CRS Leading Delivery Science and Technology

Newsletter

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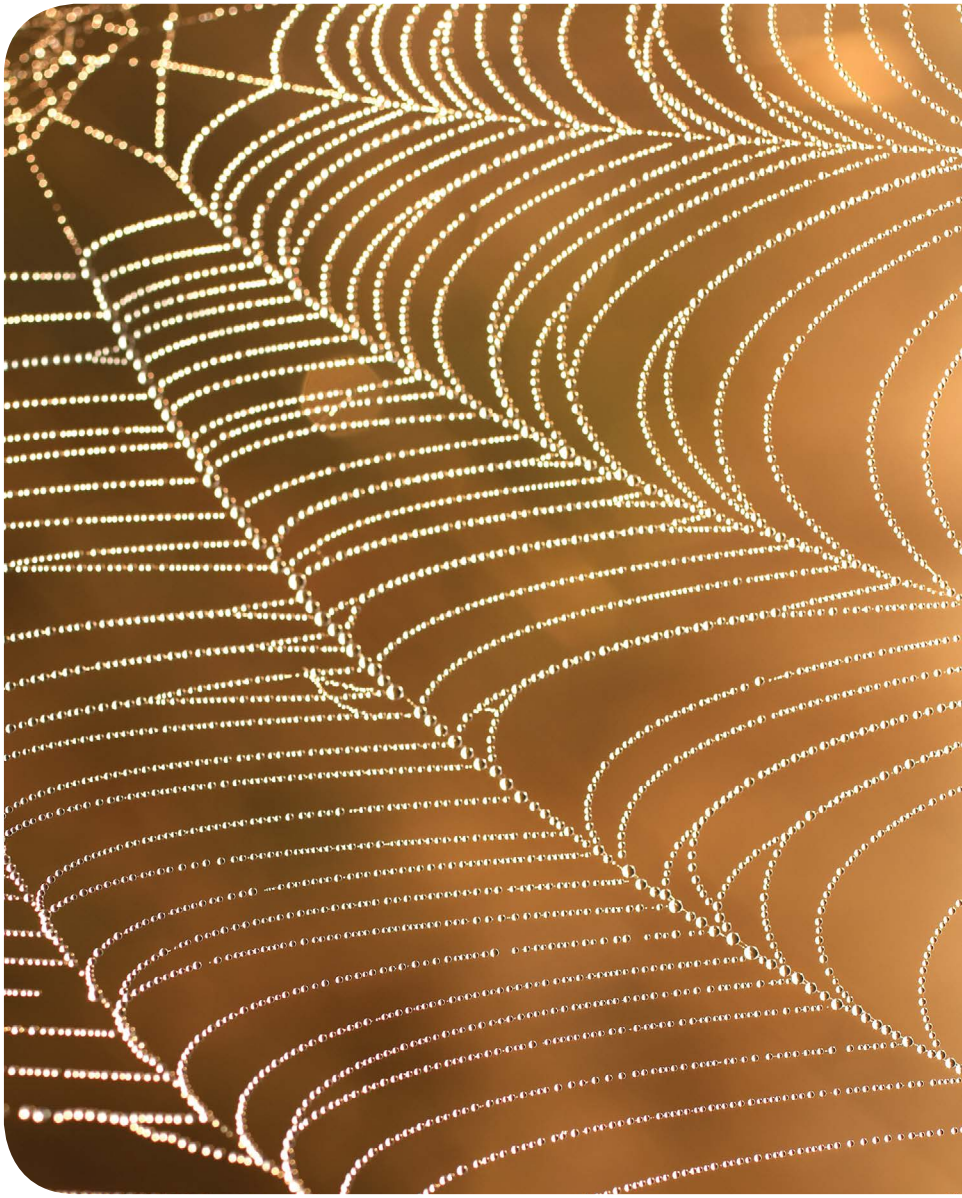
What's Inside



41st Annual Meeting & Exposition of the Controlled Release Society

July 13–16, 2014
The Hilton Chicago
Chicago, IL U.S.A.

TRANSLATION

of Delivery Technology: Innovation to Commercialization

Call For Papers
Opens
November 2013

Exhibit and
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A premiere luxury hotel since 1927, the Hilton Chicago (originally the Stevens Hotel) is among downtown Chicago's most grand and iconic buildings. With one of the largest exhibit areas on a single level of any hotel in the United States plus an array of first-class amenities, it remains a destination hotel for business travelers and tourists from around the world.

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CRS Leading Delivery Science and Technology

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Vol. 30 • No. 4 • 2013

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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 controlledreleasesociety.org.

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Visit controlledreleasesociety.org or e-mail crs@scisoc.org on questions about membership, meetings, publications, and services.

Contact dwoodard@scisoc.org for information about exhibiting, advertising or other visibility opportunities.

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

Three Things

As I attended this year's 40th CRS Annual Meeting, I knew I would be writing this, I knew it should offer a reflection of the meeting, and I knew it would be restricted to this page. A challenging task considering the meeting's scope, but with creative attention to the "between the words and letters" area, three words create a reasonable caricature: *diversity*, *investment*, and *passion*. *Voilá*, in much less than a page. Those three words, and our extended perceptions about them, create a portrait of the CRS Annual Meeting.

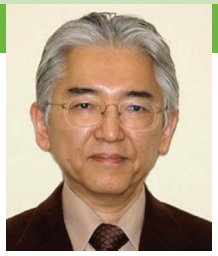
Forty years ago, CRS was all about pesticide release. The scope broadened in ensuing years to bioactive materials, inciting an uncontrolled delivery of *diversified* interests as pharmaceutical, food, personal care, household product, industrial, agricultural, and others came to participate in this unique idea and technology exchange. Pharmaceutical interests arrived in greatest numbers, but all areas are active. In fact, this year's meeting covered current work in pharmaceutical controlled release as well as the Consumer and *Diversified* Products areas of food/diet, building/construction materials, agri/aquaculture, personal care/household products, and energy conservation/production. Membership *diversity* was also evident. CRS maintains a global scope, and this year's Hawaiian venue was within reach of active membership and growing economies on the Pacific Rim. I say "well done" to the CRS Local Chapters and chapter presenters who raised laughter and keen ears during their President's Banquet presentations. The range of topics, broad geographic representation, and student to seasoned researcher participation are evidence of a rich *diversity*.

CRS is a nonprofit entity within the monetary systems that fuel our economies. Although we thrive on *investments* of ideas, research, and time, money enables us. Innovation Sunday again focused on commercial and financial elements of controlled release. One "carrot" in front of us is that possibility of contributing in some way to a useful idea or product, and Sunday afternoon's well-attended Soapbox Session provided a tool to broadcast such ideas or products. The session was followed by an Industry Roundtable discussion involving industry leaders in the areas of pharmaceuticals, foods, and finance on current trends and the future. Two financial elements come to mind from the discussion: 1) the question of how medicinal needs of developing countries can be financed, and 2) there is always money out there for a good idea. Perhaps our creative talents can be applied to join ideas from 1 with financing options from 2.

Time, ideas, and money are all *investable*, and I am certain that where any of these are involved there is *passion*. The ≈1,250 attendance, ≈900 submitted abstracts, presentations that spilled forth in the allotted times, and questions that bounced back are all tangible signs of *passions* that ensured the success of the 40th CRS Annual Meeting.

The next issue of the *CRS Newsletter* will review the Annual Meeting in more detail. In the meantime, tune into this issue and consider the *diversity*, *investment*, and *passion* involved.

Diversity. *Investment*. *Passion*. Consider their place in your sphere of influence. ■



Kazunori Kataoka
University of Tokyo
Tokyo, Japan

Of Service and Honor

In Japan, the tea ceremony has been a part of our culture for more than 1,000 years. The ceremony is an intricate one in which every detail, from the setting in which the tea is held to the fine movements of the pouring of the water, are all finely choreographed. This carefully crafted ritual is not about drinking the tea; instead, it is about pouring your attention into the movements and giving of yourself to those whom you are serving. Every aspect of the tea must be savored for what it gives the participants.

As I write this, the 2013 CRS Annual Meeting has just ended. It was the culmination of many months of preparation and careful attention to detail by the CRS Annual Meeting Program Committee chaired by Mark Saltzman and Deputy Chair Ick Chan Kwon, who, along with their fellow committee members, so graciously gave their time and attention to its planning and execution.

More than 40 countries were represented at this year's meeting in Hawaii—a true testimony to the international nature of our association. As I conclude my term as CRS President, I am reminded of the value of our global outreach and the important role that CRS has to play as host to our worldwide community of delivery science professionals.

Members of the CRS College of Fellows make a significant contribution to the facilitation of international activities within CRS, and this year's Annual Meeting Opening Session included a CRS College of Fellows panel discussion on global collaboration in delivery science. College of Fellows members are selected by the College of Fellows Award Committee from a list of nominated candidates who have made outstanding contributions to the field of delivery science and technology. With each selection, careful attention is given to ensuring that colleagues from around the world are honored and represented within this important and prestigious group. At this year's meeting, we welcomed five new members to the College of Fellows, each with an impressive list of career achievements.

When we see the full fruition of a career, as expressed in the biographies of our College of Fellows members, it serves as a reminder that at one time we were all new to the field of delivery science—that, as young professionals, the guidance of mentors and of a professional association like CRS was invaluable to our success.

Since its establishment in 2007, and through the generosity of our member donors, the CRS Foundation has awarded postdoctoral fellowships of $30,000 each to four outstanding early career professionals to assist them in furthering their work in delivery science. The CRS Foundation is working toward the next postdoctoral fellowship in honor of Sandy Florence, a respected leader in delivery science and past president of CRS. We ask that you help by making your donation to the 2014 Alexander Florence Postdoctoral Fellowship.

Whatever the level at which you give or participate within CRS, it all matters. Each act in and of itself contributes to a greater good and leaves a legacy for our association and our science. We are fortunate to be part of an organization in which our members are so generous with their time and resources. Participation on the Board of Directors level this year was excellent. The average attendance at our board meetings and telecons was 82%, which is excellent, especially given the challenges of full schedules and managing time zones. I was fortunate to work with such an engaged and committed group of CRS leaders.

The act of serving as your President is one that I have approached with great respect and heartfelt honor. I thank you for allowing me to lead such an exceptional group of colleagues as are represented within CRS. If we were together at this moment in a traditional Japanese tea house having just finished our tea, my final act as host of our tea service would be to turn to you, my guests, and give a final bow of departure.

I bow to you now, and to the work we are doing to advance our science. Together, let us welcome our new President, Ian Tucker, in whose hands we are undoubtedly well placed. ■

Interview with Mark Tracy: Insights into the Biopharmaceutical Industry

Vishwas Rai[1] and Bozena B. Michniak-Kohn[2]

Mark Tracy served as president of the Controlled Release Society (CRS) from 2010 to 2011 and on its Board of Directors (BOD) from 2008 to 2012. He also served on the CRS Board of Scientific Advisors from 2002 to 2005 and was a cochair for the CRS Annual Meeting in New York City in 2008. Highlights of his term as president and member of the BOD include establishing of the CRS College of Fellows, updating CRS governance and the strategic plan, and the launch of a new journal (*Drug Delivery and Translational Research*), a new book series, and a new website. He also helped open a new CRS chapter in China and, as president, hosted the 2011 CRS Annual Meeting comprising approximately 1,400 delegates.

Dr. Tracy is a fellow of the American Institute for Medical and Biomedical Engineering (AIMBE).

Dr. Tracy has made significant contributions in the field of biopharmaceuticals. Dr. Tracy played a key role in the advancement of nine programs into the clinic, including several that were commercialized: Nutropin® Depot, Risperdal® Consta, Vivitrol®, and Bydureon®. He is well known for successfully bringing new protein, peptide, nucleic acid, and small molecule based medicines to the clinic, incorporating recent advances in drug delivery, nanotechnology, and targeting. He has played important roles in the development of technology platforms and product pipelines for Alkermes, Inc., and Alnylam, Inc., two leading biotechnology companies, where he worked for over 20 years in various leadership roles of increasing responsibility. At Alkermes, he played a key role in building the company's parenteral product development capabilities and was a member of the team that developed the first sustained delivery system for proteins approved by the FDA. While at Alnylam, Dr. Tracy successfully brought to the clinic new nanotechnology-based products that enabled human clinical proof of concept for RNAi and a growing pipeline of clinical programs.

Before joining the biopharmaceutical industry, Dr. Tracy secured his bachelor of science in chemical engineering *summa cum laude* from the University of Illinois at Urbana-Champaign and received an M.S. in chemical engineering and Ph.D. in chemistry from Stanford University. Dr. Tracy also attended an executive program in business administration and management at MIT Sloan School of Management.

Dr. Tracy is founder and president of Tracy BioConsulting, LLC (www.tracybioconsulting.com), where he provides consulting services to biopharma clients, helping them to plan, build, and navigate a successful path from the research stages through the clinic for new platforms and drug programs, including those involving novel drug delivery systems, nanotechnology, and targeting. Also, Tracy BioConsulting provides access to an extensive network of CROs and CMOs and help in the identification of new business opportunities and creation of value from technology platforms. Tracy BioConsulting clients include startups, small and large biotech and pharmaceutical companies, CMO/CROs, and investment and VC firms.

Q *How did your educational journey lead to a career in the biotech industry?*

A When I was a kid in grade school, I remember declaring, as soon as I could pronounce the word, I wanted to be a paleontologist. Of course, finding a long-lost dinosaur skeleton was cool to me but probably more so was the act of discovery and learning that came along with it. Over the years, with many great teachers in elementary and high school and a dash of practicality added courtesy of my parents ("How many jobs are there in paleontology?"), I became interested in math and science, chemistry and engineering in particular. I was excited

Mark Tracy receiving the CRS president's gavel from Diane Burgess at the CRS Annual Meeting in Portland in July 2010.

[1] Chrono Therapeutics Inc., Waltham, MA, U.S.A.
[2] Ernest Mario School of Pharmacy, Rutgers–The State University of New Jersey, U.S.A.

to see that, when I applied to college at the University of Illinois at Urbana-Champaign, there was actually a major combining both chemistry and engineering. I was accepted, and off I went as a chemical engineering major. I was fortunate that Illinois was then and is today one of the top universities in the world in the chemical sciences and fostered close interactions between chemistry and chemical engineering. Three professors were particularly supportive and influential in my career direction. Prof. Steven Zumdahl strongly supported me and encouraged my interest in chemistry. He provided me with an opportunity to work in his lab over the summer after my freshman year doing research for the first time. Prof. Tony McHugh introduced me to polymer science and encouraged me to consider graduate school. Prof. Charles "Chip" Zukoski sparked my interest in particles and colloids and provided me the opportunity to do a senior thesis with him, which led to my first published paper. Chip's mentorship and the fun of discovery I experienced in his lab inspired me to go to graduate school at Stanford University. My experience at Illinois also taught me that I was particularly interested in research at the interfaces of traditional academic disciplines, for example, nanotechnology (also known as colloid science), polymer chemistry, and engineering. Like Illinois, Stanford also fosters close interaction between chemistry and chemical engineering. I was fortunate to combine my interests in polymers and colloids working in the lab of Prof. Robert Pecora using optical methods to study diffusion in complex fluids. Bob connected me with members of industry with whom I worked on a couple projects complementing my thesis work. Through Bob's mentorship, I honed my research and problem-solving skills as well as developed an interest in collaborative applied research with industry. So as I was about to graduate with my Ph.D., I searched for emerging interdisciplinary fields with interesting industrial applications and opportunities for discovery where I could apply my new knowledge and skills. I read an article on Prof. Robert Langer of MIT, the drug delivery field, and an emerging company he founded called Enzytech, his first startup (now he has founded more than 25). I was fortunate. Enzytech was looking for an entry-level Ph.D. scientist, and I got the job. I moved across the United States from Palo Alto, California, to Cambridge, Massachusetts, just a few weeks after defending my Ph.D. and began my career in the biotech/drug delivery industry.

Q *As a new Ph.D., what was it like to work in biotech startup?*

A Working in a startup is hard work but very exhilarating. Soon after I joined Enzytech, it merged with another startup, Alkermes, Inc. Both were exciting places to work. Things moved very fast. Our mission was to develop sustained release products based on a novel patented encapsulation process. We were blazing new ground in delivery science, including new ways to stabilize proteins, new approaches to control release from degradable polymeric particles, methods of characterization and formulation screening, new processing approaches, and regulatory precedents. It was fun and tough at the same time. There was the sense of discovery that I love combined with a focus on producing products to benefit patients. The sense of ownership and responsibility and the opportunity to make a difference in this environment were very motivating to me. In a way, this phase of my career was my "boot-camp" in pharmaceutical product development, the regulatory approval process, and building a biotech company. I was especially fortunate to work with and learn from great leaders and mentors including Howard Bernstein, Steve Zale, Jim Wright, Robert Breyer, Richard Pops, Prof. Bob Langer, Prof. Alex Klibanov, and many others. Over the period I was at Enzytech/Alkermes, I was a key member of the team that developed the first long-acting protein product approved by the FDA, Nutropin® Depot, as well as several other products that were commercialized: Risperdal® Consta, Vivitrol®, and Bydureon®.

Q *You successfully made the transition from a laboratory scientist role to a management role while at Alkermes. How did this come about? What kinds of challenges did you overcome?*

A There are two key aspects that aligned in my case that enabled my transition from lab to management: first, I came to realize, based on my work experience, that I enjoyed leading science and programs through others as a team as much or more than the direct hands-on work in the lab and, second, my projects advanced and the company grew, creating management opportunities both as group or department heads and project team leaders. I was fortunate to advance from an entry-level Ph.D. scientist to director of formulation development over my time at Alkermes. There were so many challenges: some technical, many related to the business. On the technical side, I recall discovering that our standard *in vitro* release method used for formulation screening was not an adequate predictor of release *in vivo*. This led us to transform our formulation development approach from one based primarily on screening formulations using an *in vitro* test to using a rodent *in vivo* model that was predictive across species from rodents to humans. I also found that the end group chemistry of the polymer is a key formulation parameter impacting release from poly(lactide-co-glycolide)-based particles leading to the development of improved formulations. I played a key role in scaling-up our lab scale process to one that was suitable for making lots aseptically at clinical and commercial scales. On the business side, we were very fortunate to have raised enough funds to progress our R&D work through some very challenging investment periods and regulatory and partnership setbacks. Having a small portfolio of products and technology platforms proved very helpful in overcoming setbacks on individual projects.

Q *Please share some of your lessons learned from your experience in advancing nine biotech products to the clinic and several to commercialization.*

A Here are a few important lessons I learned:

1. Have a detailed plan—at least 2 years for pre-investigational new drug (IND) programs, longer for later

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Interview with Tracy continued from page 5

stage programs—and have a backup (or better yet, several). The path to clinic and commercialization is long, with many potholes along the way. Some are technical, but many are business, regulatory, or clinical in nature. Try to anticipate as well as you can what may trip you up by regularly clarifying and aligning on your program's risks and assumptions with your team.

2. Use a science-based approach in product development. Understand to the best of your ability why each component is in your product, the most important product and process parameters impacting your product's safety, efficacy, and stability, and establish robust assays to characterize your product. These assays are your eyes and ears. Your dividend will be greater credibility with partners and regulatory agencies.
3. Be flexible and adaptable. The technology you begin with as a startup or small company is very often not the technology around which the company is ultimately built. So always be on the lookout for something better, and never close your eyes to the challenges with your technology. Challenges are also opportunities for invention.
4. Celebrate along the way with your team. Recognize the many significant accomplishments on the way to the IND, clinic, or commercialization, not just the big ones at the end.
5. Drug product development is a team sport. No one person develops a drug. High-performing teams do. The career advancement and incentives in your organization and for your team should reflect this fact.

Q *How did you get into the RNAi field? Where is the field headed?*

A I learned of an opportunity at Alnylam, Inc., a leader in the RNAi field, and was very interested to be a part of this new emerging field and company where solving delivery challenges was front and center to enabling new medicines. In RNAi, delivery to the cytoplasm inside of the cell is required. My job was to advance the delivery science and build the capabilities to turn RNAi science into products. I was very fortunate to have the opportunity to build and lead an international team of academic and industrial collaborators that developed new materials and formulations and advanced them successfully to the clinic. We were among the first to demonstrate RNAi in humans and built a pipeline of products with the potential to address serious medical conditions, including rare diseases such as TTR amyloidosis, metabolic diseases such as hypercholesterolemia, and blood diseases. I think the future of the field is bright. Over the next few years, the companies working in this field will advance the first RNAi-based therapeutics to phase II/III clinical trials and commercialization. This progress will stimulate increased interest in the field. However, delivery outside the liver and tumor tissue remains a significant challenge. Over the next few years, I hope (and think) we will see important advances in understanding delivery to different tissues and organs, which will begin to open up new biological targets for RNAi-based medicines. I expect that members of CRS will play key roles in these advances. Stay tuned!

Q *Please tell us about your plan with Tracy BioConsulting, LLC.*

A My passion is developing new medicines and products. Over the years, I have advanced nine medicines to the clinic including four that have been commercialized, including peptides, small molecules, nucleic acids, and proteins. In addition, I have been fortunate to help build two successful companies. I founded Tracy BioConsulting to provide my clients with the knowledge, experience, and connections I have developed from these and other experiences and to help them develop important new medicines. My clients include startups, small and large biotech and pharmaceutical companies, CMOs/CROs, and investment and venture capital firms. Please visit my website to learn more: www.tracybioconsulting.com.

Q *Given your experience with startups and small emerging companies, what advice would you give to entrepreneurs starting up or building a small biotech company today?*

A Prof. Bob Langer, who has started over 25 companies since Enzytech, has boiled down his formula for startup success to the following key ingredients:

- a breakthrough idea published in a top journal such as *Science* or *Nature*,
- a patent, ideally blocking,
- *in vivo* proof of principle,
- capability to have more than one product, that is, a platform, and
- passion.

Enzytech/Alkermes and Alnylam had all of these components as startups! In addition, I would add the following:

- Talk to as many people as possible who have built companies before and learn about their experiences. There are so many routes to success, so ultimately you will have to determine the path that is best for you and your company. For many of us who have science and technical backgrounds, it is also a great way to gain an understanding of the practical business aspects that you will need to build your business and raise funding.
- Know your market, key customers, and potential acquirers, not just your technology. For delivery scientists in biotech, that means you must engage biologists, clinicians, and potential customers and acquirers to understand biological targets, unmet clinical needs, and the value of your product or technology to those customers and acquirers.
- Avail yourself of the many excellent resources that exist today to support entrepreneurs and small company leaders, including the Kauffman Foundation (www.kauffman.org) and local groups in your community such as the Capital Network (www.thecapitalnetwork.org) in Boston.

Q *What accomplishments are you most proud of during your time on the CRS Board and as CRS President?*

A CRS has always been my "home" professional society. It was an honor to serve on the CRS Board from 2008 to 2012 and as CRS president for 2010–2011. I am particularly proud of working with my colleagues on the Board to establish the College of Fellows to recognize leaders in our field and our society, to launch a new website to enhance the ability of CRS to meet the needs of our members 24/7 worldwide, to launch new publications including a book series and the journal *Drug Delivery and Translational Research*, to install new chapters including one in China, and to update our governance and strategic plan to strengthen the society for the future. These efforts are already helping to enhance the society's ability to bring delivery science and technology to its members throughout the world. I look forward to seeing the society continue to develop and grow in the coming years.

Mark Tracy receiving the Distinguished Service Award at the 2013 CRS Annual Meeting. Left to right: Ian Tucker, Mark Tracy, and Kazunori Kataoka.

Q *What do you enjoy doing when you are not doing biotech?*

A I particularly enjoy the arts, travel, and the outdoors. I sing in a chorus. We sing all kinds of classical music and perform throughout the Boston area several times a year. Right now, I am quite excited because my chorus was recently selected to perform with the Boston Pops next December, which is a great honor. I enjoy all forms of travel from taking short drives near home in the Boston area to visiting destinations all over the world. I have really enjoyed attending the CRS meetings over the years because, in addition to the great science and networking, they are always in amazing places to visit. Hawaii is an excellent example! I also love the outdoors and go on hikes whenever I can. Thank you so much for inviting me for this interview. I enjoyed it very much! ■

More Educational Opportunities from CRS

These CRS workshops will take place at the 2013 AAPS Annual Meeting & Exposition
November 10–14, 2013
San Antonio, Texas, U.S.A.

Introduction to Microencapsulation Technologies Workshop

Knowledge of multiple encapsulation technologies and how they are applied is valuable information for developing new products or solving existing problems. It is important, at a minimum, to have a basic understanding of all commonly available processes and their applications. This workshop provides an introduction to common micro- and nanoencapsulation processes and their various applications. The workshop is structured to 1) introduce common encapsulation techniques, 2) review common materials, and 3) provide an overview of the wide range of applications for controlled release products.

Workshop Organizers
James Oxley, Southwest Research Institute, U.S.A.
Irwin Jacobs, Particle Dynamics International, LLC, U.S.A.

Mitigating Risks for Patients When Developing Oral Controlled Release Dosage Forms Workshop

The focus will be to understand the possible risks to patients and approaches to manage them when developing oral extended-release (ER) dosage forms. The discussion will relate to the design, development and manufacture of commonly used ER systems. Industry leaders and subject matter experts will provide scientific basis to the material science, formulation, and process attributes that will help to mitigate risks, under the umbrella of quality by design (QbD). The overall goals of such approaches are to improve quality, reduce costs, but maintain patient safety and treatment.

Workshop Organizers
Ali Rajabi-Siahboomi, Colorcon, U.S.A.
Mansoor Khan, CDER, USFDA, U.S.A.

Register online at www.aaps.org. Information about these workshops is also available on the CRS website at **controlledreleasesociety.org**.

Aloha Spirit at the 40th Annual Meeting & Exposition of the Controlled Release Society

Hawaii was a welcoming host to the more than 1,250 attendees that filled the scientific sessions, poster viewings, exposition, and special events at this year's CRS Annual Meeting & Exposition. Premeeting workshops and CRS Innovation Sunday were part of the early programming and kick-off events. More than 900 scientific presentations filled the following three days, from Monday morning's Get Up! Get Educated! session through Prof. Paula T. Hammond's closing plenary presentation. Watch for a complete recap in the next issue of the *CRS Newsletter*.

CRS President Kazunori Kataoka welcomes attendees to the 40th CRS Annual Meeting & Exposition during the Opening Session.

The Grand Opening Exposition and Welcome Reception was full, as attendees spoke with exhibitors and enjoyed time with colleagues.

2013 CRS Awards

The Controlled Release Society is proud to honor this year's awardees for their dedication and contributions to delivery science and CRS.

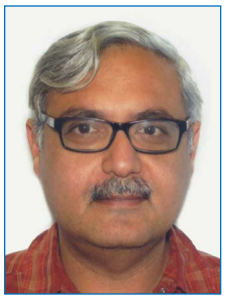
Distinguished Service Award

Established in 1994, the Distinguished Service Award is presented to a CRS member who has exhibited exceptional commitment and service to the society and is selected by the Board of Directors.

Mark A. Tracy is president of Tracy BioConsulting, LLC, a specialized biopharmaceutical consulting firm dedicated to helping clients transform research into new medicines. He is a past president of CRS and a fellow of the AIMBE.

College of Fellows

The College of Fellows recognizes those members who have made outstanding contributions to the field of delivery science and technology over a minimum of 10 years. Contributions may have been technical, scientific, and/or managerial in one or more fields of research, commercial development, education, and/or leadership within the areas of interest to CRS. Fellowship is the most prestigious level of membership in CRS.



Ashutosh Chilkoti is the Theo Pilkington Chair in Biomedical Engineering and the director of the Center for Biologically Inspired Materials and Materials Systems at Duke University, U.S.A.

Justin Hanes is the Lewis J. Ort Endowed Professor and director of the Center for Nanomedicine at the Johns Hopkins University School of Medicine, U.S.A.

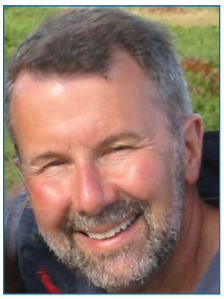
Hideyoshi Harashima is a professor of pharmaceutics and the chair of the Laboratory for Molecular Design of Pharmaceutics, Faculty of Pharmaceutical Sciences, Hokkaido University, Japan.

Claus-Michael Lehr, a professor at Saarland University, is cofounder and head of the Drug Delivery department at the Helmholtz Institute for Pharmaceutical Research Saarland, Germany.

Ijeoma F. Uchegbu is cofounder and chief scientific officer of Nanomerics, a spin-off company from University College London, United Kingdom.

Founders Award

The society grants this honor to a current CRS member who is internationally recognized for outstanding contributions in the science and technology of controlled release.



Richard Guy is a professor of pharmaceutical sciences at the University of Bath. Dr. Guy's research has focused on skin barrier function characterization, transdermal drug delivery, enhancement of percutaneous absorption, iontophoresis, noninvasive biosensing, and the prediction and assessment of skin penetration and topical bioavailability.

Young Investigator Award

Cosponsored by Aptalis Pharmaceutical Technologies

This award recognizes a CRS member, age 40 years or younger on December 31 of the current year, who has made outstanding contributions in the science of controlled release.

Ali Khademhosseini is an associate professor of medicine and health sciences and technology at Harvard-MIT's Division of Health Sciences and Technology and Harvard Medical School and associate faculty at the Wyss Institute. He is developing micro- and nanoscale technologies to control cellular behavior for tissue engineering and drug delivery applications.

CRS/T. Nagai Postdoctoral Research Achievement Award

Copsonsored by The Nagai Foundation Tokyo

This award recognizes an individual postdoc who has recently completed postdoctoral research in controlled release science and technology and the postdoc's advisor, who played an integral role in the achievements.

Shawn Owen is currently a postdoctoral fellow at the University of Toronto in Prof. Molly Shoichet's laboratory. His current research interests include the development of biomaterial scaffolds for *in vitro* cancer models and interaction and intracellular trafficking of colloids, polymeric micelles, and antibody–drug conjugates.

Molly Shoichet holds the Tier 1 Canada Research Chair in Tissue Engineering and is a professor in three departments at the University of Toronto. She founded two spin-off companies from research in her laboratory and is actively engaged in translational research.

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Annual Meeting continued from page 9

Jorge Heller *Journal of Controlled Release* Outstanding Paper Award

Cosponsored by Elsevier

This award recognizes an outstanding regular paper related to the science of controlled release (not an invited, review, or special meeting paper) that was published during 2012 in the Journal of Controlled Release.

Sungho Jin is a distinguished professor and serves as director of the Materials Science and Engineering Program at the University of California, San Diego, U.S.A. His research activities include biomaterials, nanomaterials, energy materials, and magnetic and electronic materials.

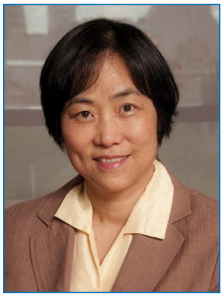
Magnetic targeting of nanoparticles across the intact blood–brain barrier

Seong Deok Kong, Jisook Lee, Srinivasan Ramachandran, Brian P. Eliceiri, Veronica I. Shubayev, Ratnesh Lal, and Sungho Jin

Drug Delivery and Translational Research Outstanding Paper Award

Cosponsored by Springer

This award recognizes outstanding research in the field of drug delivery and translational research that was published during 2012 in Drug Delivery and Translational Research.



Xiao Yu (Shirley) Wu is on the Faculty of Pharmacy at the University of Toronto. Her research interests include novel nanomedicine for enhanced therapy of multidrug-resistant and metastatic cancer, multifunctional polymers and nanocomposites for theranostics and CNS drug delivery, closed-loop insulin delivery, mechanism of controlled drug release and excipient–drug interactions, and mathematical modeling and computer-aided design of controlled release dosage forms.

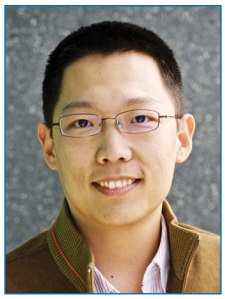
Evaluation of new bi-functional terpolymeric nanoparticles for simultaneous *in vivo* optical imaging and chemotherapy of breast cancer

Alireza Shalviri, Ping Cai, Andrew M. Rauth, Jeffery T. Henderson, and Xiao Yu Wu

Outstanding Oral Drug Delivery Paper Award

Cosponsored by Patheon

This award recognizes a CRS member whose winning abstract relates specifically to oral drug delivery.



Sifei Han
Monash Institute of Pharmaceutical Sciences, Australia

Comparison of alkyl ester versus triglyceride mimetic lipid prodrug strategies to target a model immunomodulator to the lymphatic system

Coauthors: Tim Quach, Luojuan Hu, Anisa Wahab, William Charman, Valentino Stella, Natalie Trevaskis, Jamie Simpson, and Christopher J. H. Porter

Outstanding Pharmaceutical Paper Award

Cosponsored by PharmaCircle

This award recognizes a CRS member whose winning abstract relates specifically to pharmaceutical research.

Shahriar Absar
Texas Tech University, U.S.A.

Camouflaged and thrombin-triggered delivery of tissue plasminogen activator for targeted thrombolysis

Coauthor: Fakhrul Ahsan

Outstanding Transdermal Drug Delivery Paper Award

Cosponsored by 3M Drug Delivery Systems

This award recognizes a CRS member whose winning abstract relates specifically to transdermal drug delivery research.

Katherine Moga
University of North Carolina, U.S.A.

Rapidly-dissolvable microneedles for transdermal delivery via a highly reproducible soft lithography approach

Coauthors: Lissett Bickford, Robert Geil, Stuart Dunn, Ashish Pandya, Yapei Wang, John Fain, Christine Archuleta, Adrian O'Neill, and Joseph DeSimone

Outstanding Preclinical Sciences and Animal Health Paper Award

Cosponsored by PolySciTech, division of Akina Inc.

This award recognizes a CRS member whose winning abstract relates specifically to preclinical sciences and animal health research in the field of delivery of bioactives.

Christina Hofmann
Duke University, U.S.A.

In vitro drug release and *in vivo* tumor delivery of near-infrared emissive biodegradable polymersomes containing poly(ethylene glycol) and randomized poly(trimethylene carbonate-co-caprolactone)

Coauthors: W. Qi, C. D. Landon, M. J. Therien, M. W. Dewhirst, and G. M. Palmer

CRS Outstanding Chapter of the Year Award

The CRS Chapter of the Year Award recognizes a local chapter that has provided exceptional service to its members and to the Controlled Release Society.

United Kingdom-Ireland Local Chapter

This chapter was chosen for its consistent commitment to sharing information with the CRS membership, as well as for its balanced, comprehensive events that continue to provide exceptional value to its members. Congratulations to this outstanding chapter. ■

Welcome New CRS Members

Martin Behm
Neil Berger
Vivian Bi
David Blain
John Brahms
Martin Bultmann
Calvin Carter
Kyunghee Cho
Young Suk Choi
Christina Cortez-Jugo
Debanjan Das
Yoshihito Deguchi
Thomas Durig
Michael Evangelopoulos
Sara Farahmand
Paula Garcia Todd
Elise Gill
Micah Glasgow
George M. Grass
Alessandro Grattoni
Kunal Gujraty
Umesh Gupta
Zishan Haroon
Martha Hass
Johan Hjartstam
Anran Hu
Ling-Kuen Huang
Peter Johannessen
Hiroyuki Kato
Mark A. Kendall
Hyun Koo Kim
Jong Min Kim
Tae Yoon Kim
Taek Gyoung Kim
Jeong-Tae Koh
Adam Lambert
Zhuoyang Lian
Corey A. Lohnes
Thomas D. Madden
Hiteshri B. Makwana
Antonio Mena
Juliette Merian
Daisuke Mori
Ken Morris
Kensuke Murata
Masaki Nakashima
Saumya Nigam
Natalia V. Nukolova
Yewande I. Oni
Chung Park
Nadia Passerini
Pasit Phiasivongsa
Kaushal Rege
Canan Schumann
Anita Sharma
Zoltan Szekely
Wade Tanev
Helder F. Teixeira
Divya Tewari
Shanthakumar Tyavanagimatt
Venkatta Vatti
Fumito Wada
Shunsuke Wada
Howard Wessel
Rick Witte
Jiun-Ming Wu
Emily Wyatt
Kai Xiao

CRS
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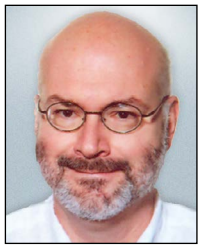
CRS Election Results

The 2013 CRS election votes have been tallied, and the results are finalized. The nominating process, led by the Nominating Committee headed by Martyn Davies, allowed for many opportunities for member input. The newly elected Board of Directors and the Board of Scientific Advisors, listed below, began their new positions on July 24, 2013, at the conclusion of the annual meeting. For a complete list of Board of Directors and Board of Scientific Advisors members, see the CRS website.

Congratulations to our newly elected CRS Board

President-Elect
Art Tipton
Southern Research Institute, U.S.A.



Treasurer
Marcus Brewster
Johnson & Johnson, Belgium

Treasurer-Elect
Ruth Schmid
SINTEF, Norway

Secretary
Debra Bingham
Valeo Partners, U.S.A.

Director-at-Large
Andy Lewis
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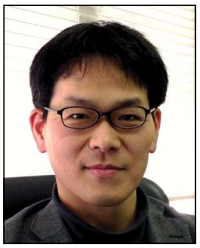
Maria Jose Alonso
University Santiago de Compostela, Spain

Board of Scientific Advisors

Claus-Michael Lehr
Saarland University, Germany

Barbara Lueckel
F. Hoffmann-La Roche Ltd., Switzerland



Akihiko Kikuchi
Tokyo University of Science, Japan

Richard Korsmeyer
Pfizer Inc., U.S.A.

Glen Kwon
University of Wisconsin, U.S.A.

James Oxley
Southwest Research Institute, U.S.A.

Thomas Rades
University of Copenhagen, Denmark

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

Delivery of Proteins Using Spider Silk Particles as Carrier Systems

Matthias Lucke, Markus Hofer, Gerhard Winter, and Julia Engert[1]
Ludwig-Maximilians-University Munich

Introduction
Biocompatible and biodegradable polymers for drug delivery have been investigated for protein delivery in the last decades. However, most of the polymers used for this purpose have major or minor drawbacks, for instance, the essential use of organic solvents during the preparation process or the formation of an acidic environment as a result of polymer degradation. Both factors have potentially negative effects on protein stability.[1] Hence, there is to date the need to search for new excipients for drug delivery.

Silk proteins from insects and spiders gained more and more interest because of their outstanding material properties such as high tensile strength, solubility, and biocompatibility. Silkworm silk has already been used as suture material for many years, and recently extracts of silk fibroin allowed the formation into many different application forms, including films, foams, hydrogels, and particles. On the other hand, silk fibroin from silkworm still varies in quality, as it is a natural product. Additionally, the sericin coating of silkworm fibroins has a strong allergic potential and has to be removed in a first step prior to further processing the protein into the final application form.[2]

Recombinant-produced spider silk proteins can overcome these drawbacks, as a well-controlled production method exists, allowing for tailor-made protein properties. The recombinant-produced spider silk protein eADF4(C16) is an engineered form of the natural spider silk protein ADF4 from the European garden spider *Araneus diadematus.* Spiess and coworkers developed this recombinant protein and already described the formation of particles and films in an all-aqueous preparation process.[3]

Lammel *et al.* then investigated the potential of eADF4(C16) nanoparticles as drug delivery vehicles.[4] The colloidal stable particles were loaded with 12 different small-molecular-weight model drugs, and release rates were studied. The loading mechanism was mainly driven by electrostatic interactions between the negatively charged spider silk particles and the positively charged model drugs. Loaded drugs were then slowly released from the particle matrix, with constant release rates of up to two weeks at physiological conditions.

These findings encouraged us to further understand the particle preparation process as well as to investigate the loading mechanism of macromolecular drugs such as proteins, as the complete loading process can be realized in an all-aqueous environment under ambient conditions.

Experimental Methods
Particle Preparation
The spider silk protein eADF4(C16) used in this study was kindly provided by AMSilk GmbH (Martinsried, Germany) as a spray-dried powder. The basis of the recombinant protein is the natural sequence of the dragline silk ADF4 from *A. diadematus*. The spider silk protein has a molecular weight of 47.7 kDa. The spray-dried eADF4(C16) protein was dissolved in guanidinium thiocyanate and dialyzed at room temperature against 10 mM tris(hydroxymethyl)aminomethane (Tris)/HCl, pH 8. The resulting eADF4(C16) solution was centrifuged, filtrated, and the protein concentration determined by UV-Vis spectroscopy.

Processing of the spider silk solution into nanoparticle dispersions was carried out by micromixing using a syringe pump system. Briefly, two cylinders of the syringe pump system were filled with pretempered eADF4(C16) solution or pretempered 2M potassium phosphate or 2M ammonium sulphate solution at 20, 60, or 80°C, respectively. The pumps were connected via a T-shaped mixing element into which the solutions were pumped at a flow rate of 50 mL/min. Resulting particle dispersions were centrifuged and washed three times with highly purified water. A short ultrasonication and filtration step completed the particle preparation procedure. The final particle concentration in mg/mL was determined gravimetrically.

Particle size and size distribution were measured in triplicate by dynamic light scattering using a Zetasizer Nano ZS (Malvern Instruments, Malvern, U.K.). Additionally, particle size, size distribution, and particle shape were confirmed by transmission electron microscopy (Jeol JSM-6500F, Jeol Inc., Peabody, MA, U.S.A.).

Loading of Spider Silk Particles with Proteins
Spider silk particles were loaded with proteins such as fluorescein isothiocyanate (FITC)–lysozyme from chicken egg white (molecular weight: 14.307 kDa), FITC–bovine serum albumin (BSA) (molecular weight: 66 kDa), or FITC-dextran (average molecular weight: 21.2 kDa) at pH 2.0 or 7.0 to investigate the loading process as a function of overall charge of the particles and loaded macromolecules. To visualize the loading procedure, microparticles were prepared by dialysis, loaded with the macromolecules, and subsequently analyzed by confocal laser scanning microscopy. The ratio of FITC-labeled protein to spider silk particles was adjusted to 15% (w/w) for all samples.[1]

Scientifically Speaking continued on page 14

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Scientifically Speaking continued from page 13

Results and Discussion

The unfolded spider silk protein can be rapidly processed into solid particles simply by the addition of kosmotropic ions. Potassium phosphate or ammonium sulphate were used, which represent kosmotropic ions according to the Hofmeister series. As determined by FTIR spectroscopy, protein particles showed a β-sheet-rich structure (Figure 1) after the phase separation and structure formation process.

The spider silk particles display a negative zeta-potential, and their size can be tailored by adjusting the processing parameters. Preparation of the particles using pretempered solutions at a temperature of 20°C and then increasing the temperature to 80°C decreased the particle size almost twofold. Particle sizes of around 300 nm can be achieved at a temperature of 80°C. The polydispersity index (PI) was lower than 0.2, indicating a uniform particle size distribution. In contrast to changes in process temperature, no considerable differences between 2M ammonium sulphate and 2M potassium phosphate were observed, although both salts are strong kosmotropic agents in the Hofmeister series. Both types of salts resulted in comparable particle sizes, and the type of salt had no significant influence on the salting out process (Figure 2). The processing temperature had no influence on the particle shape or surface characteristics, as shown by scanning electron microscopy (Figure 3).

Loading of the spider silk particles with FITC-labeled macromolecules was attempted, and the loading mechanism was investigated by confocal laser scanning microscopy (CLSM) (Figure 4). The CLSM images showed that high matrix loading of FITC-lysozyme was achieved at a pH value of 7.0. At this pH, lysozyme has a positive net charge in contrast to negatively charged eADF4(C16) particles (Table 1). Loading is mainly driven by electrostatic interactions. The FITC-lysozyme loaded eADF4(C16) particles appear as filled green spots on a dark background, showing that FITC-lysozyme is not only loaded onto the surface of the particles but also diffuses into the particle matrix.

In contrast, FITC-BSA with a negative net charge at pH 7.0 was not loaded on or into the particles. However, at pH 2.0, when FITC-BSA had a positive charge, loaded particles

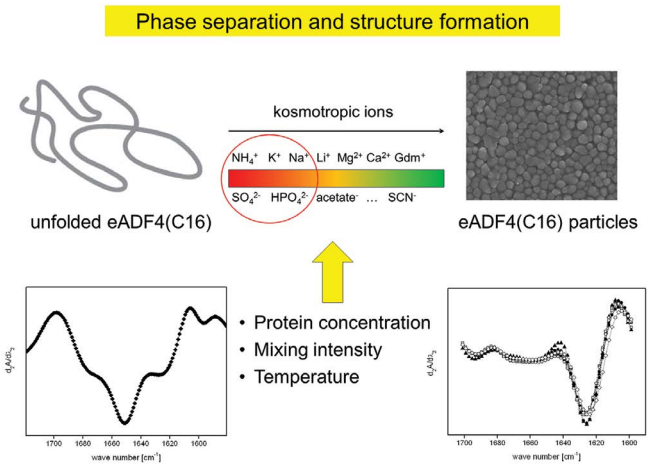

Figure 1. *Particle preparation process. The unfolded protein is processed into solid particles by a phase separation and structure formation process induced by the addition of kosmotropic ions. Particle size can be influenced by the protein concentration, mixing intensity, and temperature. After structure formation, particles display high β-sheet content, as shown in the FTIR spectra (second derivative).*

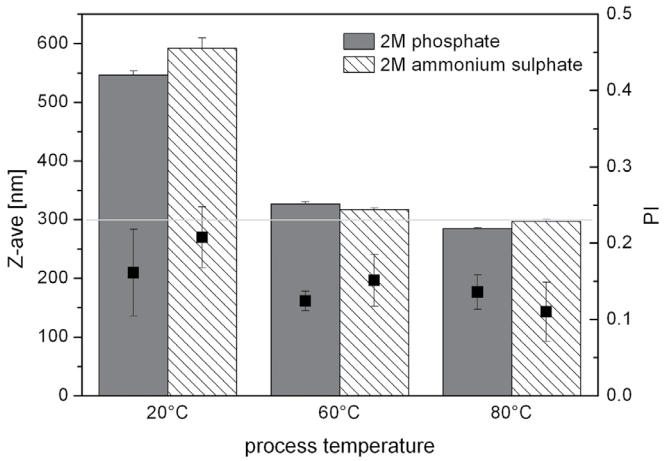

Figure 2. *Particle formation process at different temperatures induced by different kosmotropic ions of the Hofmeister series.*

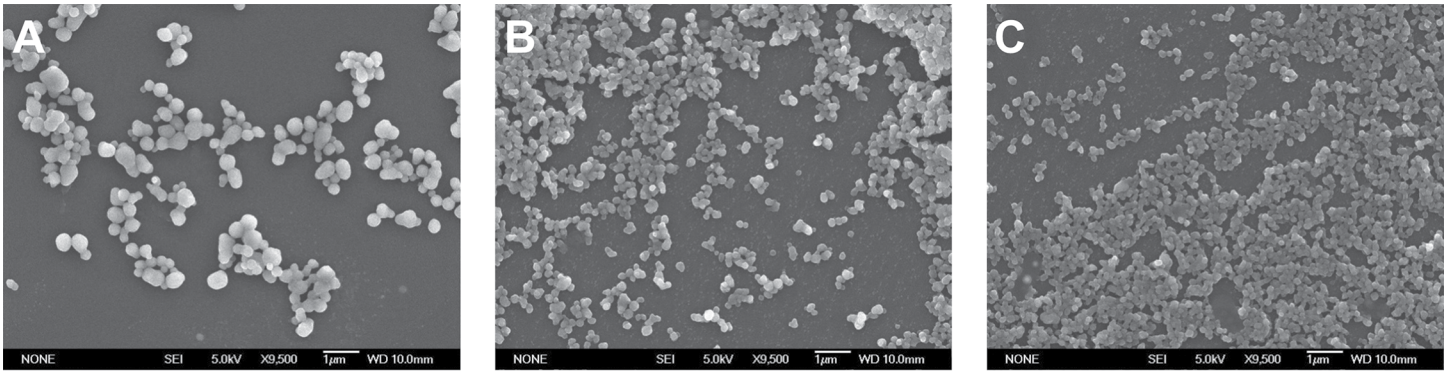

Figure 3. *Scanning electron micrographs of spider silk particles prepared at different temperatures using the micromixing system: 20°C (left), 60°C (center), and 80°C (right). Bar = 1 μm.*

Table 1. Properties of macromolecules for loading at different pH values.

pH	eADF4(C16)	FITC-lysozyme	FITC-BSA	FITC-dextran
2.0	Positive net charge	Positive net charge	Positive net charge	Uncharged
7.0	Negative net charge	Positive net charge	Negative net charge	Uncharged

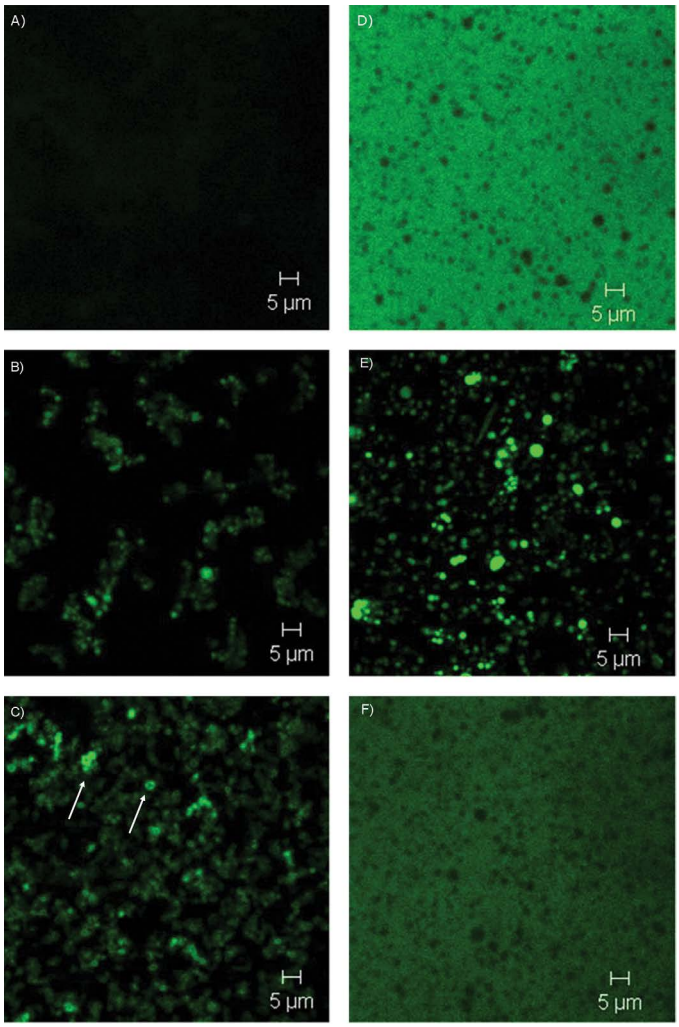

Figure 4. *Confocal micrographs of dispersed and positively charged eADF4(C16) particles after loading with FITC-dextran (A), FITC-lysozyme (B), and FITC-BSA (C) at pH 2.0. Confocal micrographs of dispersed and negatively charged eADF4(C16) particles after loading with FITC-dextran (D), FITC-lysozyme (E), and FITC-BSA (F) at pH 7.0. Figure reprinted from Hofer et al. (2012) with permission from Elsevier.[1]*

appeared as hollow spheres with a green ring at the surface. FITC-BSA failed to permeate into the particle matrix, and only surface loading was observed (Figure 5). The reason for the surface loading instead of matrix loading can be explained by the molecular weight of the macromolecules. The molecular weight of FITC-BSA is about fourfold higher compared to FITC-lysozyme (66 kDa for FITC-BSA vs. 14.3 kDa for FITC-lysozyme). Therefore, macromolecules with a higher molecular weight are not able to permeate into the matrix of eADF4(C16) particles and may only bind to the surface.

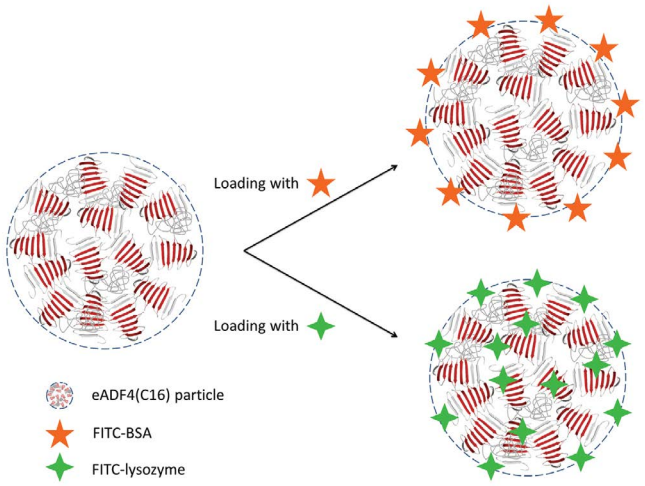

Figure 5. *Schematic illustration of the loading process of spider silk microparticles with fluorescently labeled macromolecules (FITC-BSA, FITC-lysozyme). FITC-lysozyme is loaded into the particle matrix, whereas FITC-BSA is only adsorbed onto the particle surface and does not penetrate into the matrix.*

Conclusion

Particles made of the recombinant spider silk protein eADF4(C16) can be formed using an all-aqueous preparation process. The particle size can easily be adjusted by increasing or decreasing the processing temperature. Subsequently, loading with FITC-labeled macromolecules was proven for eADF4(C16) particles and allowed a distinction between surface and matrix loading. Therefore, spider silk particles are a promising delivery system in particular for sensitive drugs such as proteins.

Acknowledgement

The authors wish to thank AMSilk GmbH (Martinsried, Germany) for kindly providing the eADF4(C16) spider silk protein. Dr. Ute Slotta and Dr. Lin Römer are thanked for their scientific support. This work is supported by the BioTransporter grant of the Federal Ministry of Education and Research (BMBF), Germany (grant number: 13N11341).

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4. Lammel, A, Schwab, M, Hofer, M, Winter, G, Scheibel, T. Recombinant spider silk particles as drug delivery vehicles, Biomaterials 32: 2233-2240 (2011). ■

Technologies for Tissue Engineering and Drug Delivery: An Interview with CRS Young Investigator Award Winner Ali Khademhosseini

Ali Khademhosseini, M.A.Sc., Ph.D., is an associate professor of medicine at Harvard-MIT's Division of Health Sciences and Technology and Harvard Medical School, Brigham & Women's Hospital, and associate faculty at the Wyss Institute. He received his Ph.D. in bioengineering from MIT, and master's and bachelor's degrees from University of Toronto, both in chemical engineering. Dr. Khademhosseini is developing micro- and nanoscale technologies to control cellular behavior for tissue engineering and drug delivery applications.

Cell-laden microscale hydrogels are useful for creating microenvironments that have a controlled architecture and can induce cells to reorganize themselves into functional tissues. Controlled release technologies can be combined with such microfabricated gels to help regulate these microenvironments by delivering chemicals to cells in a defined manner.

The biocompatibility of hydrogels, as well as their mechanical and biological tenability, has made them the material of choice in regenerative medicine. They serve as scaffolds to provide structural integrity, control drug and protein delivery to tissues and cultures, and serve as barriers or adhesives between tissue and materials surfaces.

Microgels provide a porous aqueous environment with the ability to create microcapsules of bioactive substances such as peptides, proteins, enzymes, DNA, drugs, and cells. Some can be stimuli responsive and enable drug release on demand in precise concentrations. Controlled release technology is expected to have an effect in the foreseeable future by developing new drug delivery systems superior to those we have currently.

Aptalis Pharmaceutical Technologies, cosponsor with CRS of the 2013 CRS Young Investigator Award, spoke with Dr. Khademhosseini about drug delivery and tissue engineering and how these two fields of medical research are expected to benefit from the availability of applied nanomedicine.

Q *What would you say are the most significant advances made in the field of tissue engineering in the last five years?*

A The field of tissue engineering has made major advances that have resulted in a number of high-profile breakthroughs in treating patients. These include clinical successes in engineering artificial tracheas, as well as various types of cardiovascular and musculoskeletal tissues. Other major advances have come in our understanding of the fundamental science that can be used for enabling tissue engineering. For example, a key challenge in tissue engineering is cell source. Recently, the development of new cell sources, such as induced pluripotent stem cells, promise to overcome major hurdles in the field. Also, major advances have been made with respect to using biomaterials and controlled release technologies to modulate the "microenvironment" of the nascent tissue. In addition, there have been new applications of tissue engineering, which have further enhanced its usefulness. For example, we can now make human tissues in a dish that can be used to test drug toxicity or develop models of diseases that can be used to test drug efficacy.

Q *Can you provide some examples of why nanomaterials are well suited for drug delivery?*

A Nanomaterials are particularly attractive for drug delivery since they enable the targeted delivery of the drug to specific sites in the body as well as regulate the release profile of the drug at various sites. For example, with respect to cancer therapies, chemotherapeutic drugs are often toxic when administered systemically. Delivery of such drugs using nanomaterials can significantly enhance the effectiveness of the drug while minimizing side effects.

Q *How can this enable more effective therapeutics?*

A I think that nanomaterials are already enabling major advances in various aspects of drug delivery, such as targeted therapeutics. For example, we can now engineer the surface of nanoparticles to make them interact with particular cell or tissue types, while minimizing interaction with other types of cells or tissues. This will enhance the effect of therapeutics by minimizing the dosage of the drugs as well as off-target side effects.

Q *How can engineered human tissue be used to assess the delivery of drug particles? What are the advantages?*

A An enabling area of tissue engineering is to engineer tissues that can be used to assess the effectiveness of drug delivery platforms. For example, it is possible to engineer an artificial vasculature that mimics various aspects of the human vasculature, such as microarchitecture and endothelial cell coverage. Then one can study and optimize the interaction of the drug-containing nanoparticles with cells prior to costly animal experiments or clinical trials. Appropriately engineered human tissues can also help us understand the pharmacodynamics and pharmacokinetics of drug candidates. Furthermore, such systems will enable us to assess the delivery of particles of different sizes, shapes, and coating chemistries.

Q *Can the knowledge from this work be applied to other drug delivery methods?*

A Yes. The knowledge learned from such platforms can be used to optimize dosages and release profiles from other types of drug delivery platforms.

The CRS Young Investigator Award recognizes a CRS member who has made outstanding contributions in the science of controlled release and is 40 years of age or younger in the year the award is presented. Aptalis Pharmaceutical Technologies congratulates Dr. Khademhosseini on his achievement.

Aptalis Pharmaceutical Technologies is your trusted oral drug delivery partner for overcoming even the most demanding delivery challenges, using proprietary technologies and development expertise for bioavailability enhancement, custom release profiles, and taste-masking for dosage forms including orally disintegrating tablets, resulting in patient-optimized products.

We provide flexible and tailored codevelopment and product out-licensing opportunities that can enable partners to successfully bring IP-protected, value-added Rx and OTC products to market. We have multinational and integrated R&D and manufacturing teams and facilities in the United States and Europe to offer global solutions to companies in various regions around the world.

For more information about Aptalis Pharmaceutical Technologies, visit www.aptalispharmatech.com. ■

Articles on Animal Models of Disease, Cross-Species Comparisons, and "One Health"

David Brayden[1] *and Terry Bowersock*[2]

One of the roles of the Preclinical Sciences & Animal Health (PSAH) Division is to identify important articles on the overlap between animal and human health, as well as to focus on identifying useful information on selected animal models used in understanding disease mechanism and their use in drug discovery and drug delivery programmes. Recent articles that caught our attention include:

1. A major review of animal models used in translating medicines for orphan drugs for rare diseases since 2000 has been compiled by a scientific team led by the European Medicines Agency.[1] This authoritative study provides extensive tables and analysis of what has been learned primarily from genetically modified (GM) rodent models of rare metabolic diseases including lysosomal storage diseases (e.g., Fabry's disease and Pompe disease). Of note is that naturally occurring mutations present in cats and dogs were regarded as a relevant genotype for human mucopolysaccharidosis (MPS) disorders. Assessment was also made of rare neuromuscular disease models (e.g., amyotrophic lateral sclerosis, Huntington's disease). While GM murine and rat models predominated for this class of disease, the analysis gave an objective and critical review of their relevance to the human phenotype in terms of pathogenesis, progression, and responsiveness to therapeutic intervention. Well known to veterinarians is the spontaneous canine model of myasthenia gravis, which has been used to screen long-acting cholinesterase inhibitors and therapeutic vaccines for small-animal myasthenia treatment. There are videos on YouTube of dogs suffering from this condition making a remarkable (albeit temporary) recovery of limb neuromuscular function upon injection of a short-acting cholinesterase inhibitor (Tensilon®), a tool used for myasthenia diagnosis. An example is at www.youtube.com/watch?v=k7YX9kuWrxA. The final group of rare diseases examined was in ophthalmologic diseases, where there was a dog model of retinal degeneration cited as having phenotypic relevance to man. The conclusion of the study was that there is need to develop more predictive animal models for these types of orphan diseases.

2. Lymphatic drug transport for lipophilic drugs and delivery systems remains an important topic of oral formulation research. Trevaskis and colleagues provided an extensive characterisation of the cannulated mesenteric lymph duct of the mouse and compared data with the rat and dog model using intraduodenal instillations of the highly lipophilic molecule radiolabelled halofantrine.[2] The main conclusions were that lymphatic lipid transport on a mg/kg basis was quite similar across species and between male and female when the impact of lipid dose was assessed. Nonetheless, differences in halofantrine delivery to lymph emerged with dogs > rats > mice, and this seemed in part to be related to lower overall oral bioavailability in rodents. The work has implications for lipid-based delivery studies in recently developed transgenic mouse models and for cross-species comparisons.

3. Mouse models of disease continue to attract controversy, as evidenced by an editorial in the April edition of *Nature Medicine* comparing leukocyte gene expression and transcriptional changes in mice and humans exposed to inflammatory challenges including sepsis, burns, endotoxemia, and trauma.[3] The editorial cited a study that used new and historical data and found that the mice poorly reflected human inflammatory disease and that various human inflammatory conditions had much more in common at the leukocyte gene expression and transcriptional change level with each other compared with challenges in mice.[4] *Nature Medicine* has a strong emphasis on human data and on preclinical models that closely mimic the pathology and clinical signs of human disease. The conclusion was that current focus should be initially on better understanding molecular changes in human conditions and clinical phenotypes and to assess whether animal models replicate these. The editors' argument was that there is a tendency to go in reverse, to over-rely on animal models to understand human disease. For drug delivery researchers using such animal models, not only is there the difficulty of disease correlation with the human condition but there are also the additional issues of likely different pharmacokinetics and pharmacodynamics of drugs released from delivery systems in mice and humans.

4. In acknowledging the limitations of some mouse models of disease, particularly in CNS conditions, Morton and Howland have provided an extensive review of large animal models of Huntington's disease.[5] The authors discuss the important discoveries made in the transgenic R6/2 mouse model, but then they objectively assess the limitations: differences in neuroanatomy and brain size versus humans, as well as a shorter lifespan and more rapid pathology. Following mouse studies,

[1] School of Veterinary Medicine, University College Dublin, Ireland.
[2] Zoetis Global Biologics Research, U.S.A.

they advocate use of large animals with large brains, more humanlike anatomy, and a longer lifespan, and they discuss their potential benefit in gene therapy, implant, and trophic therapy studies where intracerebral administration is more practical and where more accurate imaging by CT and MRI is possible. Transgenic sheep and mini-pig models have been created whereby the human mutant *HTT* fragment is expressed in the CNS. These models show anatomical changes in the nigrostriatum within 16 months and are being used to assess adeno-associated viral gene therapy and other therapeutic approaches in delivery systems. The authors make an interesting point regarding access to such models when they are fully developed and made available to the research community. They foresee that new funding mechanisms and international consortia will be needed to run prioritised studies for possibly 5–10 years in purpose-built core facilities.

5. Regenerative medicine and tissue implants are an important research theme of CRS. A fascinating bioengineering paper by Song and colleagues in *Nature Medicine* described studies where they made a rat donor kidney scaffold comprising connective tissue and blood vessels and then decorated the scaffold with rat kidney cells and human endothelia.[6] The system was matured to achieve a functional kidney construct *in vitro*. When the implant was then transplanted into rats, it was perfused by the recipient's circulation and filtered blood and produced urine. This is regarded as an important study, given the requirement for kidney transplantations in 100,000 people in the United States and the huge amounts of people in end-stage renal disease. The technical challenge will be to replicate it for human kidneys, where there are major challenges over and above those of rats.

6. Finally, here is an interesting article on how dogs were used to study an extremely rare and fatal form of autosomal recessive human myopathy affecting 6 out of 100,000 babies. Böhm and colleagues studied the veterinary records from a number of veterinary teaching hospitals and discovered a muscle weakness disease, inherited myopathy of Great Danes (IMGD), in which the mutation found in 5 dogs, *BIN-1*, led to myotonic dystrophy. *BIN-1* codes for a T-tubule protein in muscle fibres, and the rare mutation was found in humans and dogs.[7] Deleting the *BIN-1* gene in mice, however, did not replicate the disease. This model can be used to study disease progression and test new drug therapies and gene therapies for humans. The article was also discussed in *Science Now*.[8]

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CRS Nordic Local Chapter News

Christel Bergström, Bente Steffansen, and Martin Brandl
CRS Nordic Local Chapter Board Members

The annual Nordic Local Chapter meeting of the Controlled Release Society was held in Uppsala, Sweden, June 26–28, 2013. It included a board meeting, a social event, and a Ph.D. course in Oral Bioavailability Research: Approaches and Pitfalls, with representatives from Sweden, Denmark, Finland, Belgium, and Australia.

The 2013 course was organized by a committee from the CRS Nordic Local Chapter board, including Martin Brandl (University of Southern Denmark), Bente Steffansen (Copenhagen University, Denmark), and Christel Bergström (Uppsala University, Sweden). The course started with a poster session and a social event during which Hans Lennernäs (Uppsala University) and Patrick Augustijns (University of Leuven, Belgium) shared "Pearls of Wisdom of Oral Bioavailability Research."

The Ph.D. course covered state-of-the-art techniques and methodologies currently in use to perform pharmaceutical profiling. The impact of drug properties and their interplay with excipients commonly used in oral dosage forms were discussed to understand dissolution, solubility, supersaturation, precipitation, permeability, and interactions with transporter proteins and enzymes. The course covered *in silico, in vitro,* and *in vivo* techniques that are used to predict oral bioavailability in humans, with a special emphasis on *in vitro* methods.

Students work in groups on case studies.

Prof. Hans Lennernäs (Uppsala University) shares his wisdom with Ph.D. students.

The Ph.D. program included keynote lectures by Christel Bergström, Annette Bauer-Brandl (University of Southern Denmark), Martin Brandl, Bente Steffansen, Lena Gustavsson (Lund University, Sweden), and Maria Karlgren (Uppsala University). Topics included investigating solubility and dissolution rate of drug substances; *in vitro* permeability of drug substances, including transporter-mediated permeability and influence of solubilising agents; and *in vitro* drug metabolism.

The lectures were followed by a lab tour of the Uppsala University Drug Optimization and Pharmaceutical Profiling Platform. The students also spent several hours on case studies in biopharmaceutics, during which they actively contributed to the program through faculty-supported group discussions in which real-life examples were analyzed and discussed. The program concluded with oral presentations and a plenary discussion. Many participants gathered Thursday evening at a local restaurant, Katalin, in downtown Uppsala.

The board decided during their meeting that the next CRS Nordic Local Chapter event will be a scientific meeting held in Copenhagen in 2014, organized by a joint committee with representatives from universities in Copenhagen, Lund, Gothenburg, and Odense. ■

DDTR Special Issue "Nano/Bio Interface: Impact on Drug Delivery Applications"

Vinod Labhasetwar, Editor-in-Chief

This special issue of *Drug Delivery and Translational Research* (*DDTR*) focuses on nanotechnology applications for drug delivery presented at the NanoBio Collaborative International Conference 2012 held at the University of South Florida (USF), U.S.A.

The preface to the issue is by Sir Harold (Harry) Kroto, "Nanoscience and Nanotechnology in the Twenty-first Century." Prof. Kroto shared the 1996 Nobel Prize in Chemistry with Robert Curl and Richard Smalley. He is currently the Francis Eppes Professor of Chemistry at Florida State University.

The compendium features four reviews: self-assembling peptide scaffolds as innovative platforms for drug and cell delivery to restore cardiac tissue after myocardial infarction; cyclodextrin-based supramolecules comprising polymers and nanoparticles bearing targeting moieties such as folates, estrogen, carbohydrates, and peptides as promising drug-delivery platforms; the major barriers, nanotechnology-based solutions, and safety issues for effective drug delivery to the CNS; and recent developments in theranostic platforms, their advantages and disadvantages in the diagnosis and treatment of various lung-related diseases, and their potential application to chronic lung diseases.

In addition, there are a few research articles, including a single-step synthesis of PEGylated hybrid lipid-PLGA nanoparticles for encapsulating hydrophobic drugs without the necessity of covalently linking PLGA to PEG; the protective and anti-inflammatory effects of nanoparticles loaded with quercetin prepared with binary mixtures of cetyl alcohol and Gelucire; the feasibility and advantages of PLGA-PEG nanoparticles for delivering thyroid hormones for ischemic brain stroke; and mechanism for the protective effect of cerium oxide nanoparticles against reactive nitrogen species in reduction of peroxynitrite or its reactive breakdown products.

These reviews and research papers constitute an up-to-date cross-section of some of the most exciting and promising areas of nanomedicine today.

About the Guest Editors

Dr. Subhra Mohapatra is an associate professor of molecular medicine at the Morsani College of Medicine, USF. She received her doctorate in immunology at the University of Manitoba, Canada, and postdoctoral training at the H. Lee Moffitt Cancer Center, Tampa, Florida. Her current research focuses on the development of nanoparticle-mediated drug delivery methods and experimental therapeutics for cancer, synthesis of 3D polymeric nano/micro scaffolds for studying tumor-stroma interactions and cancer drug discovery, and establishment of nanohole sensor-based technology for biomarker detection. She has 41 publications to her credit. She has served as a reviewer for grants submitted to the American Heart Association, Department of Defense, and National Institutes of Health (NIH). Her research is funded by the NIH and Florida Department of Health.

Dr. Srinivas Nagaraj is an assistant professor of internal medicine and translational medicine at Morsani College of Medicine, USF. Following his graduate work at St. Johns Medical College, Bangalore, India, he performed postdoctoral research at University Clinic, Bonn, Germany, and H. Lee Moffitt Cancer Center, investigating the role of dendritic cell cancer therapy and tumor-derived suppression. In 2009 he joined the Nanomedicine Research Center at USF, and his research focuses on nanotherapeutic approaches to modify chronic inflammation and cancer. He has published in journals such as *Nature Medicine, Nature Reviews Immunology, Journal of Experimental Medicine, Journal of Clinical Investigation,* and others.

Shyam S. Mohapatra, Ph.D., is distinguished health professor, vice chair of basic research for internal medicine, and director of the Translational Medicine-USF Nanomedicine Research Center at USF, and a research career scientist at the James A. Haley VA Hospital in Tampa, Florida. His research focuses on molecular and immunologic mechanisms of inflammation in respiratory diseases, cancers, viral infections, and traumatic brain injury. He has received more than $19 million in extramural funds including NIH, Office of Naval Research, VA Merit Review Award, and Florida Department of Health. He has published over 160 papers, some in journals such as *Nature Medicine*, and has 15 U.S. patents and numerous pending patent applications. He is a charter fellow of the National Academy of Inventors.

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People in the News

Compiled by Steven Giannos, Independent Consultant

Orexo Appoints Robert A. DeLuca as President of Orexo US Inc.

Business Wire: July 1, 2013 – UPPSALA, Sweden – Orexo AB (STO:ORX) announced today that it has appointed Robert A. DeLuca, as president of Orexo US Inc., a fully owned U.S. subsidiary of Orexo AB. Orexo US Inc. will focus on commercialization of Zubsolv™ (buprenorphine and naloxone, sublingual tablets) in collaboration with the appointed partner Publicis Touchpoint Solutions. With the establishment of a commercial leadership team in the United States, Orexo AB in Sweden will focus its resources on the development of new products including product extensions of Zubsolv, manufacturing, and quality assurance and provide overall corporate governance. Mr. DeLuca will become a member of the executive management team of Orexo AB.

Robert A. DeLuca brings an extensive and relevant experience from establishing commercial operations in the United States, which will be important for the launch of Zubsolv in September 2013. DeLuca has extensive experience within managed care, marketing, and sales from various leadership positions at Sanofi, Schering-Plough, Berlex, Pharmacia, and most recently as chief commercial officer at Archimedes Pharma.

DeLuca is a New Jersey licensed pharmacist and graduated from St. John's University in New York City. DeLuca is on the St. John's College of Pharmacy Advisory Board, serves on the Board of Trustees of the Academy of Managed Care Pharmacy Foundation, and is a member of the Academy of Managed Care Pharmacy (AMCP) and the American and New Jersey Pharmacists Association.

"Orexo provides an exciting opportunity, and I have great expectations for the launch of Zubsolv in the United States. I am impressed with the product profile, especially the data from the acceptance trial, in which 89 percent of trial participants favored Zubsolv over the conventional buprenorphine treatment modalities for opioid addiction. We feel this product will address one of the major health issues in the United States, and I am looking forward to establishing a strong organization to execute the launch of Zubsolv in a market with significant growth potential," said DeLuca.

"Establishing a commercial presence in the U.S. is a key milestone towards the launch of Zubsolv, and I am particularly pleased that we have succeeded in recruiting Mr. DeLuca to establish and lead our U.S. subsidiary and the launch of Zubsolv. He brings extensive experience in establishing commercial operations in the United States, and his background in managed care will be a major asset to ensure a successful launch of Zubsolv," said Nikolaj Sørensen, president and CEO of Orexo AB.

With the appointment of Robert A. DeLuca, Orexo AB will activate the subsidiary Orexo US Inc. registered in the state of Delaware.

Tris Pharma Hires President for Generic Pharmaceuticals Business

PRNewswire: June 20, 2013 – MONMOUTH JUNCTION, NJ, U.S.A. – Tris Pharma, a specialty pharmaceutical company focused on developing innovative drug delivery technologies, today announced that it has named Janet Penner as president of its new generic pharmaceuticals business.

Tris's generic pharmaceuticals business, with its own distinct sales, marketing, and distribution, will be responsible for commercializing Tris's Abbreviated New Drug Applications (ANDAs) while leveraging Tris's considerable manufacturing capabilities. Tris currently has 13 FDA-approved ANDA products, including several "first-to-market" generics. All of Tris's generic products are manufactured in its FDA-inspected, state-of-the art 130,000-square-foot facility in New Jersey.

"Tris's generics initiative is a natural evolution of the overall strategic vision at Tris, bringing technologically challenging, high-quality products to the marketplace," said Ketan Mehta, president and CEO of Tris Pharma.

Janet comes to Tris with a wealth of expertise in the commercialization of generic products. She brings nearly 15 years of experience in leadership roles within the generic pharmaceuticals industry, including AmerisourceBergen, where she was responsible for the purchasing of generic pharmaceuticals. Most recently, Janet headed sales & marketing at CorePharma. Janet has also held various positions of growing responsibility at General Electric and PepsiCo, and holds an MBA.

"Tris's unique technology for liquid sustained-release products, along with the continued expansion of its strategic pipeline of both liquid and solid oral dosage ANDA development projects, has me truly excited to spearhead the generic pharmaceuticals business at Tris," said Ms. Penner.

Tris Pharma is a specialty pharmaceutical company focused on the research and development of technologies-driven products. Tris has pioneered the delivery of sustained release in the liquid, chewable/ODT, and strip dosage forms so patients do not have to swallow a pill. Tris's Nobuse™ technology provides abuse deterrence for opioids and other abuse-prone drugs. Tris's R&D and manufacturing facilities are located in Monmouth Junction, New Jersey, U.S.A. For more information, please visit www.trispharma.com.

Southern Research Institute Names Arthur J. Tipton, Ph.D., President and CEO

PRNewswire: June 17, 2013 – BIRMINGHAM, AL, U.S.A. – Southern Research Institute today announced that Arthur J. Tipton, Ph.D., has been selected by its Board of Directors to serve as president and CEO of Southern Research effective July 8, 2013.

Tipton replaces John A. "Jack" Secrist, III, Ph.D., who served as president and CEO of Southern Research Institute for seven years. Secrist announced his retirement earlier this year after 34 years of service at Southern Research.

"The Board is extremely pleased that Dr. Tipton will lead Southern Research Institute, and I look forward to working with him," said Ray L. Watts, M.D., president of the University of Alabama at Birmingham and chairman of the Southern Research Board of Directors. "This is a critical time for research, with both opportunities and challenges, and his experience and strategic vision are ideal to grow the organization's portfolio of contract research in biomedical science, drug discovery, and advanced technology/engineering."

Tipton previously served as senior vice president and general manager of Evonik–Birmingham Laboratories in Birmingham, Alabama. During his career, he has helped lead the growth of three pharmaceutical/biotech companies and launched four commercial products. He holds 31 U.S. patents with numerous foreign equivalents, and he has more than 70 publications, presentations, and invited lectures to his credit.

In 2004, Tipton joined Southern Research to lead the formation of a new, wholly owned drug-delivery company—Brookwood Pharmaceuticals—which was launched with Tipton as president and CEO. When Brookwood Pharmaceuticals was acquired by SurModics in 2007 for about $50 million, Tipton oversaw the most significant payment to Southern Research in its history. The SurModics business was then acquired by Evonik Degussa Corporation in 2011.

"A Birmingham native, I know and have great respect for the record Southern Research Institute has in research initiatives and the impressive history of innovation," Tipton said. "I am familiar with the Institute's great people; I look forward to leading this exceedingly talented and dedicated team capable of pushing research and development in a range of science and engineering markets. I am equally excited to work closely with UAB and look forward to making this close relationship even stronger."

Tipton served as executive vice president at Durect Corporation, a California-based, publicly traded drug-delivery company, and held a variety of positions in Southern BioSystems, including vice president and chief scientific officer, where he led all efforts on biodegradable technology from 1993 to 2001. At Southern BioSystems, Tipton invented the SABER delivery system and led its development into multiple clinical campaigns. He was a member of the negotiating team for the acquisition of Southern BioSystems by Durect. Prior to joining Southern BioSystems, Tipton was with Atrix Laboratories (now part of QLT) from 1988 to 1993.

Tipton holds a bachelor's degree in chemistry from Spring Hill College and a doctorate in polymer science and engineering from the University of Massachusetts, Amherst. He has served on the boards of the Society for Biomaterials, American Institute of Biological and Medical Engineers, Brookwood Pharmaceuticals, and Southern BioSystems, and he serves on the boards of the Biotechnology Association of Alabama, Birmingham Venture Club, and the Controlled Release Society. He chairs the external advisory board for UAB's Biomedical Engineering Department.

Southern Research Institute is a not-for-profit 501(c)(3) scientific research organization that conducts advanced engineering research in materials, systems development, environment and energy, and preclinical drug discovery and development. Southern Research has more than 520 scientific and engineering staff that support clients and partners in the pharmaceutical, biotechnology, defense, aerospace, environmental, and energy industries. Headquartered in Birmingham, AL, Southern Research Institute has facilities/offices in Wilsonville and Huntsville, AL; Frederick, MD; Durham, NC; Houston, TX; and Washington, DC. Learn more at www.SouthernResearch.org.

Atlantic Pharmaceuticals President Named Health-Care Hero Finalist in *Atlanta Business Chronicle* for Drug Abuse Deterrent Technology

PRNewswire: May 20, 2013 – ATLANTA, GA, U.S.A. – Atlantic Pharmaceuticals, Inc., a specialty pharmaceutical company that has developed and is commercializing a unique technology to deter prescription drug abuse today announced that its founder and president, Anthony Soscia, has been chosen as a finalist for the *Atlanta Business Chronicle*'s Health-Care Heroes Awards. The awards are presented annually by the *Atlanta Business Chronicle* to honor individuals and organizations demonstrating excellence and deserving recognition in the health-care community, from the doctors finding cures for deadly diseases to organizations serving our community's health-care needs and allied professionals making a difference in the lives of many.

Atlantic's patented abuse deterrent platform has been designed to resist attempts to easily extract a drug from an oral dosage form and may sequester and reduce drug release of a pharmaceutical that has been subjected to a variety of physical methods of tampering and abuse. The technology can be applied to immediate as well as sustained release drug candidates such as oxycodone. "We believe SMART/Script™ is a unique technology that may have a significant impact on prescription drug abuse and misuse and are honored by the Health-Care Heroes recognition," said Soscia.

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People in the News continued from page 23

SMART/Script™ (SMART, simple, controllable, resistant, insoluble, physical trap), a novel, patented drug delivery technology, was designed to prevent easy drug extraction and to deter the abuse of medications via known routes of abuse or misuse, including chewing, snorting, and injecting. Orally delivered prescription pharmaceuticals, such as narcotics, are frequently subjected to abuse and misuse via chewing and swallowing or crushing and either snorting or injecting the resultant powder in order to obtain a fast euphoria. A product formulated with SMART/Script™, however, resists extraction in water or alcohol and can be used with a broad range of opioids and nonopioids in immediate or extended release forms. SMART/Script™ is also unique among competitive technologies in that physical manipulation, such as chewing or crushing, may result in reducing the release of the drug as opposed to increasing it.

Atlantic Pharmaceuticals is a specialty pharmaceutical company using its patented technology to produce novel therapeutics that resist attempts at tampering and may be useful to reduce abuse of certain prescription drugs. Based on the company's proprietary technology, SMART/Script™, Atlantic is developing a pipeline of abuse-deterrent products that are nearing pivotal testing.

The Health-Care Heroes Award winners were revealed at the 16th annual award presentation dinner on May 16 at the Cobb Energy Centre. Please visit atlanticpharma.com for more information.

UBM Canon and MD+DI, the Global Medtech Authorities, Announce Dr. Robert Langer as the 2013 MDEA Lifetime Achievement Award Recipient

PRNewswire: May 15, 2013 – LOS ANGELES, CA, U.S.A. – UBM Canon's Medical Design Excellence Awards (MDEA), the medtech industry's premier awards program, has announced Dr. Robert Langer as the recipient of the 2013 MDEA Lifetime Achievement Award. This award goes to an individual whose contributions over a long career in the medtech industry have had a significant and demonstrable impact on technological, business, and cultural advancements in the world. Each year, the UBM Canon medical content team and the MD+DI editorial advisory board select an industry pioneer to receive the MDEA Lifetime Achievement Award in recognition of the crucial role they have played in medical device innovation. Previous recipients include Dr. Thomas Fogarty and Alfred E. Mann.

"I'm tremendously honored to receive this award—all the more so because of the previous recipients," said Langer, the David H. Koch Institute Professor at the Massachusetts Institute of Technology (MIT).

Langer has lectured at MIT since 1977 and also leads the institute's Langer Lab, one of the largest biomedical engineering laboratories in the world. His vast accomplishments include groundbreaking discoveries and advancements in the fields of drug delivery, tissue engineering, nanotechnology, and personalized medicine.

"Dr. Langer has achieved more than just ground-breaking discoveries. His efforts to share his gifts through education and publishing have transformed an entire generation of work," said Pamela Moore, senior vice president, content & strategy, UBM Canon. "That's a deep achievement, and we're so lucky to be able to recognize him."

Langer sat on FDA's SCIENCE board, the agency's highest advisory board, from 1995 to 2002, serving as its chairman the last four of those years. He was the youngest person ever elected to all three U.S. National Academies and has received 20 honorary degrees from institutions of higher learning around the world. The most cited engineer ever, Langer has written more than 1,200 articles and has more than 800 pending and issued patents. He has also helped launch at least 27 companies based on his discoveries and inventions.

Read more about Langer's thoughts on the issues affecting the medtech industry and his formula for successful start-ups on MD+DI's website. For more information about the Medical Design Excellence Awards or the Lifetime Achievement Award, visit www.MDEAwards.com or e-mail mdea@ubm.com.

Zosano Pharma, Inc., Appoints Nandan Oza as Chief Operations Officer

PRNewswire: May 14, 2013 – FREMONT, CA, U.S.A. – Zosano Pharma, Inc., a privately held pharmaceutical company developing products based on its novel transdermal delivery technology, announced today a key addition to its executive team with the appointment of Nandan Oza as the company's chief operations officer. In this position, Mr. Oza will guide the company's efforts in manufacturing, quality, and engineering—vital activities to enable the company to accelerate the development of its innovative multiproduct portfolio.

"I am pleased to welcome Nandan as our COO," said Vikram Lamba, chief executive officer, Zosano Pharma. "His operational and manufacturing experience and expertise—as well as his leadership experience—will be critical in preparing Zosano for our next stage of commercial-scale manufacturing as we drive our clinical programs towards the marketplace."

Prior to joining Zosano Pharma, Mr. Oza served as vice president, chemistry, manufacturing, and controls at Talon Therapeutics. He previously held the position of vice president, manufacturing and supply chain operations at Jazz Pharmaceuticals and at Connetics Corporation (now a part of GSK). Mr. Oza also held positions of increasing responsibility at ALZA Pharmaceuticals (now part of Johnson & Johnson) in product development, quality, and technical and manufacturing operations, progressing to his role as executive director, Bay Area operations. Mr. Oza earned a bachelor's degree (with honors) in mechanical engineering from the University of Houston, pursued graduate studies in engineering from the University of California, Davis, and earned an MBA from National University, San Diego, CA.

"This is an exciting time to join the Zosano Pharma team," said Mr. Oza. "The company is well positioned to move forward in commercial scale manufacturing with its ZP Patch technology and advancing development-stage product pipeline."

Egalet Appoints Stan Musial as CFO

PRNewswire: May 8, 2013 – MALVERN, PA, U.S.A. – Egalet Ltd., a privately held specialty pharmaceutical company focused on developing safe, effective, and abuse-deterrent medications, announced today the appointment of Stan Musial as chief financial officer (CFO).

"The addition of Stan to the management team comes at a critical time as the most advanced products in Egalet's pipeline of abuse-deterrent opioids are nearing phase 3," said Bob Radie, president and CEO. "Stan's finance experience will be invaluable as we move our pipeline through development and ultimately to the commercial market."

Stan has held senior financial management positions for both publicly held and privately held companies, becoming experienced in executing growth strategies, raising capital, and mergers and acquisitions. Stan most recently spent six years as vice president of finance and administration, chief financial officer, treasurer and secretary of Prism Pharmaceuticals, a specialty pharmaceutical company, which was successfully sold to Baxter Healthcare in 2011. Prior to joining Prism he held the position of vice president, finance, and CFO for Strategic Diagnostics, Inc. (SDIX), a publicly held biotechnology company. He began his career with KPMG LLP. Stan holds an MBA in finance from Temple University and a B.S. degree in accounting from Pennsylvania State University and is a certified public accountant.

"I am excited to join Egalet—a company seeking to advance its pipeline of abuse deterrent opioids by taking advantage of the expedited 505(b)(2) regulatory pathway to address the growing need for safe pain medicines," said Stan Musial. ■

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In the News

Compiled by Steven Giannos, Independent Consultant

July

U.S. FDA Approves Zubsolv® for the Maintenance Treatment of Opioid Dependence

PRNewswire: July 5, 2013 – New York, NY, U.S.A. – Orexo U.S., Inc., announced that it has received approval from the U.S. Food and Drug Administration (FDA) for Zubsolv (buprenorphine and naloxone) sublingual tablets (CIII). Zubsolv is indicated for the maintenance treatment of opioid dependence and should be used as part of a complete treatment plan to include counseling and psychosocial support. Zubsolv is a once-daily, sublingual tablet with higher bioavailability, a fast dissolve time, smaller tablet size, and a new menthol flavor.

Opioid dependence is a disease, like hypertension, schizophrenia, or diabetes, and affects nearly 5 million people across the United States. Although it is a treatable condition, about 60 percent of opioid-dependent patients in the United States do not receive treatment. Every year thousands of patients continue to misuse opioids rather than risk public exposure by receiving treatment.

"Orexo is committed to helping patients suffering from opioid dependence effectively manage their condition," said Robert DeLuca, R.Ph., President, Orexo U.S., Inc. "The advanced formulation of Zubsolv was developed using our proprietary technology to meet the needs of patients not satisfied with previously approved buprenorphine/naloxone formulations."

Zubsolv sublingual tablets deliver more active ingredient to the bloodstream, allowing patients to use a lower strength, thereby reducing the amount of available drug for potential misuse and diversion. In addition, Zubsolv is the only opioid dependence treatment option that is available in the highest level of child-resistant unit dose F1 packaging, thereby reducing the chance of unintended pediatric exposure. Furthermore, the naloxone component of Zubsolv reduces the potential for IV misuse and diversion.

The most effective treatment for opioid dependence is the combination of pharmacological therapy and psychological counseling, which is critical in helping to prevent relapse. Relapse rates for opioid-dependent patients approach 90 percent at six months after detoxification without the use of medication-assisted treatment.

"In addiction medicine, the recovery process can be challenging. Products designed to meet patient preferences have the potential to more successfully support their recovery," said Louis E. Baxter, Sr., M.D., FASAM, past president of the American Society of Addiction Medicine. "The approval of Zubsolv provides a new treatment option that offers unique advantages specifically designed to meet the unmet needs expressed by patients. This may have the potential to improve patient adherence, thereby reducing relapse rates and improving successful patient outcomes."

Opioid dependence greatly impacts the U.S. economy, with about $56 billion spent on the disease per year. In addition, the average healthcare cost per patient with opioid dependence is eight times higher compared to nondependent patients. There is also a great impact on human life, with almost 17,000 deaths from opioid pain relievers in the U.S. every year.

Avanir Pharmaceuticals and OptiNose Announce Development and Commercialization Agreement for a New Fast-Acting Investigational Product for the Treatment of Acute Migraine

PRNewswire: July 2, 2013 – ALISO VIEJO, CA, and YARDLEY, PA, U.S.A. – Avanir Pharmaceuticals, Inc. (NASDAQ: AVNR) and OptiNose AS today announced that the companies have entered into an exclusive North American license agreement for the development and commercialization of OptiNose's novel Breath Powered™ intranasal delivery system containing low-dose sumatriptan powder to treat acute migraine. If approved, this product would be the first and only fast-acting, dry-powder nasal delivery form of sumatriptan.

Under the terms of the agreement, OptiNose received an upfront cash payment of $20 million and is eligible to receive certain shared development costs and up to an additional $90 million in total linked to the achievement of future clinical, regulatory, and commercial milestones. In addition, if approved, Avanir will make tiered royalty payments based on net sales in North America.

"The large migraine market is characterized by a high level of dissatisfaction. OptiNose has developed a unique device that has the potential to transform the clinical profile of the leading migraine drug, resulting in a new product candidate that we believe can significantly improve upon the current treatment options," said Greg Flesher, senior vice president of corporate development and chief business officer of Avanir Pharmaceuticals. "In clinical trials, this innovative and easy-to-use device has demonstrated rapid absorption and migraine relief using approximately 80% less drug than the most commonly prescribed oral sumatriptan. This NDA-ready asset fits well with our current commercial infrastructure and is strategically aligned with strengthening our position as a leading CNS specialty company."

Under the terms of the agreement, Avanir will assume responsibility for regulatory, manufacturing, supply-chain, and commercialization activities for the investigational product, now named AVP-825. Both parties will work together on the

remaining activities in support of the NDA submission. Avanir will begin preparing the NDA immediately and expects to file the application with the U.S. Food and Drug Administration by early calendar 2014.

"Avanir is an ideal partner given its proven track record of successfully developing and commercializing neuroscience products," said Peter Miller, chief executive officer of OptiNose. "The results from our phase III clinical study were extremely encouraging, and we believe we have a potential treatment that provides pain relief quickly and with few adverse events. This new delivery method offers significant benefits, and we look forward to working with the Avanir team to bring an important new treatment option to people who continue to suffer from migraines."

In November 2012, OptiNose reported results from its pivotal phase III study in 212 subjects. The TARGET study tested delivery of 16 mg of sumatriptan using OptiNose's Breath Powered delivery technology. The study found that the product provided headache relief for 68% of subjects with moderate to severe migraines after two hours ($p < 0.01$ compared to placebo). The trial found subjects began to experience headache relief as quickly as 15 minutes after administration, with nearly 42% reporting pain relief at 30 minutes posttreatment ($p < 0.05$ vs. placebo at 30 minutes).

In this multicenter, double-blind, placebo-controlled study, migraine sufferers were randomized to self- administer either OptiNose sumatriptan (AVP-825) or placebo using the Breath Powered device when they had moderate to severe migraine pain. Pain scores were then assessed at various time points after administration. Pain was evaluated using a four-point scale, with headache relief defined as a reduction from moderate (grade 2) or severe (grade 3) pain to mild (grade 1) or complete relief (grade 0). The data show pain relief for some subjects began as early as 15 minutes after treatment, and a statistically significant greater number of subjects receiving OptiNose sumatriptan (AVP-825) experienced headache relief compared to placebo at all times from 30 minutes through two hours. At two hours after taking the medication, 70% of subjects taking OptiNose sumatriptan (AVP-825) reported that they were experiencing meaningful relief from their headache pain.

There were no serious adverse events associated with OptiNose sumatriptan (AVP-825) in the study. There were also no systemic adverse events reported in more than a single subject, and local adverse events reported in the nose were generally mild and transient.

OptiNose's Breath Powered delivery technology is unique in that it uses the natural function of a user's breath to propel medications beyond the nasal valve into the deep, targeted areas of the nasal cavity more effectively, efficiently, and consistently than current treatments. A user exhales into the device, automatically closing the soft palate and sealing off the nasal cavity completely. The exhaled breath carries medication from the device into one side of the nose through a sealing nosepiece. Narrow nasal passages are gently expanded, and medication is transported well beyond the nasal valve to targeted sites. After delivering medication to the targeted sites, air painlessly flows around to the opposite side of the nasal cavity and exits through the other side of the nose rather than into the throat or lungs.

InSite Vision Receives Notice of Allowance from USPTO for Patent on DuraSite® 2 Ophthalmic Drug Delivery System

Business Wire: July 2, 2013 – ALAMEDA, CA, U.S.A. – InSite Vision Incorporated (OTCBB: INSV) today announced that it has received a Notice of Allowance from the U.S. Patent and Trademark Office (USPTO) on its DuraSite® 2 next-generation enhanced drug delivery system. DuraSite 2 provides a broad platform for developing topically delivered ocular drugs with enhanced tissue penetration in order to improve efficacy and dosing convenience. The patent is expected to provide protection to 2029 for both the delivery system and the drugs that are formulated with DuraSite 2.

"DuraSite 2 has demonstrated increased drug retention and tissue penetration up to four-fold greater than a commercial ophthalmic pain reliever in preclinical studies. Based on its potential to significantly increase efficacy and reduce dosing requirements, we believe DuraSite 2 could serve as a standard drug delivery technology across ophthalmic therapeutics," said Timothy Ruane, chief executive officer of InSite Vision. "We plan to utilize the DuraSite 2 platform in the development of all future pipeline products. Additionally, once the patent issues, InSite plans to initiate a broad licensing program that provides access to industry partners through both exclusive and nonexclusive licensing and/or commercialization agreements."

In a large-scale comparative study, a drug formulated with DuraSite 2 demonstrated significantly enhanced retention on the eye and tissue penetration as compared to the same product alone or formulated with InSite's DuraSite® technology. Results of that study showed that the DuraSite 2 formulation achieved more than 2× and 4× concentrations in the aqueous humor of the eye compared to the DuraSite formulation or marketed drug, respectively. The robust results of this study suggest that DuraSite 2's increased tissue penetration may enable it to be used in the treatment of back-of-the-eye diseases with a topical eye drop when formulated with drugs that must currently be administered by injection. InSite presented detailed data from this study at the Association for Research in Vision and Ophthalmology (ARVO) 2013 Annual Meeting. The ARVO poster presentation is available in the publications section of InSite Vision's website at www.insitevision.com/publications.

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Novati Technologies Launches Nanofabrication Center with World's Largest Portfolio of Product Development Materials

Business Wire: July 1, 2013 – AUSTIN, TX, U.S.A. – Novati Technologies announced today the launch of its nanofabrication services and manufacturing site, featuring the world's broadest portfolio of product-development capabilities and materials. The newly named company builds on 25 years of technology leadership cultivated from its roots at SEMATECH and, most recently, the SVTC fabrication foundry.

Citing an acute need for leadership in the rapid evolution of technologies away from the historic guidance of Moore's Law and toward a larger set of emerging opportunities, Novati's team of expertise and assets has been assembled to provide the leading edge for an effort aimed at creation of new markets that don't depend on the smallest feature sizes but rather on driving new combinations of materials for products. This drive to incorporate new functionalities for devices that don't necessarily need to scale is regarded as "More-than-Moore."

Offering a significant advantage over traditional foundries that typically limit customers to working with no more than 25 elements from the periodic table, Novati's unique position engages a world-leading 60 elements in order to move exotic ideas and breakthrough designs into development and production. Large corporations, small startup ventures, and university spin-offs alike report they will use Novati because other venues are simply not able to meet the needs of the most rapid product development criteria.

"We rely on the portfolio of development materials that Novati offers and their comprehensive suite of advanced tools as a critical piece of our equation for going to market," said Randy Goodall, CEO of NanoMedical Systems. "Novati turns our great ideas into reliable, manufacturable technologies that give the world the next game-changing medical products. The nanofluidic chips that Novati fabricates for our drug delivery implants are the first and only ones ever made with long-term Angstrom-level structural stability while inside the body."

Examples of other global advancements created with Novati's novel portfolio and development process are found in the life sciences sector, where Novati built a DNA sequencing device that enabled end customers to resolve a mysterious and deadly *E. coli* outbreak. In a consumer telecom application, Novati has developed new micro electro mechanical systems (MEMS) technology for an elastic autofocus/autozoom lens for cell phone cameras. In security, Novati has quadrupled the technology roadmap for complex night vision sensors.

"No longer dependent on shrinkage of features, today's rapidly emerging nano-electronic products are driven by heterogeneous integration of multiple technologies and novel materials. That's where Novati excels," said Dave Anderson, president of the newly formed Novati Technologies. "Offering unrivaled speed, we're spearheading the implementation of never-before-used materials and new processing methods that lead to breakthroughs in device design and drive the revolution for today's 'More-than-Moore' markets."

Formed following an unexpected closure of SVTC's foundry centers in 2012, Novati teams with its customers to leap beyond previous constraints in the services offered by its former SVTC owner. Novati is an early adopter of carbon nanotubes (CNTs) and has demonstrated integration of magnetic, phase-change materials and is a pioneer in the integration of superconducting materials and heterogeneous integration of III-V materials on silicon.

Novati Technologies is the premier innovation partner for accelerating nanotechnology development and commercialization. Novati's proven advanced technology and secure IP infrastructure combined with its technology development process supports companies developing MEMS, microfluidics, novel transistors, photovoltaics, and other nanotechnologies for the semiconductor, life sciences, and aerospace and defense markets. Novati's advanced technology center in Austin, Texas, provides customers with technology building blocks, engineering expertise, professional program management and a broad complement of flexible processing equipment that enables the accelerated development of silicon-based solutions. For more information, visit www.Novati-Tech.com.

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Eighth Patient Treated with Sealantis Novel Alga-Mimetic Sealant

PRNewswire: June 27, 2013 – HAIFA, Israel – Sealantis Ltd., a private start-up from the Technion-Israel Institute of Technology, reports that an eighth patient was treated with Seal-V, its alga-mimetic vascular sealant, as part of the company's first clinical study. Seal-V is a protein-free sealant, designed to resolve current limitations and challenges in control of surgical bleeding. It is expected to receive CE Mark within the year.

The clinical trial, taking place in Israel, is evaluating the safety and efficacy of achieving hemostasis in large peripheral blood vessels using the Seal-V protein-free sealant.

Sealantis is a 6-year-old startup, located on the campus of one of Israel's leading academic centers—the Technion. It was founded by Prof. Havazelet Bianco-Peled, a world-renowned expert in biomedical polymers.

Since the early 2000s, Prof. Bianco-Peled had been researching the adhesion mechanism of algae to rocks underwater. The research unveiled the chemical composition of the algae adhesive, but it was the professor's invention of a synthetic, alga-mimetic adhesive that enabled harnessing nature's power for practical and commercial uses.

In 2007, the invention was embraced by the Alfred Mann Institute at the Technion, which is funding the company. While having potential uses in a variety of industrial applications, Sealantis chose to focus on urgent medical needs—controlling leakage of body fluids through surgical or traumatic wounds. Such leaks can be fatal, since sutures or staples are not fully leak-proof. "Sealing surgical incisions requires sticking to wet or moist surfaces, which is a challenge that most known adhesives can't usually meet," explains Prof. Bianco-Peled.

Surgical sealants represent a market of over $1.0 billion, which grows 14% annually. "When I look at the market, it's clear to me that there is no single winning solution," says Dr. Zeev Gilkis, AMIT CEO and Sealantis Ltd. chairman, "There are some good products, but each one has drawbacks or is limited to a specific application. Sealantis brings a versatile yet simple technology, addressing unmet clinical needs."

"Seal-V is overcoming a clinical need with its unique features, which offer simultaneous sealing and hemostasis for native and synthetic vascular fields," explains Prof. Vincent Riambau, chief of the Vascular Surgery Division, Hospital Clínic, University of Barcelona, and past president of the European Society of Vascular Surgery (ESVS), who serves on the clinical advisory board of Sealantis. "It is accomplishing valuable qualities for vascular surgery, being quick, easy to use, effective, and safe. It will surely be most welcome to the vascular community."

Sealantis Ltd. is currently planning its next regulatory steps toward a PMA study and FDA approval of Seal-V and is working on strategic partnerships towards the coming market launch.

Highland Therapeutics Announces Positive Clinical Results for HLD-200—A Novel ADHD Therapeutic

PRNewswire: June 25, 2013 – TORONTO, Canada – Highland Therapeutics, Inc. ("Highland"), a specialty pharmaceutical company based in the MaRS Discovery District in Toronto, today announced that its wholly owned subsidiary has generated positive phase 1 results for HLD-200—a novel formulation of methylphenidate being developed to treat the symptoms associated with attention-deficit/hyperactivity disorder (ADHD). The study was conducted in collaboration with the Harvard Clinical Research Institute (HCRI) and Massachusetts General Hospital (MGH), and with Dr. Joseph Biederman as senior study adviser and medical monitor. Dr. Biederman is chief of the clinical and research programs in pediatric psychopharmacology and adult ADHD at MGH and professor of psychiatry at the Harvard Medical School.

Consistent with the observations from the HLD-100 (amphetamine) phase 1 trial, Highland's proprietary drug-delivery technology performed exceptionally well in delivering the active pharmaceutical ingredient consistently across the entire group of healthy adult volunteers. In addition, the study data revealed an absorption window for HLD-200 that is longer than that of the leading methylphenidate product on the market today.

The study, "A Phase 1, Single-Center, Single-Dose, Open-Label, Randomized, Crossover, Comparative Bioavailability Study to Compare Two Methylphenidate HCl Modified Release and an Immediate Release Methylphenidate HCl Marketed Formulation in Healthy Adult Volunteers," examined the pharmacokinetics of HLD-200 and represented the first study in humans for HLD-200. A total of 12 patients were enrolled in the study—six men and six women—each of whom received the three different methylphenidate formulations after a washout period between treatments.

While the data are strong overall, Highland is particularly pleased by the class-leading low level of variability seen with respect to the time to maximum concentration, or Tmax. This parameter is critical given Highland's unique approach to dosing its drugs. The low coefficient of variation (CV%) seen in the HLD-200 study is similar to that seen in the HLD-100 phase 1 study, demonstrating the robustness of Highland's drug-delivery platform. According to the article "Pharmacokinetic Variability of Long-Acting Stimulants in the Treatment of Children and Adults with Attention-Deficit Hyperactivity Disorder" by James C. Ermer et al, published in *CNS Drugs*, HLD-200's level of variability is significantly lower than that of the leading stimulants, including Vyvanse (marketed by Shire US Inc.), Concerta (Janssen Pharmaceuticals, Inc.—a Johnson & Johnson company), and Focalin XR (Novartis Pharmaceuticals Corporation).

Commenting on the study, Dr. Biederman said, "The data suggest that Highland has developed a potential new treatment option for ADHD that could consistently deliver the medication so that the symptoms of ADHD can be controlled immediately upon wakening while also providing once-daily coverage."

Dr. Bev Incledon, Highland's senior vice president, research and development, added, "We are pleased to once again see such low levels of variability with our technology. The consistent delivery of their medication is a great benefit for patients, as it enhances the predictability of their response, which is clinically desirable."

"The data we have generated for both our amphetamine and methylphenidate programs suggest our drug-delivery technology is a platform technology, applicable to other active ingredients in a wide range of therapeutic categories," said David Lickrish, chief executive officer of Highland Therapeutics, Inc. "In ADHD, our products are designed to address a significant unmet medical need in the treatment of the disease. The third-party market research we have conducted indicates substantial pent-up demand for Highland's products, which could become first-line therapy in both the adult and pediatric/adolescent patient populations."

"We are grateful for the support of MaRS, which provides an ideal environment for innovative life sciences companies to thrive. MaRS has been instrumental in Highland's success to date," added Mr. Lickrish.

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Based on the strength of the phase 1 data, Highland anticipates initiating phase 2 studies with both HLD-100 and HLD-200 in the third quarter of 2013. The phase 2 trials will be conducted in two stages—one in adolescent patients (ages 12–17), the other in pediatric patients (ages 6–11) with ADHD. Data from these studies are expected in the fourth quarter of 2013 and will be critical in guiding the design of the phase 3 clinical trial programs, anticipated to begin in the first quarter of 2014.

mPhase Will Include Research and Development of Drug Delivery Systems to Its Path-Breaking Smart NanoBattery Technology

PRNewswire: June 24, 2013 – LITTLE FALLS, NJ, U.S.A. – mPhase Technologies, Inc. (OTCQB: XDSL) said today that is broadening its focus on its path-breaking battery technology to include research and development of drug delivery systems. In February of 2013 mPhase filed a U.S. Letter Patent Application for a novel drug delivery system based on its smart surface technology.

The drug delivery patent is based on mPhase's smart surface technology enabling the automatic dispensing of a preset dosage of a drug agent or medication. mPhase believes the research could lead to a novel drug delivery system, possibly creating greater shareholder value.

Last week mPhase received the 2013 North America Frost & Sullivan Technology Innovation Award for its pioneering nanobattery technology.

mPhase Technologies is a leading nanotechnology innovator in smart surfaces. Potential applications include energy storage systems, drug delivery systems, self-cleaning systems, liquid and chemical sensor systems, and filtration systems. mPhase has pioneered its first smart surface enabled product, the mPhase Smart NanoBattery.

In addition to the smart surface technology, mPhase, in collaboration with Porsche Design Studio, has developed a world class automotive jump starter. See www.mpowertech.com. More information about the company can be found at www.mphasetech.com.

JDRF Extends Collaboration with BD to Develop Combined Infusion and Monitoring Products for People with Type 1 Diabetes

PRNewswire: June 18, 2013 – FRANKLIN LAKES, NJ, and NEW YORK, NY, U.S.A. – JDRF and BD (Becton, Dickinson and Company) (NYSE: BDX) are accelerating the development of new products that combine BD's proprietary insulin infusion and glucose sensing technologies through a new collaboration announced today. This new, three-year commitment is an extension of existing JDRF-BD collaborations focused on type 1 diabetes (T1D).

Many patients with T1D not only take daily insulin via an insulin pump—requiring a catheter to be placed in the body for a number of days—but are also checking their glucose levels via a continuous glucose monitor (CGM), which also requires a catheter-like sensor to be placed in the body for a number of days.

While BD has been working to improve the products used for insulin infusion and CGM, the new collaboration with JDRF will enable additional research to develop a single optimized device that will perform both functions and eliminate the need and complexities of multiple in-dwelling catheters. The ability to perform these discrete metabolic actions automatically and accurately, with little patient intervention, defines the artificial pancreas concept.

"Providing the best tools that not only improve patient care but ease the daily burden of managing diabetes are important goals for BD and JDRF," said Linda Tharby, President, BD Medical–Diabetes Care. "This latest collaboration with JDRF demonstrates both parties' commitment to improve patients' experiences and outcomes. Combining these novel technologies will address two key components of an advanced artificial pancreas system."

"As the world's largest charitable funder of type 1 diabetes research, JDRF is committed to advancing therapies that improve the lives of people living with this disease," said Jeffrey Brewer, president and chief executive officer of JDRF. "We are excited to continue our collaboration with BD and support efforts to develop novel technologies enabling advanced artificial pancreas systems that will both measure glucose and administer insulin. Joining these capabilities into a single solution will address significant patient needs and help reduce the daily burden of managing type 1 diabetes."

T1D is an autoimmune disease in which the body's pancreas stops producing insulin, a hormone needed to turn food into energy. BD's culture of innovation and continuous improvement has enhanced the patient experience to help improve therapy and outcomes for people with diabetes worldwide. BD devices support earlier initiation and better adherence to prescribed therapies to help all diabetes patients live healthier lives.

Mapi Pharma Granted United States Patent for Pain Relief Medication Tapentadol

PRNewswire: June 18, 2013 – NESS ZIONA, Israel – Mapi Pharma Ltd. (Mapi), developer of complex bulk active pharmaceutical ingredients (APIs), generic and innovative intermediates, and finished dosage forms based on selected drug delivery systems, announced today that the company has been granted a U.S. patent for tapentadol. Tapentadol is indicated in the United States and Europe for the oral treatment of moderate-to-severe acute pain.

U.S. patent number 8,410,176 B2 is titled Intermediate Compounds and Processes for the Preparation of Tapentadol and Related Compounds. Mapi's innovative process enables the company to obtain tapentadol in an optically active pure form.

The process is cost effective, uses easily available reagents, and fits scalable industrial processes.

Tapentadol is indicated for the relief of moderate-to-severe acute pain. This segment of pain relievers has continuously grown during the last decade as a result of improved delivery technologies, increased physician recognition of the need for effective pain treatment, and the rising requirement for pain medication by the growing ageing population.

"The patent acceptance announced today is Mapi's second in just one month. The first was for a long-acting depot formulation of glatiramer acetate for the treatment of MS. Both patents strengthen Mapi's patent position, support the business plan, and advance the company one step closer to bringing patients improved medications at affordable prices," said Mapi Pharma president and CEO Mr. Ehud Marom. "The pain relief market requires a specific expertise in dealing with potent pharmaceuticals. Mapi is uniquely positioned to answer the growing needs of this market."

The moderate-to-severe acute pain relief market is a growing therapeutic area. It is currently estimated at about US$10 billion and is expected to continue expanding for the foreseeable future.

Imprimis Pharmaceuticals, Inc., Acquires Intellectual Property Assets from Buderer Drug Company

PRNewswire: June 17, 2013 – SAN DIEGO, CA, U.S.A. – Imprimis Pharmaceuticals, Inc. (NASDAQ: IMMY) today announced it has completed the acquisition of intellectual property (IP) rights related to certain proprietary innovations from the compounding pharmacy operations of Ohio-based Buderer Drug Company. The acquisition allows Imprimis to pursue the commercial development of these proprietary innovations and also provides Imprimis with a right of first refusal on additional Buderer Drug Company intellectual property and drug development opportunities.

Buderer Drug Company, which has served the needs of patients and physicians in Ohio since 1878, is a compounding pharmacy member of PCCA. This IP acquisition is the first to emerge from the Imprimis-PCCA relationship.

"Buderer Drug Company is a leading compounding pharmacy organization in the United States, and we are extremely pleased to announce this asset purchase," said Mark L. Baum, Imprimis CEO. "This new relationship, which could lead to up to three new development programs, is a good example of our plan to begin to leverage our agreement with PCCA into proprietary IP that may ultimately lead to the FDA approval of new medicines to address unmet patient needs. We are in the process of preparing filings with the USPTO related to the acquired assets and intend to communicate with the marketplace with more specificity in the near-term. Ultimately, we intend to develop and commercialize any drug development assets we decide to pursue by utilizing the U.S. Food and Drug Administration (FDA) 505(b)(2) regulatory pathway. The 505(b)(2) pathway has the ability to significantly reduce both cost and duration of the FDA approval process, bringing quality medications more quickly to patients who need them."

"We are excited at the potential development and commercialization prospects of our ideas. We believe that Imprimis understands and appreciates the important role of the compounding pharmacist in the healthcare system. Further, Imprimis understands that the ideas we generate come from a 'boots on the ground' approach—dealing directly with doctors and their patients to address specific and often unmet patient needs. We also appreciate that some drugs are demonstrably difficult for compounders to make and that oftentimes additional research and development is required before a drug can be used in humans, including more formal preclinical and clinical research. We are looking forward to strengthening the bond between our companies and working toward bringing these medicines through the FDA approval process, and then to the marketplace, where they can help people with a myriad of different medical conditions," said Matt Buderer, R.Ph., vice president and chief compounding pharmacist with Buderer Drug Company.

Compounding pharmacies work with physicians to develop medications for individual patients. Examples are alternative dosage strengths, or unique dosage forms, such as topical creams or gels, suspensions, or solutions with more tolerable drug delivery vehicles.

Access to these formulations may be limited if patients don't live near a compounding pharmacy or cannot cover the out-of-pocket costs or if their physician is simply unaware of compounding options available to them. Baum said, "Commercialization of formulations developed by Buderer Drug Company by taking them through a regulated FDA process would in the long run allow more patients to benefit from these medications. At the same time, Imprimis respects the rights of pharmacists and physicians to continue to serve their patients' needs. Imprimis believes having an FDA-approved derivative of compounding's innovations will enhance the overall acceptance of compounding and develop new opportunities for compounders to serve patients."

Gus Bassani, Pharm.D., vice president of consulting, R&D, and formulations with PCCA, and also an Imprimis board member, said, "Buderer Drug Company and its novel drug technologies are just one example of the depth of creativity and innovation possessed by PCCA's members. We've desired to create a pathway for our members' innovations that have commercial potential to get FDA approval. Imprimis has developed this pathway for PCCA pharmacy members, and we hope to see more in the future."

Baum added, "We will continue to be open to the ideas, innovation, and unique 'proximity to the patient' of the more

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than 4,000 compounding pharmacy members that are a part of the proprietary PCCA network worldwide."

Teva Strengthens Respiratory Franchise with Acquisition of MicroDose Therapeutx

Business Wire: June 17, 2013 – JERUSALEM, Israel – Teva Pharmaceutical Industries Ltd. (NYSE: TEVA) today announced that it has entered into a definitive agreement to acquire MicroDose Therapeutx, a privately held pharmaceutical and drug delivery company focused on inhalation technologies and products for lung diseases and infections with the potential to dramatically improve efficacy and patient compliance.

With the addition of MicroDose's technologies and products, Teva is taking a significant step toward expanding its respiratory pipeline. Teva will now have access to MicroDose's proprietary technology including its multi-dose dry powder nebulizer device, which requires no preparation and can be administered in under 30 seconds. MicroDose's current pipeline is anchored by MDT-637 for respiratory syncytial virus (RSV)—an inhaled, low dose, small molecule, fusion inhibitor, which prevents viral replication, delivered via MicroDose's technology.

"I am thrilled that Teva can now count the exciting MicroDose products and technologies amongst our growing respiratory portfolio. The MicroDose platform is both simple and attractive, and their addition will help us to address the unmet needs of the youngest and oldest patients, who have a requirement for a better way of taking the medicines they rely upon," stated Michael Hayden, president, Teva Global R&D, and chief scientific officer.

Under the terms of the deal, Teva will acquire all of MicroDose's outstanding shares for a payment at closing of $40 million, additional payments of up to $125 million upon achievement of regulatory and development milestones, plus sales-based milestones and tiered royalty payments upon commercialization of MDT-637 and an earlier stage asthma/COPD medicine.

Anand V. Gumaste, president, CEO, and chairman of MicroDose, stated, "We believe this agreement provides a unique opportunity to advance MicroDose's platform technology and development programs for the greatest benefit of patients. Teva has a strong and growing franchise in respiratory diseases, with extensive experience in both delivery mechanisms and novel therapeutic modalities. Teva also has a worldwide market presence and leading global supply chain."

Micell Technologies Receives CE Mark Approval for MiStent SES

PRNewswire: June 12, 2013 – DURHAM, NC, U.S.A. – Micell Technologies, Inc. received CE (Conformite Europeenne) Mark approval for its MiStent® sirolimus eluting absorbable polymer coronary stent system (MiStent SES®) introducing a thin-strut stent that features elimination of the coating from the stent in 45–60 days and the complete absorption of the polymer coating within 90 days. The MiStent SES is unique in providing local drug delivery both during and after the period of polymer absorption, thereby eliminating long-term polymer exposure, a potential cause of delayed healing and late adverse events.

Micell's chief executive officer, Arthur J. Benvenuto, commented, "The MiStent SES brings a new paradigm of safety without compromise to efficacy or deliverability. With polymer absorption faster than any other DES currently available, we believe the MiStent SES provides a long-term safety profile of a highly deliverable bare metal stent."

The MiStent SES approval is supported by in-depth clinical analysis from the DESSOLVE I and DESSOLVE II clinical trials. The DESSOLVE II trial met its primary end point: superiority of MiStent SES in minimizing in-stent late lumen loss (LLL) at nine months as compared to Medtronic's Endeavor® Sprint DES ($p < 0.001$). The trial was a randomized, multicenter study of 184 patients with documented stable or unstable angina pectoris. At nine months' follow-up, in-stent LLL was 0.27 mm with a target lesion revascularization rate of 0.9%. The major adverse cardiac events (MACE) rates were 4.3% for MiStent SES and 6.7% for Endeavor. In a subgroup of patients, optical coherence tomography (OCT) and endothelial function testing confirmed good vessel healing with excellent strut coverage and normal endothelial function.

The DESSOLVE I first-in-human study provides additional evidence for the potential clinical advantages of MiStent SES's unique features, with serial angiographic, intravascular ultrasound (IVUS), and OCT assessment of patients at early (6/8 month) and late (18 month) time points. Data analysis of the groups using matched pairs shows no progression of LLL (0.10 / 0.09 mm and 0.09 mm, respectively).

Patrick W. Serruys, M.D., Ph.D., professor of interventional cardiology at the Erasmus University, Rotterdam, The Netherlands, said, "MiStent SES uniquely offers physicians an effective DES that converts to a bare metal stent (BMS) in 45–60 days while still providing drug for suppression of neointimal hyperplasia up to 9 months. The MiStent SES brings us a step closer to the ideal DES, which may provide long-term efficacy while still allowing normal vessel healing."

The company is preparing for a postmarketing clinical program of 2,000 patients comparing the MiStent SES to the Xience® everolimus eluting coronary stent system in a randomized design to show noninferiority of target lesion failure at 12 months and superior performance by the MiStent SES at 24 months with significantly less progression of LLL.

With this CE Mark approval, Micell is preparing to make the MiStent SES commercially available in Europe and other markets where CE Mark approval can expedite the registration process. The MiStent sirolimus eluting absorbable polymer coronary stent system is not currently available for sale in any market.

Catalent Pharma Solutions Breaks Ground on a Major Expansion of Its Winchester, Kentucky, Controlled Release Manufacturing Facility

PRNewswire: June 12, 2013 – SOMERSET, NJ, U.S.A. – Catalent Pharma Solutions, a leading global drug delivery technology and advanced supply solutions company, has announced a major expansion of its controlled release drug manufacturing facility in Winchester, Kentucky. The company is to invest nearly $35 million to expand the 100,000 square-foot facility by almost 80,000 square feet of modern manufacturing space and will add as many as 90 new employees at the expanded site. Construction will commence on June 12, 2013, with a ceremony led by Kentucky governor Steve Beshear and Catalent president and CEO John Chiminski. Catalent expects to complete the expansion by October 2014 and will welcome customers to tour the facility at that time.

The Governor of the Commonwealth of Kentucky, Steve Beshear, made the following statement, "Catalent is making tremendous strides forward in Winchester, and we're excited to see such success for a global company in the Commonwealth. The numbers speak for themselves, with 90 new jobs and $35 million in investment, but this also shows the level of confidence that Catalent has in Kentucky's high quality workforce."

Opened in 1992, Catalent's Winchester facility has evolved into one of the industry's premier sites for advanced oral controlled-release drug formulation and manufacturing, launching over 100 products for Catalent's pharmaceutical and consumer health customers. As industry demand for innovative dose forms continues to increase, Catalent is responding through expansion of its manufacturing premises and continuous improvement of equipment and workflows.

"Catalent is a fully integrated formulation, regulatory, and manufacturing solutions partner, helping pharmaceutical and consumer healthcare companies differentiate their products and reach markets faster," commented Steve Havel, general manager of Catalent's Winchester facility. "The expanded Winchester facility will provide our customers with enhanced access to custom equipment capabilities and our market-leading controlled release solutions and technologies."

The Winchester expansion comes on the heels of several significant investments Catalent has made in advanced delivery technologies globally. "Catalent has continued to build on its global leadership in advanced drug development solutions and advanced delivery technologies with major recent investments in controlled release forms, including fluid bed capacity, OptiMelt hot melt extrusion, and OSDRC OptiDose advanced tableting technologies," noted Mr. Chiminski. "As with Winchester, Catalent continues to invest to meet the most critical needs of the industry, including recently announced inhalation facility expansion in North Carolina, our recently completed biologics expansion in Wisconsin, and our two new ventures in China, which will focus on softgel technologies and clinical trial supplies." To learn more about Catalent's modified release technologies, please visit www.catalent.com/index.php/delivery.

Arcturus Therapeutics Raises $1.3 Million in Series Seed Funding

PRNewsire: June 3, 2013 – SAN DIEGO, CA, U.S.A. – Arcturus Therapeutics, Inc., an industry leader in RNAi technologies for the treatment of disease, today announced it has raised $1.3 million in a seed funding round led by multiple high-net-worth private investors from the United States and Canada.

Arcturus Therapeutics, a San Diego–based company focused on the discovery and development of therapeutic modalities, was founded in 2013 to pursue RNA interference (RNAi) solutions for rare diseases for which there is no adequate treatment.

"Researchers have made great strides in recent years in diagnosing, treating, and even preventing a variety of rare diseases. Still, much more remains to be done because there are no treatments for the vast majority of rare diseases, which affect an estimated 25 million to 30 million Americans," said Joseph E. Payne, president and CEO, Arcturus. "Arcturus is poised to contribute significant disruptive and promising treatments for rare diseases, contributing to improved quality of life and betterment of society."

Arcturus's recent round of funding underscores the significant potential represented by the RNAi market and its role in the development of innovative pharmaceutical therapies. According to a new report by Global Industry Analysts, Inc., the global RNA interference (RNAi) market is expected to reach $4.04 billion by 2017.

The new round of funding will support the purchase of capital equipment and further development of Arcturus's intellectual property of RNAi delivery technologies, along with RNAi target selection, design, and *in vitro* proof of concept studies.

Arcturus Therapeutics was founded by Joseph Payne and Pad Chivukula, pharmaceutical scientists and experts in nanoparticle delivery technology and who have previously executed a preclinical development project through IND filing for a novel RNAi therapeutic to treat fibrosis. The Arcturus founders have substantial experience delivering multiple drug products for reputable companies, such as DuPont Pharmaceuticals, Merck, Bristol-Myers Squibb, Kalypsys, and Nitto Denko.

Arcturus Therapeutics is located in San Diego–based Janssen Labs, where disruptive research is underway by some of today's leading scientists and up-and-coming technologists who are working side-by-side to develop pioneering medical treatments. Recently, Arcturus announced new appointments to its Board of Directors and Scientific Advisory Board.

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Founded in 2013 and based in San Diego, California, Arcturus Therapeutics is poised to become an industry leader in the application of RNAi technologies for the treatment of disease and improved quality of life. The company's aim is to develop breakthrough technology and novel therapeutics for rare diseases for which there is no adequate treatment. Backed by a management team with extensive experience in the discovery and development of therapeutic modalities, Arcturus is on the forefront of research and development of nanoparticle siRNA drug delivery systems. For more information, visit us at www.ArcturusRx.com.

May

TWi Pharmaceuticals' Manufacturing Site for the Generic Version of Lidoderm® (Lidocaine 5% patch) Passes U.S. FDA cGMP Audit and Preapproval Inspection

PRNewswire: May 29, 2013 – TAIPEI, Taiwan – TWi Pharmaceuticals, Inc., today announced that Teh Seng Pharmaceutical Mfg. Co. (Teh Seng), the manufacturing partner for its generic version of Lidoderm® (5% lidocaine patch) located in Taiwan, has completed the cGMP audit and preapproval inspection (PAI) by the U.S. Food and Drug Administration (FDA) and been granted "acceptable" status under the FDA's regulatory guidelines. "We are pleased to know Teh Seng has received the 'acceptable' status upon the completion of cGMP audit and PAI by U.S. FDA," said Calvin C. Chen, president of TWi Pharmaceuticals. "TWi has worked closely with our manufacturing partner on meeting FDA's regulatory requirement for our lidocaine patch product. Getting the 'acceptable' status not only shows TWi and its manufacturing partner's continuing commitment to the high standard production quality but also brings TWi one step closer to getting the ANDA approval and launching this important product in the U.S."

Lidocaine patch is currently marketed under the trade name Lidoderm® by Endo Pharmaceuticals Inc. in the United States and has been approved for relieving postherpetic neuralgia. According to IMS Health data, in 2012, the total sales figure of Lidoderm® in the United States is over US$1.2 billion.

TWi Pharmaceuticals, Inc., is a leading specialty pharmaceutical company based in Taipei, Taiwan, focusing on the development of high-barrier generic prescription products ranging from oral controlled release dosage forms to novel drug delivery systems including the utilization of nanoparticles, transdermal, and polymeric oral delivery systems. Leveraging its internal research and development capabilities, together with operational flexibility, process development, and manufacturing and regulatory expertise, TWi Pharmaceuticals concentrates on products and technologies that present significant barriers to entry or offer Paragraph IV first-to-file or first-to-market opportunities in the United States. For more information on TWi Pharmaceuticals, please visit www.twipharma.com.
Teh Seng Pharmaceutical is among the global leaders in topical patch manufacturing. Located in Tainan, Taiwan, the company has developed and manufactured over sixty patch products for various medical and cosmetic applications. The products are distributed in several countries across Asia, Europe, and in the United States. For more information on Teh Seng Pharmaceutical, please visit www.tehseng.com.

ULURU Inc. Announces Publication on Altrazeal® in the *International Journal of Molecular Sciences*

PRNewswire: May 28, 2013 – ADDISON, TX, U.S.A. – ULURU Inc. (OTCQB: ULUR) today announced the publication, in the *International Journal of Molecular Sciences*, of an article titled "Bacterial Growth Kinetics Under a Novel Flexible Methacrylate Dressing Serving as a Drug Delivery Vehicle for Antiseptics."

The article describes the investigation of the antimicrobial efficacy and influence on bacterial growth kinetics in combination with three antiseptics in an *in vitro* porcine wound model. The study demonstrated that a methacrylate dressing (Altrazeal®) applied into an experimental wound as a powder, which then transforms into a flexible, wound-contouring dressing, can be combined with a number of antiseptics and serve as a drug delivery system for antimicrobial compounds. Depending on the antiseptic chosen, bacterial load can be controlled up to 5 days (length of the study), and controlled non-antimicrobial or antimicrobial effect may be achieved using the same type of wound dressing.

Commenting on the publication, Kerry P. Gray, president and CEO of ULURU Inc., stated, "This is an important publication for the company in a peer-reviewed journal. This opens new possibilities for topical antimicrobial treatment and prophylactic strategies in wound care management. Clinicians have experienced favorable clinical results using antimicrobials in combination with Altrazeal®. This could represent a major advancement in controlling microbial contaminants in acute and chronic wounds and avoid, in many cases, the use of antibiotics."

ULURU Inc. is a specialty pharmaceutical company focused on the development of a portfolio of wound management and oral care products to provide patients and consumers improved clinical outcomes through controlled delivery utilizing its innovative Nanoflex® aggregate technology and OraDisc™ transmucosal delivery system. For further information about ULURU Inc., please visit our website at www.uluruinc.com. For further information about Altrazeal®, please visit our website at www.altrazeal.com.

Echo Therapeutics Announces Institutional Review Board (IRB) Approval for Its Clinical Trial of the Symphony® CGM System

PRNewswire: May 21, 2013 – PHILADELPHIA, PA, U.S.A. – Echo Therapeutics, Inc. (Nasdaq: ECTE), a company developing its needle-free Symphony® CGM system as a noninvasive, wireless, transdermal continuous glucose monitoring system, announced today that the company's clinical trial of its Symphony CGM system has received Institutional Review

Board (IRB) approval. The IRB approval enables the commencement of a clinical evaluation of Symphony that will support the company's CE Mark technical file.

"It's gratifying to see this important technology advance. This IRB approval signals a long-awaited CE Mark regulatory trial initiation," commented Dr. Mooney. "Our team's hard work and extreme dedication have put us in a very strong position to begin the process of securing Symphony's market approval by European regulatory agencies."

Echo Therapeutics is developing the Symphony CGM system as a noninvasive, wireless, transdermal continuous glucose monitoring system. Our target is patients who could benefit from glucose monitoring in the hospital setting, including critical care. Significant opportunity also exists for patients with diabetes to use Symphony in the outpatient setting. Echo is also developing its needle-free skin preparation component of Symphony, the Prelude® SkinPrep system, as a platform technology to enhance drug delivery of topical pharmaceuticals.

Phosphagenics Signs Research Agreement with the Agricultural Research Service

PRNewswire: May 20, 2013 – MELBOURNE, Australia – Australian drug delivery technology company Phosphagenics Limited (ASX: POH, OTCQX: PPGNY) will collaborate with the U.S. Department of Agriculture's (USDA's) Agricultural Research Service (ARS) to develop and trial products targeting the serious bacterial infection mastitis in dairy cows. ARS is the USDA's chief intramural scientific research agency.

Under the agreement, Phosphagenics and ARS will formulate and evaluate products containing active ingredients in combination with the company's TPM® delivery technology to enable superior absorption and efficacy. The products will include the formulation previously trialed by Phosphagenics with good results, as well as a formulation containing a vitamin D derivative.

A preliminary study conducted by ARS in 2012 demonstrated that directly infusing the vitamin D derivative into infected quarters of the mammary gland in infected dairy cows was able to significantly lower bacteria counts and clinical symptoms of mastitis. The study also showed that cows treated with the derivative exhibited superior milk production.

The trials will begin mid-2013 and will be conducted in the United States by ARS. Researchers will examine the effects and efficacy of the TPM® formulated products delivered via intra-mammary infusion using a protocol developed by ARS.

Phosphagenics CEO Dr. Esra Ogru said mastitis typically affected around 15% of the world's dairy herd at any given time. In the U.S.A. alone, economic losses resulting from this infection are estimated at US$2 billion per annum.

"This is a significant problem for farmers worldwide, as it affects milk quantity and quality," Dr. Ogru said.

"Current standard of care for mastitis is antibiotic treatment, but there are widespread concerns globally around antibiotic-resistant bacteria. It is important to develop new therapeutics that bypass these problems and that are also effective."

Phosphagenics' proprietary TPM® delivery technology enables the superior absorption of key active ingredients across a range of platforms.

Dr. Ogru added: "There are 250 million dairy cows globally, and the U.S. dairy industry represents just 4% of this market. Clearly, progressing these kinds of products presents a major market opportunity for our company."

Phosphagenics Limited is commercialising drug delivery applications based on its novel transdermal (drugs administered via skin) TPM®—Targeted Penetration Matrix technology. TPM® is a patient friendly and cost-effective system used to deliver proven pharmaceutical and nutraceutical products.

The lead products advancing through clinical trials are an oxycodone and oxymorphone matrix system for the relief of chronic pain.

Phosphagenics' shares are listed on the Australian Securities Exchange (POH), and its ADR–Level 1 program in the United States is with The Bank of New York Mellon (PPGNY). www.phosphagenics.com

BioRestorative Therapies Signs Agreement with Dexterity, Inc., to Advance Production of the Company's Novel brtxDISC™ Stem Cell Therapy Device

PRNewswire: May 20, 2013 – JUPITER, FL, U.S.A. – BioRestorative Therapies, Inc. ("BRT" or the "company") (OTC BB: BRTX), a life sciences company focused on developing stem cell based therapies for various personal applications, announces the signing of a consulting agreement with Dexterity, Inc. ("Dexterity"). Dexterity is a product design and bioengineering firm that will provide services to further the development and production of BRT's proprietary therapeutic delivery device for its intervertebral disc stem cell therapy program brtxDISC™ (disc implanted stem cells).

Dexterity's work is intended to advance the design and production of the disc therapeutic delivery device toward a final version, to be eventually used in a clinical trial as a stem cell delivery system for the treatment of bulging and herniated discs. BRT expects to have a pre-IND/IDE meeting with the FDA to discuss the clinical trial by fourth quarter of this year.

The company's brtxDISC™ program is being developed as an alternative to surgical intervention for patients suffering from bulging or herniated discs and could bridge the gap between noninvasive and invasive surgical back procedures. The therapy is a regeneration repair process using a patient's own stem cells that

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are implanted using BRT's proprietary therapeutic delivery device. The company has data on treated humans in the United States and is compiling results in preparation for clinical trials in the United States.

"We are very excited to be working with BioRestorative Therapies on the development of its novel, proprietary brtxDISC™ intervertebral disc stem cell therapy," commented Eric Simon, president of Dexterity. "Our experience with laparascopic and catheter-based devices, cell culture systems, and drug-delivery devices will assist in advancing the development and production of BRTX's disc stem cell delivery device as the company moves through its next phase of clinical trials."

"We are fortunate to be working with Dexterity," commented Mark Weinreb, chief executive officer of BioRestorative Therapies. "With their depth of experience in 3D-CAD, biomaterials, and advanced prototyping and manufacturing, they are the perfect partner to work on the design and final engineering of our medical disc delivery device. We are confident our device will have the performance and quality to operate as intended and will be commercial-ready when we are able to launch our brtxDISC™ program."

Dexterity, Inc., is a full-service product design and development resource. The company has extensive experience in the design of tangible goods in the medical/biotechnical, consumer, and industrial markets. Dexterity specializes in 3D-Solids CAD modeling and analysis, employing rapid prototyping and tooling technologies to accelerate products to market. Dexterity's broad manufacturing experience assists its clients in designing toward the appropriate production technology for its clients' and consumers' needs. The company has designed and implemented a diverse range of medical and biotechnical products including *in vitro* diagnostic systems, laparoscopic instrumentation, high-performance cell culture ware, drug-delivery devices, and various implantable products.

BRT, www.biorestorative.com, develops medical procedures using cell and tissue protocols, primarily involving adult stem cells, designed for patients to undergo minimally invasive cellular-based treatments. BRT is developing the following scientific initiatives:

brtxDISC™ program (disc implanted stem cells), a nonsurgical treatment for bulging and herniated discs that addresses the gap between noninvasive and invasive back procedures. This research is still in the nonclinical, investigational stage. The ThermoStem® program is a treatment for metabolic disorders (diabetes, heart disease, etc.) and obesity using brown fat stem cells. The company also offers plant stem cell-based facial creams and beauty products under the Stem Pearls® brand at www.stempearls.com.

Oramed Receives FDA Clearance to Initiate Oral Insulin Trials in the United States

PRNewswire: May 17, 2013 – JERUSALEM, Israel – Oramed Pharmaceuticals Inc. (NASDAQCM: ORMP) (www.oramed.com), a developer of oral drug delivery systems, announced today that the U.S. Food and Drug Administration (FDA) has cleared the company's Investigational New Drug application (IND) for ORMD-0801, its oral insulin capsule.

"We are very pleased to have the FDA clearance to proceed," stated Nadav Kidron, CEO of Oramed. "The upcoming trial is a major milestone for Oramed, and we look forward to continuing to progress ORMD-0801's clinical development in the U.S."

Oramed's ORMD-0801 is an orally ingestible insulin capsule indicated for the early stages of type 2 diabetes, when it can still slow the rate of degeneration of the disease by providing additional insulin to the body and allowing pancreatic respite. Moreover, orally administered insulin has the potential benefit of enhanced patient compliance at this crucial stage as well as the advantage of mimicking insulin's natural location and gradients in the body by first passing through the liver before entering the bloodstream.

Oramed Pharmaceuticals is a technology pioneer in the field of oral delivery solutions for drugs and vaccines currently delivered via injection. Established in 2006, Oramed's technology is based on over 30 years of research by top research scientists at Jerusalem's Hadassah Medical Center. Oramed is seeking to revolutionize the treatment of diabetes through its proprietary flagship product, an orally ingestible insulin capsule (ORMD-0801), currently initiating phase 2 clinical trials under an Investigational New Drug application with the U.S. Food and Drug Administration, and with its oral exenatide capsule (ORMD-0901, a GLP-1 analog), currently approaching phase 2a trials. The company's corporate and R&D headquarters are based in Jerusalem.

Halo Pharma and Altus Formulation Announce New Formal Collaboration

PRNewswire: May 14, 2013 – MONTREAL, Canada – Halo Pharma today announced that it has taken a minority ownership position in, and established a formal collaboration with, the drug formulation and development company Altus Formulation Inc. Altus uses proprietary technologies and approaches to solve pharmaceutical formulation and delivery problems.

Halo is focused on satisfying the pharmaceutical client's development and manufacturing needs, whether those needs are straightforward or complex. On a fee for service basis, Halo will always remain committed to practical facilitation and implementation of nonproprietary and client based solutions to scientific and technical challenges in the areas of preformulation, analytical method development, formulation, scale up, regulatory submission, and commercial manufacturing. These approaches typically generate significant new wholly client owned IP.

With this new investment in, and association with, Altus Formulations, Halo takes a first step in offering to clients, when needed, an entire suite of proprietary scientific and technical solutions designed to solve intractable issues in such areas as drug solubility, bioavailability, tamper and abuse deterrence, and precisely managed drug dosage delivery. These proprietary solutions cover a wide range of nonsterile and sterile dosage forms. One such area requiring solution is the currently much-discussed question of the need for abuse resistance for narcotic analgesic and other frequently abused CNS drugs.

In commenting on the collaboration with Altus, the CEO of Halo Pharma, Clive Bennett, said, "We are delighted to have this new association with Altus, as it will allow Halo to provide novel proprietary solutions to clients with difficult formulation problems in addition to those already-available public domain and client originated solutions that we have historically offered."

Damon Smith, CEO of Altus Formulation, remarked, "The Altus team is extremely excited to be collaborating with Halo Pharma with their track record of excellence in the contract development and manufacturing fields. By combining our strengths, Altus and Halo offer a full range of development and delivery options that are ideally placed to meet the needs of the industry."

Halo Pharma is a privately held company with operations in the New Jersey pharmaceutical corridor and in Montreal, Quebec. Halo is a significant provider of drug development and commercial manufacturing services to the pharmaceutical industry. The company provides the highest quality products and services to some of the world's leading pharmaceutical and biotechnology companies.

The development services of Halo cover the entire development cycle from preclinical to clinical trial materials to registration, including project management, preformulation, formulation, analytical development, clinical manufacturing, scale-up, and validation at commercial scale. Commercial manufacturing covers postapproval launch of new and established molecular entities through late product life cycle strategies. A wide range of dosage forms is supported both in development and commercial manufacturing.

Altus Formulation is a Quebec-based drug formulation and development company using its proprietary and patent protected drug delivery technologies to generate novel, differentiated, and cost-effective new products for its clients. With a focus on an improved patient experience, Altus technologies include Intellitab tamper and abuse resistant technologies, Contramid®, for high-dosage product delivery, MicroSpheres Plus for taste-masked controlled release liquids, and the PNDS micellar technology platform that enables delivery of insoluble small and large molecules via both oral and parenteral routes to achieve increased bioavailability and low volume intravenous administration.

Contramid is a registered trademark of Paladin Labs Inc. (TSX: PLB). Each of these technologies are under exclusive global license from Paladin. Halo and Paladin are both minority shareholders in Altus Formulation.

Aegis Awarded Second Patent for Fast-Acting Migraine Nasal Spray Treatment

PRNewswire: May 14, 2013 – SAN DIEGO, CA, U.S.A. – Aegis Therapeutics LLC announced today that it has been awarded U.S. Patent No. 8,440,631, its second patent providing fast-acting formulations for triptans, a class of drugs that are effective in treating migraine headaches and include sumatriptan, zolmitriptan, naratriptan, rizatriptan, eletriptan, almotriptan and frovatriptan. Human clinical trials have shown that the Intravail® formulation of sumatriptan achieves therapeutic drug levels at approximately 2 to 3 minutes, 20 to 30 times faster that the currently marketed noninjectable sumatriptan products. For comparison, the most widely used triptan formulations, namely sumatriptan nasal spray or tablet formulations, both reach maximum blood levels of drug in about 60 to 120 minutes, thus delaying onset of relief.

The enabling Aegis Intravail formulation technology is broadly applicable to a wide range of small molecule and biotherapeutic drugs to increase noninvasive bioavailability by the oral, nasal, buccal, and sublingual routes and to speed attainment of therapeutic drug levels in cases where speed is important to the patient, for example, in the treatment of pain, nausea, emesis, convulsive disorders, spasticity, and the like.

Aegis technology is commercialized by our licensees, who conduct the actual product development and marketing activities. Aegis's licensees include four of the top 10 largest pharmaceutical companies and two of the top 10 largest generics companies, along with many public and private biotech companies. Aegis's growing patent portfolio currently has more than fifty issued and pending drug formulation patents covering peptide, protein, and small-molecule drugs.

Aegis Therapeutics LLC is a drug delivery technology company commercializing its patented drug delivery and drug formulation technologies through product-specific licenses. Our Intravail® drug delivery technology enables the noninvasive delivery of a broad range of protein, peptide, and nonpeptide drugs that can currently only be administered by injection, via the oral, buccal, and intranasal administration routes, and with high bioavailability. Our ProTek® excipients stabilize, prevent aggregation, and reduce unwanted immunogenicity of protein and peptide therapeutics while avoiding the oxidative damage caused by polysorbate surfactants. For more information about Aegis, please visit www.aegisthera.com. ■

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

Calendar of Events

2013

Advances in Tissue Engineering Short Course
Sponsored by CRS
August 14–17
Houston, TX, U.S.A.
http://tissue.rice.edu/

11th International Nanomedicine and Drug Delivery Symposium (NanoDDS'13)
October 25–27
La Jolla, CA, U.S.A.
http://nanomedicine.ucsd.edu/nanodds13

Mitigating Risks for Patients When Developing Oral Controlled Release Dosage Forms
Sponsored by CRS
November 9–10
San Antonio, TX, U.S.A.
controlledreleasesociety.org

Introduction to Microencapsulation Technologies
Sponsored by CRS
November 10
San Antonio, TX, U.S.A.
controlledreleasesociety.org

New Vision for the Eye: Unmet Ocular Drug Delivery Needs Workshop
Sponsored by CRS
November 10
San Antonio, TX, U.S.A.
www.aaps.org

2014

5th FIP Pharmaceutical Sciences World Congress
April 13–16
Melbourne, Australia
www.fip.org/pswc2014