology, and the Prostate Cancer Foundation.

"These seminal data on BIND's first clinical stage Accurin, BIND-014, demonstrates for the first time that it is possible to generate medicines with both targeted and programmable properties that can concentrate the therapeutic effect directly at the site of disease, potentially revolutionizing how complex diseases such as cancer are treated," commented Omid Farokhzad, M.D., BIND Founder and Associate Professor, Harvard Medical School. "BIND's data are a giant leap forward in achieving the true promise of nanomedicine by enabling the design of therapeutics with highly differentiated efficacy and safety that go above and beyond the capabilities of traditional drug design through medicinal chemistry."

"Previous attempts to develop targeted nanoparticles have not translated into clinical success because of the inherent difficulty of designing and scaling up a particle capable of targeting, long-circulation via immune-response evasion, and controlled drug release," commented Robert Langer, Sc.D., BIND Founder and David H. Koch Institute Professor at MIT. "BIND-014 is the first therapeutic of its kind to reach clinical evaluation and has demonstrated increases of up to tenfold in drug concentration in tumors, which lead to substantially better efficacy and safety." With these findings, multiple phase I/II trials targeting other cancers expressing PSMA can be accelerated safely.

Neupro® Approved by U.S. FDA for Parkinson's Disease and Restless Legs Syndrome

Business Wire: April 3, 2012 – BRUSSELS, Belgium & ATLANTA, GA, U.S.A. – UCB announced today that the U.S. Food and Drug Administration (FDA) approved Neupro® (Rotigotine Transdermal System) for the treatment of the signs and symptoms of advanced stage idiopathic Parkinson's disease (PD) and as a treatment for moderate-to-severe primary Restless Legs Syndrome (RLS). Neupro® was previously approved by the FDA for the signs and symptoms of early stage idiopathic PD. Neupro® is a dopamine agonist patch that provides continuous drug delivery for patients with PD and RLS. The FDA has also approved UCB's new formulation of Neupro®.

"Neupro® represents an innovation in the treatment of Parkinson's disease and restless legs syndrome," said Prof. Dr. Iris Loew-Friedrich, Chief Medical Officer and Executive Vice President of Global Projects and Development at UCB. "UCB is thrilled to make Neupro® available to patients living with these serious diseases."

"RLS can be a serious condition with symptoms that affect patients during the day as well as at night, and Parkinson's disease symptoms can have a broad impact on patients. Neupro® provides a novel way of treating RLS and PD through continuous transdermal dopaminergic delivery. It can help patients manage the unpredictable nature of these chronic conditions," said William Ondo, M.D., Professor, Department of

Neurology, University of Texas Health Science Center at Houston.

As a PD treatment, the mechanism of action of Neupro® is thought to be related to its ability to stimulate dopamine receptors within the caudate-putamen, the region of the brain that regulates movement. Similarly, in RLS, the mechanism of action of Neupro® may be related to its ability to stimulate dopamine receptors. The precise mechanism of action of Neupro as a treatment for these diseases is unknown.

The effectiveness of Neupro® in the treatment of the signs and symptoms of idiopathic PD was established in five parallel-group, randomized, double-blind placebo-controlled trials conducted in the U.S. and abroad. Depending on trial design, patients underwent a weekly titration of Neupro® in 2 mg/24 hours increments of either the randomized dose or optimal dose.

In three trials, statistically significant improvements in the combined scores on the Unified Parkinson's Disease Rating Scale (UPDRS) were observed in early stage PD patients receiving Neupro® compared with patients receiving placebo. The UPDRS is a multi-item rating scale intended to evaluate mentation, activities of daily living (ADL), motor performance, and complications of therapy. The three trials measured only the ADL and motor performance sections of the UPDRS. The UPDRS contains 13 questions relating to ADL, such as speech, dressing, and cutting food with utensils, and 27 questions related to the cardinal motor symptoms in PD patients—i.e., tremor, rigidity, bradykinesia, and postural instability.

Two trials of Neupro® in patients with advanced PD examined change from baseline in "off" time, periods when the effectiveness of medication wears off and PD symptoms return. Statistically significant changes in off-times were observed in advanced PD patients receiving Neupro® compared with those who received placebo.

The efficacy of Neupro® in the treatment of RLS was primarily evaluated in two fixed-dose, randomized, double-blind, placebo-controlled trials with six-month maintenance periods. Patients received Neupro® doses ranging from 0.5 mg/24 hours to 3 mg/24 hours, or placebo, once daily.

Statistically significant improvements in sum scores on the International RLS Rating Scale (IRLS Scale) and the Clinical Global Impression–Improvement (CGI-I) assessment were observed in RLS patients receiving Neupro® compared with those receiving placebo. The IRLS Scale contains 10 items designed to assess the severity of sensory and motor symptoms, sleep disturbance, daytime somnolence, and impact on activities of daily living and mood associated with RLS. The CGI-I is designed to clinically assess RLS symptoms on a 7-point scale.

In clinical trials, the most common adverse reactions (≥5% greater than placebo) for the highest recommended doses of Neupro® for treatment of Parkinson's disease were nausea, vomiting, somnolence, application site reactions, dizziness, anorexia, hyperhidrosis, and insomnia. The most common adverse reactions (≥5% greater than placebo) for the highest recommended dose of Neupro® for treatment of Restless Legs Syndrome were application site reactions, nausea, somnolence, and headache.

PolyTherics and Spirogen Announce a Research Collaboration to Develop Novel Antibody-Drug Conjugates for the Treatment of Cancer

Business Wire: April 2, 2012 – LONDON, U.K. – PolyTherics Limited ("PolyTherics"), a provider of solutions to enable the development of better biopharmaceuticals, and Spirogen Limited ("Spirogen"), a leading oncology-focused company developing DNA sequence-targeted agents, announce that they have formed a research collaboration to develop antibody drug conjugates (ADCs) that combine PolyTherics' proprietary site-specific conjugation chemistry with Spirogen's highly potent novel cytotoxic drugs to produce novel ADCs for the treatment of cancer.

Under the collaboration, the two companies will produce the ADCs using PolyTherics' proprietary TheraPEG™ linker technology to site-specifically conjugate Spirogen's potent pyrrolobenzodiazepines ("PBDs") cytotoxic agents—known as warheads—to antibodies and antibody fragments. The companies will then test the potency of the resulting ADCs in preclinical models of cancer. PolyTherics and Spirogen will jointly seek partners to develop the most promising ADC candidates that arise from the collaboration.

John Burt, CEO of PolyTherics, commented, "This is an exciting opportunity to combine our validated conjugation technology with Spirogen's potentially best-in-class PBD warheads. The novel antibody-drug conjugate reagents that we develop will have broad application for the development of ADCs as new cancer therapies."

Chris Martin, CEO of Spirogen, added, "We believe that ADCs will represent a significant medical breakthrough in cancer therapy over the coming decade, and that PolyTherics' TheraPEG™ conjugation technology will broaden the applications where our PBD warheads and linkers can create highly potent potentially market-leading ADC candidates." For more information, please visit www.polytherics.com.

March 2012

Supreme Court Denies Apotex's Petition for a Writ of Certiorari

PRNewswire: March 22, 2012 – BOONTON, NJ, U.S.A. – Unigene Laboratories, Inc. (OTCBB: UGNE), a leader in the design, delivery, manufacture, and development of peptide-based therapeutics, today reported that the U.S. Supreme Court denied Apotex's Petition for a Writ of Certiorari on March 19, 2012, in Apotex, Inc., et al. v. Unigene Laboratories, Inc., et al., Supreme Court Docket No. 11-879. Thus, the validity of Unigene's U.S.

In the News continued on page 44

In the News continued from page 43

patent on Fortical® has been confirmed by the District Court and the Court of Appeals for the Federal Circuit. The August 25, 2011 decision of the Court of Appeals in favor of Unigene now stands as the final decision. The Court of Appeals ruled for Unigene affirming the District Court's grant of summary judgment of nonobviousness in favor of Unigene, affirmed the District Court's denial of Apotex's motions, and affirmed the District Court's dismissal of Apotex's new claims and defenses.

Particle Sciences and Pernix Therapeutics Enter into an Agreement to Develop a Pediatric Dermatology Product

PRNewswire: March 21, 2012 – BETHLEHEM, PA, U.S.A. – Particle Sciences, Inc., a leading pharmaceutical CRO, today announced that it is developing with Pernix Therapeutics, a specialty pharmaceutical company, a new topical dermatology product for the pediatric market.

Mark Mitchnick, CEO of Particle Sciences, said, "There are multiple treatments for many pediatric skin conditions. The unmet need is in the delivery of these agents via a more convenient and improved vehicle. Particle Sciences is applying advanced drug delivery and formulation technologies to an established pediatric product category. For parents, this product is designed to be a potentially better and easier to use product."

Cooper Collins, Pernix Therapeutics' President and CEO, said, "We are enthusiastic about working with Particle Sciences for this product candidate, which may be another opportunity to further expand our pediatric product line."

Fuisz Pharma Announces Filing of Patent Application Relating to Breath-Based Diagnostics

PRNewswire: March 21, 2012 – MIAMI, FL, U.S.A. – Fuisz Pharma today announced the filing of a patent application with the United States Patent and Trademark Office relating to the field of breath-based diagnostic systems.

Joseph Matus Fuisz Esq., commented, "The field of breath diagnostics holds enormous potential to extend the range of convenient and portable non-invasive diagnostic techniques. This patent application is directed towards addressing some of the challenges that have prevented commercial adoption of breath diagnostic systems, and specifically those challenges relating to addressing contaminants that can confuse results."

Richard C. Fuisz M.D., a co-inventor with Joseph Fuisz, stated, "This is an exciting and very important application. In the future, it will be thought of as bedrock to the advancing use of the breath for diagnosis. Diagnostics are moving toward the breath and with our interest in diagnostics we, of course, shall be there."

Fuisz Pharma is a private pharmaceutical technology company originated by the Fuiszes. The Fuiszes have made substantial contributions in drug delivery including orally dissolving tablets and novel particle coating systems at Fuisz Technologies, inventing and developing thin-film drug delivery technologies at Kosmos Pharma and MonoSol Rx, as well as independently developing extruded sheet technology, and have extensive experience working with big and specialty pharma. Fuisz Pharma has its headquarters in Miami. www.fuisz.com.

Nautilus Neurosciences, Inc. Announces a New Approval for CAMBIA® for the Acute Treatment of Migraine

PRNewswire: March 19, 2012 – BEDMINSTER, NJ, U.S.A. – Nautilus Neurosciences announced today that their Canadian promotional partner, Tribute Pharmaceuticals, a wholly owned subsidiary of Stellar Pharmaceuticals, was granted a Notice of Compliance (NOC) approval from Health Canada for CAMBIA® (diclofenac potassium for oral solution) in the treatment of acute migraine with or without aura in adults. CAMBIA® is expected to be launched in Canada during the second half of 2012. CAMBIA® has been available to patients in the United States since May 2010.

Nautilus Neurosciences has exclusive marketing rights for CAMBIA® in the United States and Canada, which they obtained from APR, a Swiss drug delivery and drug development company. Patents have been granted that protect the product in the United States through 2026.

"We congratulate our partners at Tribute Pharmaceuticals on the Health Canada approval and look forward to continuing to work with them on the Canadian launch of CAMBIA®. We are excited that CAMBIA® will be available as a treatment option for physicians and patients in Canada," said William Maichle, the CEO of Nautilus Neurosciences. Mr. Maichle highlighted, "With CAMBIA® now approved in both the United States and Canada, this marks another major milestone in the evolution of Nautilus to a best-in-class neurology-focused specialty pharmaceutical company."

Mr. Maichle added, "Looking forward, our strategy is to build an increasingly valuable company through the addition of complementary neurology-targeted therapies through in-licensing and acquisition opportunities." Mr. Maichle concluded, "[I] expect Nautilus Neurosciences to experience record growth in 2012 as CAMBIA® continues to fill an important unmet need for patients suffering from the debilitating effects of migraine."

CAMBIA® (diclofenac potassium for oral solution) is the lead product from Nautilus Neurosciences and has been available for sale in the United States since May 2010. It is indicated for the acute treatment of migraine attacks with or without aura in adults 18 years of age or older. For more information about Nautilus Neurosciences, please visit www.nautilusneurosciences.com. For further information on Stellar Pharmaceuticals, visit http://www.stellarpharma.com, and for information on its subsidiary, please visit http://www.tributepharma.com. For more information about APR, please visit www.apr.ch.

Piedmont and Hisun Sign Agreement to Develop Animal Pharmaceuticals

PRNewswire: March 15, 2012 – NEW YORK, NY, U.S.A. – Piedmont Pharmaceuticals, a privately held strategic pharmaceutical development, licensing, and marketing company headquartered in Greensboro, N.C., U.S.A., and Zhejiang Hisun Pharmaceuticals (SSE stock code 600267), a leading Chinese pharmaceutical company headquartered in Zhejiang, China, announce the signing of a joint agreement to develop companion animal health pharmaceuticals for China and other markets worldwide.

"New products are the lifeblood of every pharmaceutical company," says Roland Johnson, chairman and CEO of Piedmont Pharmaceuticals. "Hisun is a globally recognized pharmaceutical provider that demonstrates excellence in every facet of their business operations. This partnership will allow the team at Piedmont to develop and bring even more innovative animal health products to strategic business partners and pet owners worldwide."

Hua Bai, CEO and chairman of Hisun Pharmaceuticals, notes, "Hisun is very pleased to enter this partnership with Piedmont Pharmaceuticals. The Piedmont team has tremendous depth of expertise and 25 years of proven success with some of the most successful animal health products ever introduced. This product development agreement is a significant component of our strategy to become a leading global supplier of animal health pharmaceuticals. Products emerging from this collaboration will not only help Chinese consumers ensure the health of their pets, but will serve pet owners in other global markets as well."

Current estimates place China's pet population at 200 million, with that number expected to reach 500 million by 2015. China is the world's second largest economy behind the U.S., and in the last 30 years, economic growth in China has averaged 8 percent gross domestic product (GDP) annually. Many analysts predict that China will become the largest economy in the world this century.

Formed by a group of industry veterans, Piedmont Pharmaceuticals develops and achieves regulatory approval for its innovative animal health and human products, then licenses them to strong commercial partners. Piedmont has licensed a number of its novel animal health products to U.S.-based Pfizer, U.K.-based Dechra Pharmaceuticals, and Germany-based Bayer Animal Health.

Foamix's Minocycline Foam—100% Effective in Impetigo Phase II Clinical Trial With No Side Effects—80% Improved Significantly After 3 Days of Treatment

PRNewswire: March 14, 2012 – REHOVOT, Israel – Foamix, a clinical stage specialty pharmaceutical company, announced today the successful completion of the phase II clinical trial of minocycline foam in impetigo patients. Minocycline foam has shown to be highly effective against bacteria, including some multi-drug resistant strains (such as MRSA).

The randomized double-blind phase II clinical study, conducted in pediatric patients with impetigo, was designed to assess the efficacy, safety, and tolerability of two strengths of the minocycline foam. Patients received the foam twice daily for 7 days, and they were checked again on day 14.

Robust efficacy was demonstrated in both 1% and 4% strength doses in this randomized, double-blind, dose-ranging study enrolling 32 patients ages 2 to 15. Clinical response at the end of the treatment was 92% and 100%, respectively, for the low or high doses, and all patients (100%) showed success on day 14. Notably, 80% of the total patients cured or improved significantly after 3 days of treatment. Eight patients had MRSA, and in all of them the bacterial infection was eradicated on day 7.

"These results are excellent, especially considering this study is the first to treat patients with topical minocycline. The results confirm the efficacy of our minocycline foam in skin infections. It is also significant that our minocycline foam was well-tolerated and that there was no evidence of clinical safety concerns since one of the persistent barriers to the development of new classes of antibiotics has been the issue of patient safety," commented Dov Tamarkin, Foamix CEO. "We intend to aggressively pursue the development of our minocycline foam as a first-line treatment for a range of skin conditions, including acne, rosacea, impetigo, and other skin infections." ■

Controlled Release Society
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Calendar of Events

2012

39th Annual Meeting & Exposition of the Controlled Release Society
Sponsored by CRS
July 15–18
Centre des congrès de Québec
Québec City, Canada
www.controlledreleasesociety.org/meeting

Advances in Tissue Engineering Short Course
Sponsored by CRS
August 8–11
Houston, TX, U.S.A.
www.ruf.rice.edu/~mikosgrp/pages/ATE/ate.htm

2nd Symposium on Innovative Polymers for Controlled Delivery (SIPCD 2012)
September 11–14
Suzhou, China
http://www.sipcd.cn

10th International Nanomedicine and Drug Delivery Symposium (NanoDDS '12)
Sponsored by CRS
October 28–30
Atlantic City, NJ, U.S.A.
http://nanodds2012.com

Drug Delivery Australia Conference
Sponsored by CRS
November 26–27
Melbourne, Australia
http://www.crsaustralia.org

2013

40th Annual Meeting & Exposition of the Controlled Release Society
Sponsored by CRS
July 21–24
Hawaii Convention Center
Honolulu, Hawaii, U.S.A.
www.controlledreleasesociety.org