CRS Leading Delivery Science and Technology

Newsletter

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What's Inside

CRS Newsletter

Leading Delivery Science and Technology

Vol. 32 • No. 1 • 2015

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

Arlene McDowell
University of Otago
New Zealand

Unexpected Things

With the start of a new year, thinking can turn to wondering what the year will hold. iCal, doodle, and deadlines make sure we plan for some of the things we do, but there will always be unexpected things.

Unexpected things can be tragic, and I am reminded of the untimely passing of Marcus Brewster—a wonderful friend of so many in CRS. I am sure that Marcus would attest that unexpected things can also provide us with a great opportunity to do something that we would not normally do. Personally, CRS has provided me with opportunities that I did not foresee (including co-editing a book, eating from a chocolate fountain in the penthouse at the New York Hilton, and going behind the scenes at the Minneapolis zoo to fulfil a long-term wish to meet an opossum). This has all been through my contribution to CRS committees. Recently, I have been serving on the CRS Volunteer Recruitment Committee, where we have been looking at strategies to broaden participation in the operation of CRS as well as enhancing the volunteer experience. I strongly encourage you to get involved in a CRS committee and see what unexpected things you can encounter. The CRS local chapters are an excellent way to begin your involvement and can enable you to contribute more than your science to CRS.

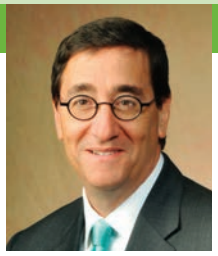
In this issue of the *CRS Newsletter* you can read about a new initiative by the *DDTR* journal to now consider publishing research that has a negative or unexpected finding. This is an excellent initiative, and our lab group has often lamented the lack of this type of forum. CRS members get free access to the online journal content. We also have all our regular forums, including Scientifically Speaking, Patent Watch, and an interesting interview with Prof. Paolo Colombo from Universita degli studi di Parma, Italy. Prof. Gregory Gregoriadis has also written a compelling account of his foray into writing a novel.

Edinburgh is the place to be in 2015 for our CRS Annual Meeting. It seems like many of you agree, because a record number of abstracts have been submitted for this conference. I am excited to see the new format for the conference closing reception in Edinburgh. Plan to be there and to be open to the unexpected things that can happen.

On behalf of the *CRS Newsletter* editorial team, I wish you a happy, healthy, and successful 2015.

I will leave you with a relevant quote from Oscar Wilde: "To expect the unexpected shows a thoroughly modern intellect."

Best wishes,
Arlene McDowell ■



Art Tipton
Southern Research Institute
Birmingham, Alabama, U.S.A.

Celebrate Our History!

For many of us, January is the month when we come back from a brief end-of-the-year break. Like many, I took some time off as the year ended, reflected on 2014, and spent time planning for 2015. I unwound with a few books, including *All the Light We Cannot See*, the Anthony Doerr novel set during World War II that is currently on best-seller lists, and the final book of Ken Follett's Century Trilogy, *Edge of Eternity*. Those books got me thinking about history. As I write this in mid-January, we just commemorated Martin Luther King Jr. Day and reflected on his pivotal role in history. For us in North America, King is the person most identified with human rights, and he joins Nelson Mandela from Africa, Lech Walesa from Europe, Mahatma Gandhi from Asia, and others around the world who as individuals made a strong historical difference.

In our own way, we at CRS have a great history we should also commemorate. For many years we have acknowledged our leaders with awards. In 2009 we created a special way to acknowledge the luminaries in our field with a Foundation Award. In that year and subsequent years we have honored Joe Robinson, Jorge Heller, Tsuneji Nagai, Sun Wan Kim, and Sandy Florence. I am pleased to announce we will continue this recognition in Edinburgh in 2015, recognizing Nicholas Peppas. In previous years CRS has recognized these leaders by establishing a one-year postdoctoral position for one individual in a lab of their choosing. Going forward we are electing to use those funds to more aggressively sponsor young scientists to attend our annual meeting. With this new focus, the program is designed to support multiple students to attend the CRS meeting so those students have a chance to experience the signature event in our society and to learn from and meet with other delivery scientists. This new focus is consistent with the long-term vision of CRS and provides an even better way to honor our luminaries and continue the wonderful history of our society.

You were probably already excited about the meeting in Edinburgh. Now you should be even more so given the opportunity to acknowledge Nicholas. Please also read more at our website on how you can contribute and be part of this opportunity, both to recognize Nicholas's many accomplishments in our field and contributions to our society and to invest in the next generation of scientists.

I want to provide a few more updates on the annual meeting. While we appreciate and will build on our great history, as you have probably seen from emails and other communications, we are working to add some changes so that we have the most interactive and enjoyable meeting ever. Many of the leading scientists around the world have seen this updated format and are responding by submitting what looks to be a record-breaking number of abstracts. Also, as you know, we will have an increased industry focus, once again renewing our commitment to that fruitful exchange between academia and industry that has been an integral part the rich CRS history. Our annual banquet, once a highlight of our yearly gathering, has over recent years been more sparsely attended due to extra costs for attendees. This year we have developed an updated event, included in the meeting registration, that will be a fun taste and experience of Scottish history. This event will be a great networking experience for all attendees.

Finalize your plans to join us in Edinburgh this July. Come and celebrate the history of CRS, and build (or start) your own history within our society. Plan a few extra days to enjoy Edinburgh and Scotland, and as I am telling people, "Come for the Science, Stay for Some Haggis!" ■

An Interview with Paolo Colombo from University of Parma

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

Colombo (left) with Nicholas Peppas (right) on a spring day in Parma for Verdi composer celebrations.

Dr. Paolo Colombo is an international expert in the field of pharmaceutical technology, swellable matrices for oral delivery of drugs, iontophoresis, nasal and pulmonary administration of drugs, and pharmaceutical micro- and nanoparticles and generic preparations.

Dr. Colombo received his Pharm.D. (master course in pharmacy) in November 1968 and an honorary Ph.D. from the University of Athens in 2010. He joined the Università degli studi di Parma as a professor of pharmaceutical technology in 1986 and since then has published over 250 articles in international journals, made over 275 communications to scientific meetings, and presented over 130 lectures as an invited speaker on various research topics. He has been a part of peer societies such as CRS, Italian Pharmaceutical Technology Teachers, Italian Society of Pharmacokinetics and Biopharmaceutics, Industrial Pharmacists Association, American Association of Pharmaceutical Scientists (AAPS), European Federation for Pharmaceutical Scientists, and Association de Pharmacie Galénique Industrielle.

During his career, Dr. Colombo has received many awards, including the Award for Scientific Production at the University of Pavia (1973), Colorcon Award (1991), Jorge Heller *Journal of Controlled Release* Outstanding Paper Award (1999), Maurice-Marie Janot Award for Pharmaceutical Sciences (2004), CRS Reiner Hofmann Award (2007), CRS Founders Award (2014), and Ralph Shangraw IPEC Award (2014). He is a foreign correspondent of the Association Française des Enseignants de Pharmacie Galénique, a foreign member of the Academie de Pharmacie Française (1999), and an AAPS fellow (1996). His recent projects are related to microparticle design and testing for lung delivery, thalidomide for telangiectasia by nasal delivery (Telethon), gastroretentive dosage forms for drug combination modified release, inhalation therapy in tuberculosis, and new dry powder inhalation in cystic fibrosis.

Q *How did you get to join the University of Parma, and what inspired you to stay at this place for all of your working career?*

A I graduated in pharmacy in Pavia, an old university close to Milan, studying for my thesis with Aldo La Manna, who was the first Italian researcher in pharmaceutical technology. Then I progressed to an assistant and then an associate professor in his group together with Ubaldo Conte and Carla Caramella. In 1986 I won a position as a full professor in Parma, where the Faculty of Pharmacy called on me to implement the research and teaching in pharmaceutical technology. The faculty, in particular the dean, Tullo Vitali, supported me a lot, and when the faculty got a new building I decided to move my family and stay in Parma. There are also collateral reasons to the scientific interests that convinced me to stay there, such as the music (Parma is the city of Verdi and Toscanini), the excellent food, and the good quality of life in this city.

Q *You have worked closely in collaboration with different professors and scientists. What are your closest ties? What do you think made these relationships so special?*

A Apart from the colleagues mentioned before, I have to acknowledge Piero Catellani, who collaborated with me in Parma on many research subjects, and my first students there, now professors in Parma: Patrizia Santi and Ruggero Bettini. The risk to miss someone is high, but I cannot forget the time spent and collaborations done with Michel Traisnel, Jean Claude and Anne Guyot in Lille, Pierre Buri and Eric Doelker in Geneva, Dominique Duchene, Francis Puisieux, Patrick Couvreur and Elias Fattal in Paris Sud, Bob Langer at Massachusetts Institute of Technology, Richard Guy at University of California, San Francisco, Tsuneji Nagai in Tokyo, Hans Junginger in Leiden, Dimitri Rekkas in Athens, and Maria José Alonso in Santiago de Compostela. However, what gave decisive input to my career was the scientific and friendly collaboration with Nicholas Peppas at Purdue. We spent many days together working on matrices, swelling, disintegration, and release mechanisms. Very often this was done in the car, moving around Italy for meetings or lectures. It continues to be a fantastic interaction between a pharmacist and a chemical engineer. We have a common passion that helps: opera. We exchanged many students for collaborative research projects as well as Ph.D. theses.

Q *What are some of your most interesting research projects?*

A The most interesting has been the Geomatrix technology for oral drug delivery control. The idea of modifying the release kinetics without changing the matrix composition was first described in a thesis done in Pavia by one of my students, Didi Sangalli. She became a young professor in Milan, but she left us prematurely five years ago. Didi's thesis provided the scientific basis for making the matrix prototypes appear as partially coated swellable matrices. The coating position on the matrix core affects the matrix swelling and, as a consequence, the drug release rate and kinetics. However,

1 Chrono Therapeutics Inc., Hayward, CA, U.S.A.
2 Ernest Mario School of Pharmacy, Rutgers–The State University of New Jersey, U.S.A.

ideas can become products if a mind open to the market contributes, and in this case the fortune was to meet Jacques Gonella, the founder of Yagotech, who put the product on the U.S. market. Today, the evolution of this product is another matrix delivery system known as Dome Matrix, which is a modular system used for drug combination products.

Q *Please list the five publications from your research lab that were most significant in your research career.*

A Harland, RS, Gazzaniga, A, Sangalli, ME, Colombo, P, Peppas, NA. Drug/polymer matrix swelling and dissolution, Pharm. Res. 5(8): 488-494 (1988).

Colombo, P, Conte, U, Gazzaniga, A, Maggi, L, Sangalli, ME, Peppas, NA, and La Manna, A. Drug release modulation by physical restrictions of matrix swelling, Int. J. Pharm. 63: 43-48 (1990).

De Ascentiis, A, Bettini, R, Caponetti, G, Catellani, PL, Peracchia, MT, Santi, P, Colombo, P. Delivery of nasal powders of beta-cyclodextrin by insufflation, Pharm. Res. 13(5): 734-738 (1996).

Young, PM, Cocconi, D, Colombo, P, Bettini, R, Price, R, Steele, DF, Toby, MJ. Characterization of a surface modified dry powder inhalation carrier prepared by "particle smoothing," J. Pharm. Pharmacol. 54: 1339-1344 (2002).

Sonvico, F, Mornet, S, Vasseur, S, Dubernet, C, Jaillard, D, Degrouard, J, Hoebeke, J, Duguet, E, Colombo, P, and Couvreur, P. Folate-conjugated iron oxide nanoparticles for solid tumor targeting as potential specific magnetic hyperthermia mediators: Synthesis, physicochemical characterization and *in vitro* experiments, Bioconjugate Chem. 16: 1181-1188 (2005).

Q *Please list the five most important publications (not from your lab) that you think have had the greatest impact in the pharmaceutical science field during your research career.*

A Peppas, NA. Analysis of Fickian and non-Fickian drug release in polymers, Pharm. Acta Helv. 60: 110-111 (1985).

Brigger, I, Dubernet, C, Couvreur, P. Nanoparticles in cancer therapy and diagnosis, Adv. Drug Delivery Rev. 54(5): 631-651 (2002).

Gref, R, Minamitake, Y, Peracchia, MT, Trubetskoy, V, Torchilin, V, Langer, R. Biodegradable long-circulating polymeric nanospheres, Science 263(5153): 1600-1603 (1994).

Potts, RO, Guy, RH. Predicting skin permeability, Pharm. Res. 9(5): 663-669 (1992).

Amidon, GL, Lennernäs, H, Shah, VP, Crison, JR. A theoretical basis for a biopharmaceutic drug classification: The correlation of *in vitro* drug product dissolution and *in vivo* bioavailability, Pharm. Res. 12(3): 413-420 (1995).

Q *What is role of government in academic research in Italy? What is the status of government-sponsored and private research funding? How has that changed over the years?*

A Academic research today is not supported enough by national governmental funding. The economic situation in recent years reduced the possibilities of access to funding. This access is still too much related to lobbying. In contrast, being renowned in research opens one to contracts with companies. Today, 90% of my funds come from industry. I hope that will continue.

Q *How has the European economy affected research activity in Italy in last few decades?*

A There is a great expectation from the new EU program Horizon 2020, and we have applied to this program recently. The European Union is now favoring the contacts with European industries from other countries.

Q *For international students and professionals, would you suggest advanced education in Italian schools? What is the language for day-to-day activities? Is financial aid available to foreign students?*

A Education in Italy is certainly advantageous for classic disciplines. Also, technological fields that are very advanced in the country attract researchers in science. We receive many students from EU countries because of the Erasmus program, which allows EU students to follow undergraduate courses at foreign universities and have recognition of the credits at their original universities. Presence in class requires a minimum understanding of the Italian language. In a laboratory, the language for communication and collaboration is English. It is not easy to find a local grant for a foreign student. Sometimes the Italian embassy in the country of origin provides financial support.

Q *Your main hobbies are skiing and sailing. What fascinates you about these sports? What else do you do like to do in your spare time?*

A The two sports have in common being outdoors. Maybe I like them since I am always inside during working hours in a lab or classes. In reality, these sports are also shared by my family, and they are a good opportunity for keeping all of us in contact.

The Colombo family on a magnificent winter day in the Livigno Alps (Italy): Paolo, Gaia (associate professor at University of Ferrara), Miti (letter professor), and Marcello (a police officer in Rome).

I like to spend my free time with my students too. Every year, we organize a few days all together for skiing or mountaineering. ■

42ND CRS ANNUAL MEETING & EXPOSITION

July 26–29, 2015
Edinburgh, Scotland

The Annual Meeting Call for Abstracts closed in mid-January 2015. Nearly 1,000 abstracts were submitted from individuals representing 56 countries. "CRS leadership is excited about the strategic changes planned for this meeting," said Susan Kohn, CRS Executive Director. "The six-year high in abstract submissions is both an enthusiastic endorsement of the new scientific session format and an early indicator of strong attendance in Edinburgh. The CRS Board and Program Planning Committees are delighted with the response." The Annual Meeting website is your go-to link to the latest scientific content, discounted housing, online registration, exhibit and sponsorship opportunities, and schedule-at-a-glance. Be sure to bookmark controlledreleasesociety.org/meeting and visit often.

NEW! 90-minute scientific session format moderated by a CRS Fellow or society leader

40 minutes	Two Invited Speakers: 1 from industry, 1 from academia
30 minutes	Research Highlight Talks: 5 chosen from submitted abstracts *Speakers will prepare a corresponding poster presentation*
20 minutes	Q&A Session with All Speakers

Scientific Sessions: New Format to Deliver a Balanced Program

Watch the website and the next issue of the *CRS Newsletter* for scientific sessions developed using the new 90-minute format. This approach will offer meeting attendees expanded opportunities to exchange information on cutting-edge research, new technologies, and emerging growth areas.

Mini-Symposia: Multiple Perspectives from Invited Speakers

Mini-symposia offer in-depth knowledge into a specific area of delivery science and technology, featuring multiple invited speakers sharing their research on the topic. Symposia descriptions, moderators, and invited speakers are listed on the Annual Meeting website.

Cost-Effective Encapsulation for Industrial Applications: Limitations and Solutions
Moderators: Doug Dale, Dupont Industrial Biosciences, U.S.A.; and Igor Bodnár, Firmenich, Switzerland

European Technology Platform on Nanomedicine: Translation of Nanomedicines
Moderator: Patrick Boisseau, Nanomedicine European Technology Platform, Germany

Modeling and Simulation of Oral Absorption – A Progress Report from the EU/IMI Project OrBiTo
Moderators: Peter Langguth, Johannes Gutenberg University of Mainz, Germany; and Clive Wilson, University of Strathclyde, United Kingdom
Opening Comments: A Tribute to Dr. Marcus Brewster

Next-Generation Vaccine Development and Delivery Technologies
Moderators: Sevda Senel, Hacettepe University, Turkey; and David Brayden, University College Dublin, Ireland

Therapeutic Cancer Nanomedicines
Moderators: Lawrence Mayer, Celator Pharmaceuticals, Inc., U.S.A. and Canada; and You Han Bae, University of Utah, U.S.A.

Premeeting Workshops: Deep Discussion on Diverse Topics

Workshops offer focused presentations on specific topics by noted speakers and are open to a limited number of participants for an additional fee. All workshops will be held prior to the annual meeting. Advance registration and payment required. You may register for a workshop even if you do not plan to attend the annual meeting.

Advanced Pulmonary Drug Delivery: From Generating Aerosols to Overcoming Biological Barriers
Saturday, July 25 (one-day workshop)
Organizers: Claus-Michael Lehr, Saarland University, Germany; and Heidi Mansour, University of Arizona, U.S.A.

Delivery of Therapeutic Bioconjugates: From Polymer Conjugates to Antibody-Drug Conjugates
Sunday, July 26 (half-day workshop)
Organizer: Roger Pak, Pfizer Inc., U.S.A.

Introduction to Microencapsulation
Saturday–Sunday, July 25–26
(1.5-day workshop)
Organizers: James Oxley, Southwest Research Institute, U.S.A.; and Jean-Antoine Meiners, Laboratoire Meiners Sàrl, Switzerland

Ocular Drug Delivery – Challenges of Matching New Technologies with Drug Pharmacokinetics
Saturday, July 25 (one-day workshop)
Organizers: Ilva Rupenthal, University of Auckland, New Zealand; and Michael O'Rourke, Graybug, LLC, U.S.A.

Plenary Speakers: Internationally Recognized Experts

This year, CRS is pleased to offer a featured speaker on each day of the meeting. The first plenary speaker is slated to address the general audience on Sunday, July 26, at 3:00 p.m.

Polymers and Nanomedicines – The Promises and Pitfalls of New Materials

Cameron Alexander
Head of the Division of Drug Delivery and Tissue Engineering, School of Pharmacy, University of Nottingham, United Kingdom

Global Efforts and Successes in Needle-Free Peptide Delivery

María José Alonso
University of Santiago de Compostela, Spain, and coordinator of the TRANS-INT European Consortium

Customized Drug Delivery: A Personal Odyssey

Vincent H. L. Lee
School of Pharmacy, Faculty of Medicine, Chinese University of Hong Kong

Ligand-Directed Therapy and Molecular Imaging Based on *In Vivo* Phage Display Technology

Renata Pasqualini
University of New Mexico Cancer Center, U.S.A.

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2015 Annual Meeting Program Committee

Chair:
Justin Hanes, *Johns Hopkins University, U.S.A.*

Deputy Chair:
Kinam Park, *Purdue University, U.S.A.*

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You Han Bae, *University of Utah, U.S.A.*
Igor Bodnar, *Firmenich, Switzerland*
David Brayden, *University College Dublin, Ireland*
Doug Dale, *DuPont Industrial Biosciences, U.S.A.*
Bill Lambert, *MedImmune, U.S.A.*
Yvonne Perrie, *Aston University, United Kingdom*
Suzie Pun, *University of Washington, U.S.A.*
Ilva Rupenthal, *University of Auckland, New Zealand*
Ron Smith, *Merck & Company, Inc., U.S.A.*

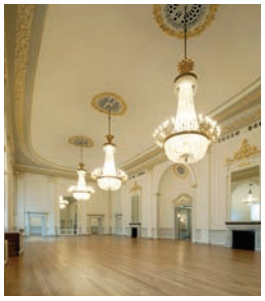
Book Your Room: Many Choices at a Variety of Price Points

This year, CRS-negotiated accommodations include a large variety of hotels offering discounted rates. The best news? You can view, select, and book your choice of accommodations from one link to Marketing Edinburgh Ltd./Convention Edinburgh—the ***only*** housing bureau authorized to book CRS Annual Meeting hotel reservations. **Don't wait until the June 11 reservation deadline—book now to get the accommodations that best fit your needs.**

Annual Meeting Closing Reception

New Event Included in Your Registration Fee

Since 1787, the Assembly Rooms in Edinburgh have been in continuous use for grand assemblies, balls, musical performances, and many other public and private events. CRS is proud to be hosting a Closing Reception with drinks and hors d'oeuvres at this UNESCO World Heritage Site on Tuesday, July 28, from 7:30–10:00 p.m. You'll enjoy the sights, sounds, and flavors of Scotland as all come together to celebrate. More details to come!



Registration Opens Late March

2015 CRS Registration Types and Fees

All CRS registration fees are in U.S. dollars (USD)

EARLY REGISTRATION

(March 23–May 14, 2015)

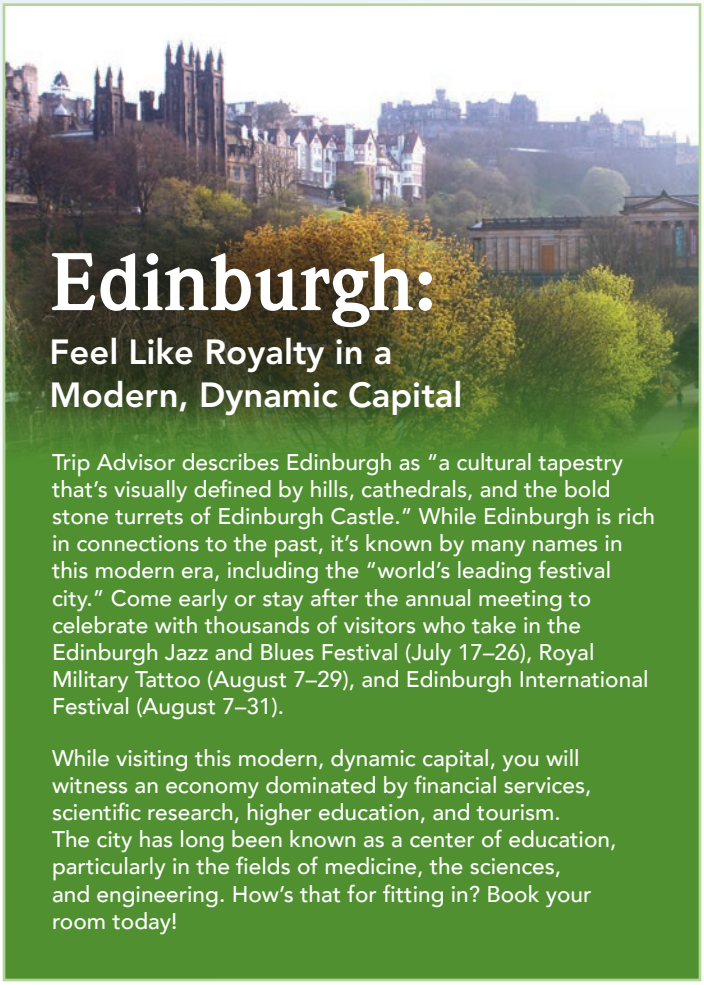
	Member Rate	Meeting PLUS Membership	Nonmember Rate
Regular	$875	$1,045	$1,050
Student*	$450	$500	$495
Postdoc*	$495	$550	$525

REGULAR REGISTRATION

(after May 14, 2015)

	Member Rate	Meeting PLUS Membership	Nonmember Rate
Regular	$1,075	$1,245	$1,249
Student*	$540	$590	$585
Postdoc*	$585	$640	$615

*Full-time student/postdoc rates: full-time students and postdocs qualify for discounted registration rates. Proof of graduate student or postdoctoral research status will be required when registering for the annual meeting.



Edinburgh:

Feel Like Royalty in a Modern, Dynamic Capital

Trip Advisor describes Edinburgh as "a cultural tapestry that's visually defined by hills, cathedrals, and the bold stone turrets of Edinburgh Castle." While Edinburgh is rich in connections to the past, it's known by many names in this modern era, including the "world's leading festival city." Come early or stay after the annual meeting to celebrate with thousands of visitors who take in the Edinburgh Jazz and Blues Festival (July 17–26), Royal Military Tattoo (August 7–29), and Edinburgh International Festival (August 7–31).

While visiting this modern, dynamic capital, you will witness an economy dominated by financial services, scientific research, higher education, and tourism. The city has long been known as a center of education, particularly in the fields of medicine, the sciences, and engineering. How's that for fitting in? Book your room today!

Courtesy Sheraton Edinburgh

Access the Future of Delivery Science and Technology with Key CRS Resources

Essential Delivery Science Webcasts

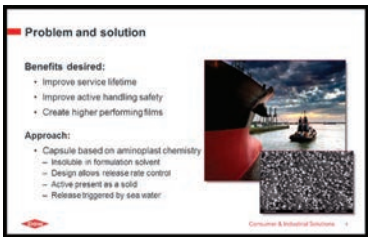
CRS is committed to delivering content that's relevant, peer reviewed, and convenient to access from around the globe. Recorded presentations from the annual meeting are available to CRS members indefinitely and to registered meeting attendees for one year after the meeting date. Take advantage of this important benefit of membership, on demand.

View over 70 recorded presentations from the 2014 Annual Meeting. Topics include:

- Advances in Drug Delivery to the Eye and Lung
- Advances in Process Engineering
- Advances in RNA and DNA Delivery
- Cells as Delivery Vehicles
- Controlled Release Applications in Food, Feed, and Beverages
- Controlled Release of Actives in Consumer Products
- Innovations in Micro- and Nano-Based Delivery
- Innovations in Oral Drug Delivery
- Intracellular Delivery of Nucleic Acids and Proteins
- Nanoparticle-Based Delivery to the Brain
- Nanoparticles in Tumor Treatment
- Overcoming Barriers in the GI Tract
- Proteins, Peptides, and Vaccines
- Transdermal Delivery

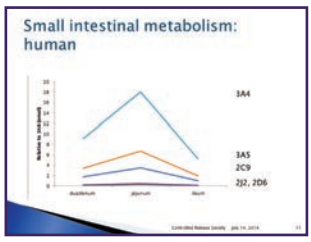
Recorded presentations are also available for the 2009–2013 annual meetings. ■

Members Highlight the Value of Webcasts



Nilesh Shah's presentation "shows clear examples of true market applications of encapsulation and controlled release technologies outside of the pharma market: marine coatings, wood, textile and personal care."

— Nicole Papen-Botterhuis, TNO, the Netherlands

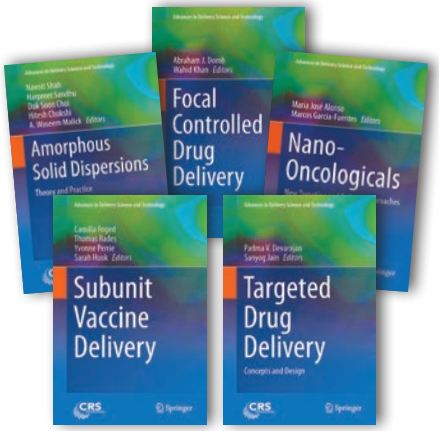


Steven Sutton's meta-analysis provides "invaluable info for designing oral studies in different species."

— Peter Cheifetz, Merial Inc. ■

Comprehensive Guides to Delivery Science

Build your knowledge base with the CRS *Advances in Delivery Science and Technology* book series. CRS books deliver essential knowledge on delivery science and technology, written and edited by scientific authorities and opinion leaders from around the globe.



The series includes:

- **NEW!** Amorphous Solid Dispersions
  Shah, N.; Sandhu, H.; Choi, D.S.; Chokshi, H.; Malick, A.W. (Eds.)
- Controlled Release in Oral Drug Delivery
  Wilson, Clive G.; Crowley, Patrick J. (Eds.)
- Controlled Pulmonary Drug Delivery
  Smyth, Hugh D.C.; Hickey, Anthony J. (Eds.)
- **NEW!** Focal Controlled Drug Delivery
  Domb, A.J.; Khan, W. (Eds.)
- Fundamentals and Applications of Controlled Release Drug Delivery
  Siepmann, Juergen; Siegel, Ronald A.; Rathbone, Michael J. (Eds.)
- Long Acting Animal Health Drug Products
  McDowell, Arlene; Rathbone, Michael J. (Eds.)
- Long Acting Injections and Implants
  Wright, Jeremy C.; Burgess, Diane J. (Eds.)
- **NEW!** Nano-Oncologicals: New Targeting and Delivery Approaches
  Alonso, María José; Garcia-Fuentes, Marcos (Eds.)
- RNA Interference from Biology to Therapeutics
  Howard, Kenneth A. (Ed.)
- **NEW!** Subunit Vaccine Delivery
  Foged, C.; Rades, T.; Perrie, Y.; Hook, S. (Eds.)
- **NEW!** Targeted Drug Delivery: Concepts and Design
  Devarajan, Padma V.; Jain, Sanyog (Eds.)

For more information, visit **controlledreleasesociety.org**. ■

pH-Responsive Fluorescence Polymer Probe for Tumor pH Targeting

Yuki Hiruta,[a,b] Takaaki Funatsu,[a] Yutaro Maekawa,[a] Minami Matsuura,[a] Teruo Okano,[c] and Hideko Kanazawa[a]

Introduction

The consistent differences between tumor cells and normal cells are often not enough to distinguish tumor cells from normal cells in order to destroy only cancer cells selectively. Features of the tumor microenvironment that are slightly different from normal tissues include acidity, hypoxia, overexpressed proteases, and so on.[1] Therefore, we have developed a highly sensitive pH-responsive fluorescence polymer probe for selective imaging of acidic tumor cells, because the probe will only respond to the weakly acidic tumor environment (Figure 1).

Poly(*N*-isopropylacrylamide) (PNIPAAm) exhibits thermally reversible soluble–insoluble changes in an aqueous solution in response to temperature changes across a lower critical solution temperature (LCST) at 32°C. Additionally, the LCST of PNIPAAm can be increased to near body temperature with more hydrophilic comonomers, such as *N*,*N*-dimethylacrylamide (DMAAm). pH-sensitive monomers are copolymerized with PNIPAAm, and a phase transition can also be induced by a change in the specific pH near p*K*a of pH-sensitive monomers, such as sulfamethazine acrylamide (SMZ). Therefore, we designed a pH- and temperature-responsive fluorescence polymer probe (ID48S10-FL), comprising p(NIPAAm42%-*co*-DMAAm48%-*co*-SMZ10%), which exhibited phase transition via environmental pH change at 37°C, near body temperature (Figure 2). pH-Dependent intracellular uptake of ID48S10-FL was evaluated.

Experimental Methods

ID48S10 was synthesized by reversible addition-fragmentation chain transfer (RAFT) radical polymerization. RAFT polymerization can control the molecular weight of polymer chains with narrow molecular-weight distribution. The pH-dependent LCST of the polymer was determined by measuring the optical transmittance in aqueous buffer solutions (0.5 w/v%) at 500 nm. ID48S10 was grafted to 5-aminofluorescein (FL) using the formation of an amide bond between the carboxyl end group of ID48S10 and the amino groups of FL, to obtain ID48S10-FL.

HeLa cells were seeded into 35 mm glass-bottom dishes (5×10^4 cells, 2 mL/dish) and cultured for one day at 37°C in minimal essential medium (MEM) with nonessential amino acids (NEAA) with 10% fetal bovine serum (FBS) with 5% CO_2. Cultured cells were exposed to ID48S10-FL (400 μg/mL) in MEM at pH 7.4 or 6.8 at 37°C for 4 h with 5% CO_2. After incubation, HeLa cells were rinsed with Dulbecco's phosphate-buffered saline (DPBS) three times. HeLa cells were fixed with 4% paraformaldehyde phosphate buffer solution (Wako) for 20 min and rinsed with DPBS twice. Samples were visualized with glass-bottom dishes by a confocal laser scanning microscope.

Results and Discussion

Sharp transmittance curves of ID48S10 in aqueous buffer solutions were observed regardless of pH (Figure 3). LCST and zeta potentials of ID48S10 as a function of pH values are shown in Figure 3B. The zeta potentials of ID48S10 showed only negative values. As the pH value decreased, the zeta potential increased. The charge neutralization of SMZ by protonation of the sulfonamidic group (-SO_2N*H*-) with decreasing pH values can be attributed to increasing zeta potential as well as to hydrophobization of polymer chains. Consequently, LCST of

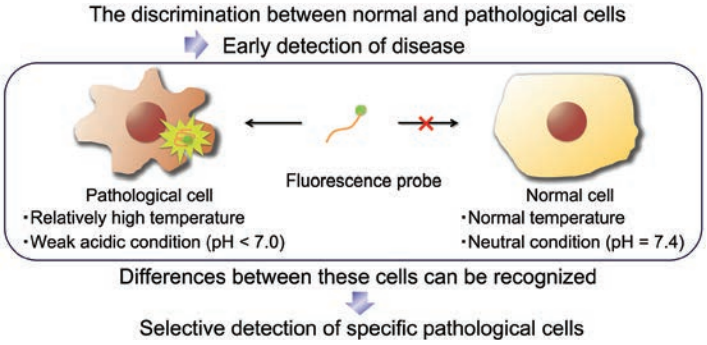


Figure 1. *Tumors absorb a fluorescence probe under weakly acidic conditions.*

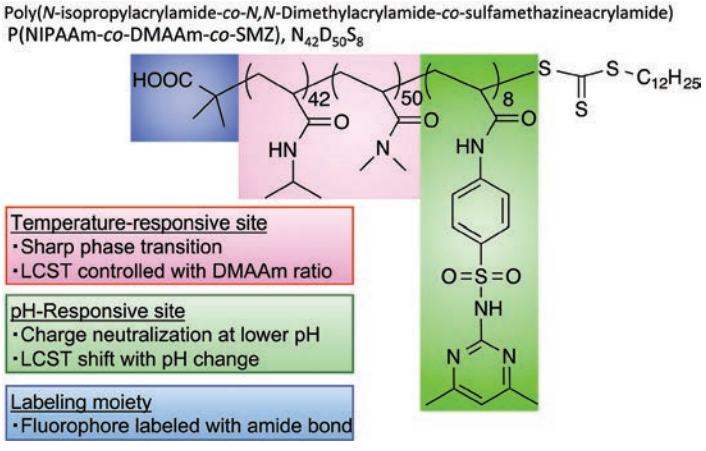


Figure 2. *The design of the pH-responsive fluorescence polymer probe.*

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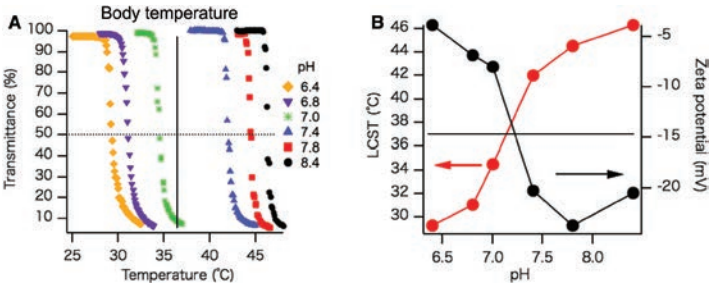

Figure 3. *(A) Temperature-dependent optical transmittance of ID48S10 as a function of pH; (B) LCST and zeta potential of ID48S10 as a function of pH. Reprinted from Hiruta et al. (2015), with permission from Elsevier.*[2]

ID48S10 drastically decreased as the pH value decreased. ID48S10-FL was incubated at two pHs (6.8 and 7.4). While the green fluorescence derived from ID48S10-FL was hardly observed at pH 7.4, fluorescence can be clearly observed at pH 6.8 (Figure 4). The cellular uptake of ID48S10-FL in only weak acidic conditions seems to be because of two factors: 1) hydrophobization of the polymer chains via protonation of the sulfonamidic group, and 2) increasing hydrophobic interactions between the polymer chains and cell membranes. In addition, ID48S10-FL was merged with LysoTracker by utilizing multistaining with LysoTracker, and Hoechst 33342 and ID48S10-FL were merged with LysoTracker. These results indicated that ID48S10-FL might be internalized by HeLa cells, by way of endocytic pathways into the lysosomes.

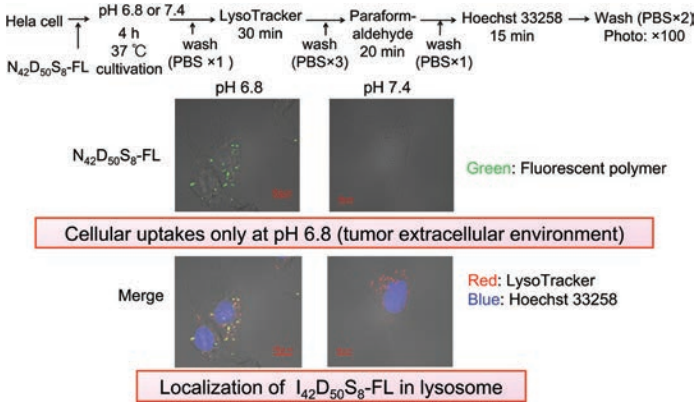

Figure 4. *pH-dependent cellular uptake as shown by fluorescence microscopy images of HeLa cells incubated with ID48S10 at pH 6.8 or 7.4. Green: ID38S10; blue: Hoechst 33342; and red: LysoTracker.*

Conclusion

In conclusion, we have developed a highly sensitive pH- and temperature-responsive fluorescence polymer probe. ID48S10 showed drastic phase transition (hydrophobic/hydrophilic) change at pH-dependent temperatures. While the zeta potential closed to 0 mV by neutralization of the SMZ moiety, LCST temperatures decreased with decreasing pH values. ID48S10-FL was internalized by HeLa cells at only the pH of 6.8, confirming the pH-dependent cellular uptake of ID48S10. These results indicated that a pH- and temperature-responsive fluorescence polymer probe has the potential to be applied for selective imaging of acidic tumor cells. Thus, these methods could provide new opportunities for the development of molecular diagnostics, drug deliveries, biosensing, and bioimaging technologies.

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In Situ-Gelling Hydrogels for Ophthalmic Drug Delivery Using a Microinjection Device

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McMaster University, Canada

The primary causes of vision loss in developed nations are related to diseases of the posterior eye (age-related macular degeneration, diabetic retinopathy, posterior uveitis, retinitis due to glaucoma, etc.).[1,2] However, this is a particularly difficult target tissue because of anatomic and physiologic limitations, resulting in few intravitreal treatment options being available. Intravitreal injections have been the preferred option because they are a facile, direct method of delivering therapeutic or delivery systems. Unfortunately, to maintain therapeutic levels frequent injections are typically required, which greatly increases the risk of complications over time and is inconvenient and uncomfortable for the patient.[2]

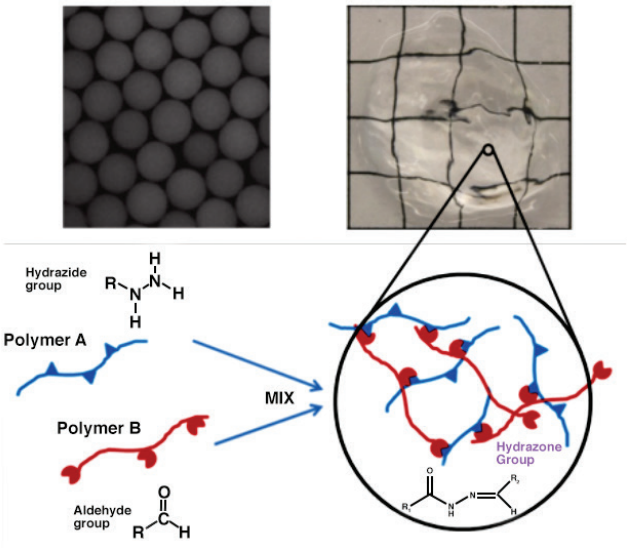

Figure 1. *In situ-gelling system to create hydrogels and microgels.*

Hydrogels are a potential solution to this issue, because they can facilitate prolonged delivery of a drug to the eye and limit the number of required injections for effective treatment. Our research group has developed injectable, degradable hydrogel-based materials for ophthalmic applications that could prolong drug release and have highly adjustable properties (swelling, refractive index, gelation time, and API uptake and release). The hydrogels utilize the rapid chemical reaction of hydrazide-functionalized and aldehyde-functionalized polymers to form hydrolytically degradable hydrazone bonds that are the basis of the crosslinks in the hydrogel structure (Figure 1).[3]

These materials have also shown promising *in vitro* results in many cases, including a hydrogel that does not swell after injection that also matches the refractive index of the vitreous humour. However, assessing the *in vivo* characteristics of these materials is difficult because these experiments require injections in the range of 1–5 µL (and up to 10 µL for humans). While this is facilely done with single component systems, no suitable system exists for the administration of *in situ*-gelling hydrogels at such low volumes. Furthermore, single-component microliter-scale syringes cannot be used with these materials because the *in situ*-gelling nature of these hydrogels is much too rapid to be used with such devices.

The proposed system design should (1) effectively mix the two precursor polymers from separate channels upon injection; (2) controllably and precisely inject volumes in the 1–10 µL range through a narrow-gauge needle suitable for ophthalmic applications; and (3) rapidly inject these materials to prevent gelation and blockage within the needle. Additionally, surgeons want the device to be ergonomical, the injection process to not be too rapid (surgery times may vary from 1 to

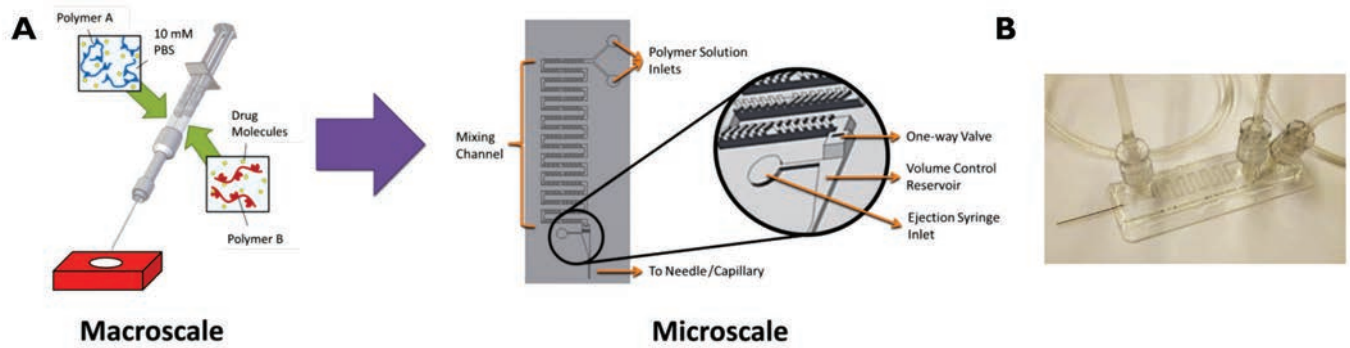

Figure 2. *(A) Macroscale double barrel syringe (left) and the microfluidics-based microinjector device design, highlighting the volume-control reservoir with the associated one-way valve (right), and (B) the polydimethylsiloxane-based device itself.*

5 min), and for the operation to be as similar as possible to the current method (summarized in the box below).

The microinjector was designed to operate analogously to this macroscale system, which involves a double-barrel syringe that has solutions of hydrazide-functionalized polymer (polymer A) and aldehyde-functionalized polymer (polymer B) in separate loading barrels (Figure 2A). Upon injection, these two solutions interact in the mixing channel and needle, forming the hydrazone bonds that crosslink the polymer to form a hydrogel.

The microinjector design (Figure 2B) consists of two separate inlets that a double-barrel syringe can be connected to, a serpentine mixing channel with herringbone grooves (developed by Strook *et al.*)[4] to promote mixing, and a volume-control reservoir with a one-way valve coupled with a second syringe input port that can be used to eject the mixed polymer solutions out the needle (into the eye). The device is operated by placing the two reactive polymer solutions in separate barrels of a double-barrel syringe and attaching that syringe to the two polymer solution inlets, and the mixed fluids can be pushed through to the needle. The needle can then be inserted into the eye, and an ejection syringe can be compressed to only eject the volume of mixed polymer solution in the volume-control region, because of the one-way valve that is present. The volume-control region can be designed to be of any volume from 1 µL to 5 mL.

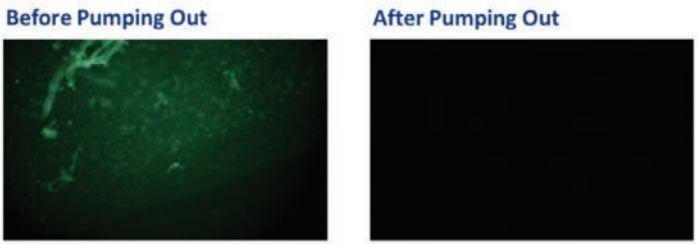

Figure 3. *Fluorescent imaging fluorescein isothiocyanate–labelled polymers before and after pumping out.*

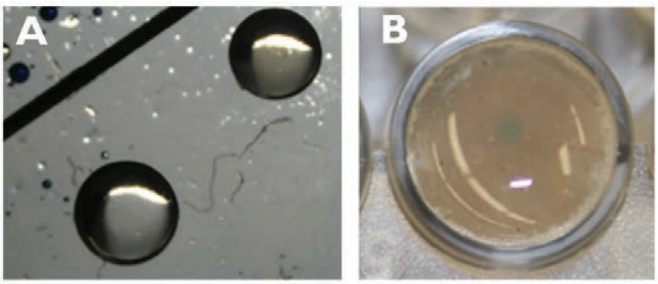

Figure 4. *(A) 2 µL gelled hydrogel droplets in paraffin oil, and (B) dyed blue in bovine vitreous humour at 37°C*

Mixing fluids within microfluidic channels is inhibited by the fact that fluid flows at microfluidic scales are laminar in nature. The addition of herringbone grooves was found to dramatically improve the degree of mixing within the channels of preliminary device prototypes, creating microvortexes and allowing for nearly complete mixing only a short distance (1.75 cm) from the point where the two separate solutions first interact within the channels.

With the volume-control chamber and the one-way flow valve, the device is able to eject droplets with controlled volumes (± around 10%) in the range of interest (1–10 µL) via an entirely handheld operation, requiring no additional equipment. The entire volume of the material can be ejected from the device, as indicated by using fluorecently labelled polymers and observing the volume-control reservoir before and after the ejection of a 2 µL sample of gel (Figure 3). These microinjectors can produce hydrogel droplets from multiple combinations of reactive polymer solutions. These hydrogels can be ejected from devices with 33G needle outlets and smaller capillary outlets (prefered in order to lower the overall cost of the devices) into various materials, including bovine vitreous humour at 37°C (Figure 4).

This microinjection device has proven capable of injecting precise small amounts (1–10 µL) of *in situ*-gelling hydrogel precursors, which allows for the *in vivo* assessment of injectable hydrogels as ocular drug delivery materials, which will be available shortly. The hydrogels that this device can deliver to the eye could provide significant improvements over current therapies in terms of treating diseases of the posterior eye.

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2. Sheardown, H. Critical role for drug delivery in the development of new ophthalmic treatments, Future Med. Chem. 4: 2123-2125 (2012).
3. Patenaude, M, Hoare, T. Injectable, degradable thermoresponsive poly(*N*-isopropylacrylamide) hydrogels, ACS Macro Letters 1: 409-413 (2012).
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Patent Watch

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

This article briefly summarizes novel aspects of selected U.S. patents involving controlled release or delivery that were issued from January 1 to June 30, 2014. Selections have been loosely categorized into interest areas; however, many overlap into multiple categories. Greater detail on each can be found on the U.S. patent website at http://patft.uspto.gov/.

Abuse Deterrent

U.S. patents 8,685,447 and 8,691,270 – A super-absorbent is incorporated into a coating layer as an abuse deterrent to swell and retard release of analgesic when crushed and exposed to aqueous media.

U.S. patent 8,685,916 – Controlled release of an opioid is achieved by enzymatic cleavage, which can be modulated with a trypsin inhibitor.

U.S. patent 8,623,412 – Waxes are applied both as a particle coating and tableting matrix to control release of analgesic materials. The resulting matrix limits extractability of the analgesic to less than 15% of the immediate release therapeutic level.

Agriculture

U.S. patent 8,741,804 – Coated magnetic nanoparticles are covalently bound to the shell of microcapsules of agricultural interest to control microcapsule shell rupture with a magnetic field.

U.S. patent 8,679,546 – A ruminant feed pellet consisting of a matrix core containing active substances and multiple coat layers is described for controlled release of the actives.

U.S. patent 8,756,862 – A structurally stable substrate with interconnecting pores is constructed of composted bark, a carbon-based fibrous material, a hydrophilic polymer, sea solid, beneficial bacteria/fungicide, and a controlled release fertilizer to provide an optimum combination of nutrients, water retention, and pest and fungus control.

U.S. patents 8,741,021 and 8,741,022 – A variation of sulfur-coated urea including an *in situ* polymerized or thermoset polymer layer provides robust, economically viable controlled release nitrogen sources.

Antibiotics

U.S. patent 8,758,804 – A gum-like device/composition for sustained delivery of rifaximin to surfaces in the mouth and similar cavities is disclosed.

U.S. patent 8,748,447 – Extended oral release of rifaximin is achieved in a spray-dried powder form.

U.S. patent 8,628,797 – Release rate of poorly soluble bioactives such as clarithromycin in a tablet is controlled by the viscosity differential of tableting polymers while eliminating or minimizing food effects.

Complexes

U.S. patents 8,709,500 and 8,747,912 – Anionic drug molecules are intercalated into layered double hydroxides for controlled oral delivery.

U.S. patent 8,734,652 – Porous metal organic frameworks of Al-fumarates are described for use as controlled release of guest materials.

U.S. patent 8,680,202 – Cyclodextrin-containing polymers are described as drug carriers for controlled delivery of therapeutics.

Devices/Implants

U.S. patents 8,647,657 and 8,722,078 – A copolymerized, biodegradable blend of poly-lactide/glycolide or the like and a poly-alkyleneneglycol are coextruded with API for sustained release of the API.

U.S. patent 8,715,707 – A freeze-thaw temperature cycle is used to modify release properties of a stent coating.

U.S. patent 8,658,195 – A polyurethane membrane is applied to implantable reservoir devices to control drug release.

U.S. patent 8,758,428 – A stent coated with a coating layer, bioactive material layer, and vapor deposited polyamide or parylene layer is used to control bioactive material release.

U.S. patent 8,709,467 – A microfilm device consisting of a para-zylylene membrane is disclosed for controlled bioactive delivery.

U.S. patent 8,628,798 – Water-swellable linear polyurethane polymers capable of swelling 300–1,700% for controlled release of high-molecular-weight bioactives are disclosed.

U.S. patent 8,623,399 – Microminerals impregnated in a porous silicon subcutaneous implant are released over a period up to a year via complete corrosion of the implant or breaching of bioerodible doors.

U.S. patent 8,679,094 – Intravesical devices that can be implanted in the bladder for controlled drug release within the bladder are disclosed.

Fragrances

U.S. patent 8,715,702 – Fragrance/surfactant compositions are encapsulated in 30 μm polymerized tetraalkoxysilane shells for controlled release in fabric softeners, hair conditioners, and the like.

U.S. patent 8,685,425 – Coacervate microcapsules possessing Lewis acid–Lewis base salt walls are used to control release of a water-immiscible core, such as insect repellent or fragrance.

Injectables

U.S. patent 8,734,852 – Injectable formulations of aceclofenac and/or diclofenac with immediate and up to 72 hours of sustained release are described.

U.S. patent 8,722,679 – A freeze-dried injectable aripiprazole formulation is disclosed for sustained release for a period up to eight weeks.

Miscellaneous

U.S. patent 8,715,478 – This invention provides a means to electrically control ion transport for physiological process control in cells.

U.S. patent 8,629,098 – Modular artificial antigen-presenting cells are described for controlled cytokine release.

U.S. patent 8,709,481 – Biodegradable polymers are used with acid-sensitive API complexes for controlled delivery up to 18 days.

U.S. patent 8,703,907 – Covalently bound drugs are released from dendrimers through controlled beta elimination.

U.S. patent 8,697,117 – A freeze-dried, inverted emulsion formulation is used to create polymeric films for controlled release in physiological fluids.

U.S. patent 8,652,378 – Processes and formulas for creating uniform thin films of taste-masked bioactives for oral delivery are described.

U.S. patent 8,691,272 – A trilayer controlled release tablet consisting of a drug-containing, nonerodible core sandwiched between two release modulating layers is described.

U.S. patent 8,674,132 – This invention involves location and nature of modulating substituents to control release of HNO from *N*-hydroxylsulfonamide derivatives for treatment of heart failure and the like.

U.S. patent 8,652,506 – Block/graft arrangement in biodegradable block co-polymers is used as a means to control drug release.

U.S. patent 8,632,798 – Cereal β(1-3) β(1-4) glucan is used as a coating for controlled delivery of pharmaceutical, medical, or confectionery agents in the mouth.

U.S. patent 8,722,067 – Ultrasonication is applied to speed silk fibroin gelation to produce a hydrogel controlled delivery matrix.

U.S. patent 8,734,850 – Orally delivered drug release is controlled with a two-coat configuration consisting of an inner layer containing a swell agent and an outer enteric layer.

U.S. patent 8,691,275 – A solubility-enhancing localized pH condition is maintained through the digestive tract in an oral controlled release melatonin formulation.

U.S. patent 8,668,954 – An extrusion of mineral particles and binder forms porous granules for incorporation and controlled release of algaecide.

U.S. patent 8,754,190 – Drugs are bound to macromolecular carriers via linker functionalities whereby drug release is controlled by beta-elimination.

Osmotic Systems

U.S. patent 8,703,193 – Osmotic tablets are described for controlled release of venlafaxine or metoprolol using controlled porosity coatings without a drilled hole.

U.S. patent 8,679,534 – An osmotic tablet consisting of a water-insoluble coating with an enteric pore former is described for controlled release of cholesterol reducing agent.

Proteins/Peptides

U.S. patent 8,623,345 – Polymer-insulin conjugates for controlled release of insulin in response to increased glucose concentration are described.

U.S. patent 8,642,082 – Controlled release oral compositions of heparin are described.

Transdermal

U.S. patent 8,747,889 – A transdermal controlled delivery system for fentanyl with abuse deterrent features consisting of drug and antagonist reservoirs is described.

U.S. patent 8,696,637 – A transdermal microneedle assembly patch is disclosed. ■

How to Be a Scientist and yet Write a Literary Novel

Gregory Gregoriadis,[1] University College London School of Pharmacy, United Kingdom

I have a confession to make: I have written a novel, a work of fiction. It has been just published. "Oh, I see," you may say. "You were a scientist and now you are an arty person. A high-brow bohemian engrossed in dreams and fairy tales, dancing on clouds." "Yes," I would reply, but, mindful of my academic record being blemished, I would add hurriedly. "I am still a scientist, you know. I publish the odd review, articulate a comment here and there, disagree in silence with someone's assertions. In silence, because of my inability to use a flask or a pipette, or to prepare a drug solution. Because I can't inject a rat, observe its reaction, and hopefully prove my point. You see," I would go on bitterly, "I do not have a lab to test my ideas. I have no affiliation either, just an emeritus at University College London. I am no longer king, head of something. Only of myself. I am retired, a superannuated has-been."

Alas, I can no longer direct others. I have no orchestra, no violins and cellos, trombones and clarinets. My concert hall is empty, the piano smothered by spider webs. Only ghosts of players, slowly fading in the mist of my receding memory. I would listen to the "Ridi Pagliaccio" threnody on the gramophone and sigh in despair, "It is not fair." Yes, grossly unfair because, after all these years of science, of publications and conferences, my creativity is still alive and kicking, violently in fact. Yet I have been condemned to paralysing inaction, to ever-decreasing years of boredom and decay, soon to be forgotten. Some may still remember me, vaguely perhaps, wondering whether I am still around, googling for my obituary. I know because I have done it myself more and more recently.

Thinking of my future, the dead end of it, has not been easy. One after the other, well-meaning colleagues lacerated me with the promise of horticulture, the martyrdom of a kitchen garden, of tomatoes, leeks, and courgettes. "But," I would protest, remembering another retired colleague, "didn't so-and-so take up gardening and pay for it? Didn't he drop dead in the midst of his cabbages?" "Well, he tried to pull out an enormous turnip with his bare hands, didn't he?" said the well-meaning colleagues. Others, wiser perhaps, would suggest philately. "Invest in stamps," they said, "look at it long term." What long term? I thought, and shivered. I had been transferred to my childhood, the abomination of stamp collecting. In my private moments I even toyed with travel, blood-curdling memories coming into me of boats of pleasure packed with fun-loving oldies. Peregrinating the oceans with them, an invisible dead soul among many.

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Until one day, the day I saw my lab to be my orchestra and the players. It was there, in my room, waiting for me. A table, a pad of A4 paper, and a fountain pen. I had seen my crucible of thoughts, of creation. I would write a story, a long one. I would be king again. And, oh boy, did I have a story to tell! I had been dreaming of it since the time of my teens. A story of things that happened to me and to my friends, my family, and neighbours, to all of us Athenians. In the shadow of the Parthenon, where we lived, under the Acropolis. I remember sitting down, a virginally white sheet of paper waiting to be relished, a pen raring to have its ink shed on paper, creating the words and the sentences. Stories of Mussolini and Hitler, of the Nazis on top of us, the executions and the great famine. Of corpses in the streets. Stories of pathos and Eros as we listened to the cicada song. I wrote and wrote, forgetting myself and the world, then stopped to refill my fountain pen. I read the lines and the paragraphs, page after page, horror after horror. This was not a literary novel! Cold sweat bathed my face. What had I done? What a literary disaster. A series of disgusting, languor-dripping sentences. The scientist in me had woken up from his stupor, spewing chunks of a Results and Discussion–like text, logically composed, expectorations of accuracy and common sense masquerading as a literary novel. It was a monstrous text. I kept writing, desperate to free myself from the shackles of scientific rationale, of cause and effect. Escape from the lexicon of irksome entries, of sterile sentences studded with pretentious epithets: "in conclusion therefore and on the basis of mellifluous statistics, the Nazis had murdered our heroes." Or, "he thought of the scrumptious results obtained under controlled conditions, and concluded the famine had killed her." The paper basket by my side overflowed with screwed up pages of aborted literary feats.

> *"It was there, in my room, waiting for me. A table, a pad of A4 paper, and a fountain pen."*

And as I sat there by the paper basket observing the ruins, my wasted hours, the never-ending labour of Sisyphus, wondering whether I should revisit the dreaded gardening, philately, and boats of pleasure, I rebelled. "No, my friend!" I said to myself in anger, my scary cry reverberating within my room. "You've got to change your ways, forget the trodden paths of scientific writing, the soulless patent-speak. This is fiction, my friend. You are in control, total unmitigated control." There was a little silence. "Total control? Really? Isn't this too good to be true?" I asked. Then the scary voice again: "Yes, total control, you dummy. You can lie *ad nauseam,* experiment on storytelling, create your narrative, be another Homer. Choose words never seen in a science paper, produce your own results, modify them, and then

adjust them to suit your needs, your plot. You are a master of marionettes, the controller of their moves, their moods and utterings. You can give them life then take it away. You can turn them into heroes, a latter-day Odysseus, merciless assassins, a tempestuous Circe. You decide. You are the god Zeus and the goddess Athena of the world you have created. But remember, my friend, should your endeavours take you to mixing history with fiction, stick to the truth, the scientific facts. Spread the facts wisely among the scenes of horror, of death and love and passion. Be a Thucydides." I had listened to the voice, mesmerised. It all sounded so exciting, so liberating. A solitary tear had exited the corner of my eye. I heard my voice, a throaty murmur: "I will write a real novel. I will."

Gregory Gregoriadis's book Still the Cicadas Sing *was published by Matador in early 2015. He is a professor emeritus at University College London and the founder of Xenetic Biosciences Inc. He introduced liposomes (1971) and polysialic acids (1991) in drug and vaccine delivery and has published extensively on the subject. Gregory Gregoriadis was the director (1981–1999) of the NATO Advanced Study Institutes "Targeting of Drugs" and "Vaccines." He was the founder (1978) of the "Drug Carriers in Medicine and Biology" Gordon Research Conference series and, since 1990, chair of the "Liposome Advances" conferences. He has received numerous awards, including the CRS Founders Award (1994), and is a CRS Fellow.* ■

Welcome New CRS Members

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CRS
Leading Delivery Science and Technology

CRS New Zealand Local Chapter (NZCRS) Events in 2014

Mimi Yang[1] and Sharan Bobbala[2]

"Controlled Release in Response to Environment" was the theme of the 2014 NZCRS Workshop, November 24–25 at the University of Auckland, which was jointly hosted by the New Zealand and Australian CRS Local Chapters. Invited speakers explored applications of controlled release in agriculture, wildlife, and animal health.

The session "Agriculture and Environment Controlled Release" commenced with plenary speaker Charles Frey, principle scientist at Coating Place (U.S.A.), who discussed the Wurster fluid bed and related coating technologies and their applications in agricultural and environmental formulation research, including the need for taste masking, enteric delivery, sustained release, and delayed release. Continuing this theme, Craig Bunt from Lincoln University (NZ) discussed important insights into microbial formulations and toxin delivery for pest and wildlife control. Ben Boyd (Monash University, Australia) discussed his research on "Nanostructured Emulsions for Agricultural Chemical Delivery—Formulation to Field."

University of Otago participants who travelled to Auckland for the NZCRS Workshop. Left to right: Arnold Lee, Siddarth Matikonda, Sasi Yarragudi, Greg Walker, Katrin Kramer, and Sharan Bobbala.

A breakout session opened the floor to delegates to briefly describe their research. Postgraduate students were invited to raise any issues they had in their experiments, and industry professionals and academics offered advice or research directions. This strategy was effective to introduce attendees to each other and enabled the identification of individuals with specific skills or knowledge.

The second session, "Targeted and Active Controlled Release," opened with Darren Svirskis (School of Pharmacy, University of Auckland, NZ), who introduced us to controlled drug release from non-biodegradable materials including stimuli-responsive delivery systems. Javad Foroughi (Intelligent Polymer Research Institute, University of Wollongong, Australia) discussed his research in the development of novel nanofibres (both biopolymers and conducting polymers) with biomedical applications in controlled release and tissue engineering. Greg Walker (School of Pharmacy, University of Otago, NZ) presented the interesting utility of electrospinning in agricultural applications and demonstrated that it is indeed possible to electrospin an entire potted plant!

Another breakout session with the translational topic of laboratory to field challenges discussed issues and challenges in this area, and insightful advice was given by our many experts, including industry delegates from Ballance Agri-Nutrients.

Postgraduate student attendees were given a three-minute time slot to talk about their research with the aid of one PowerPoint slide to highlight their poster. Interesting projects and hypotheses were brought forth in many disciplines of controlled drug delivery. Arnold Lee (School of Pharmacy, University of Otago, NZ) was the winner of the postgraduate student prize at the completion of this session.

An excellent conclusion to the day was a tour of the University of Auckland School of Pharmacy laboratories, where students were given the opportunity to show the guests the research facilities.

The theme of the third and final session of the workshop was "Wildlife and Livestock Controlled Release," which began with Lee Shapiro from Connovation Ltd. (NZ), who discussed regulatory obstacles involved with registering vertebrate toxic agents in New Zealand. Per Wessman (Innovative Farm Systems, AgResearch Ltd., NZ) continued discussions on agricultural applications of controlled release with his talk on "Microbial Formulations for Agriculture: Targeted Delivery and Controlled Release of Beneficial Micro-organisms." Charles Frey followed with his talk on "Controlled Release Coating Technologies for Animal (and Human) Applications – Taste Masking, Improved Stability, and Improved Delivery," in which he discussed processes, materials, and strategies of film coating to successfully achieve controlled release. Kate Wilson from James & Wells (NZ) discussed intellectual property and gave the audience tools to identify potentially valuable aspects of their work and steps to ensure maximum opportunity.

The 2014 NZCRS Workshop was highly informative and thought provoking, as well as excellent exposure of research for postgraduate students involved.

Mimi Yang and Dedeepya Uppalapati (University of Auckland) ready to welcome delegates for the 2014 NZCRS Workshop.

1 School of Pharmacy, University of Auckland.
2 School of Pharmacy, University of Otago.

The D[4] Conference – Devices for Diagnostics and Drug Delivery – was a joint conference of the Formulation and Delivery of Bioactives (FDB) research theme of the University of Otago, the Consortium for Medical Device Technologies (CMDT), the Centre for Bioengineering and Nanomedicine, and NZCRS.

Delegates at the D[4] conference, which took place at Hutton Theatre, Otago Museum, Dunedin, New Zealand. Photo by Len Stevenson.

The opening presentation was given by David Grainger (University of Utah, U.S.A.) on improving the performance of diagnostic devices and combination medical devices. Prof. Grainger quoted several commercial examples to support the common problems and technical approaches currently underway for these devices. Abraham Rubinstein (University of Jerusalem, Israel) addressed *in situ* diagnosis and screening of early malignancy in the gastrointestinal tract by using novel targeted delivery vehicles. David Budgett (Auckland Bioengineering Institute, NZ) spoke on monitoring of intracranial pressure in traumatic brain injury patients. He explained challenges associated with a brain pressure monitoring device in development and regulatory stages. Rajesh Katare interpreted the importance of circulating microRNAs as biomarker for the early diagnosis of cardiovascular disease in people with diabetes. Stephen Sowerby (University of Otago, NZ) gave insight into a simple portable digital microscopy system developed in their lab for imaging parasite ova in stool samples and their importance in monitoring antihelminthic drug efficacy. Ben Boyd concluded the session with a talk on development of self-assembled lipid systems as new design elements for diagnostic systems.

Invited speakers at the D[4] Conference. Left to right: Azim Ali, Andrew Taberer, Stephen Sowerby, Anand Kumbble, David Grainger, Stewart Jessamine, David Budgett, Ben Boyd, James Birchall, Quentin Pankhurst, Chuck Frey, and Shyamal Das. Photo by Len Stevenson.

James Birchall (Cardiff University, U.K.) spoke on microneedle devices for drug and vaccine delivery through skin. His explanation on microneedle usage in targeting the skin immune cells for the treatment of diabetes was the highlight. Another interesting aspect on health care biomagnetics was introduced to the audience by Quentin Pankhurst (University College London, U.K.). He described magnetic nanoparticles' role in targeting and activation for the controlled release technology. Andrew Taberner (Auckland Bioengineering Institute, NZ) presented a novel concept of fluid jets for needle-free delivery through the skin and the ability of these devices to extract fluids from the injection site. Shyamal Das (University of Otago, NZ) discussed the application of spray-dried powders in pulmonary delivery. Chuck Frey's presentation emphasized the evolution of coating equipment and different formulation strategies employed in coating. Rapid-fire oral presentations of posters from the postgraduate students concluded the session with three-minute bursts of enthusiasm.

On the second day, Stewart Jessamine (Medsafe, Wellington, NZ) discussed the regulatory concerns in translation. Anand Kumble (Pictor, Auckland, NZ) engaged all the audience by describing his experiences in translating an expensive lab ELISA technique to a low-cost immunodiagnostic for different diseases. Craig Bunt demonstrated application of 3D printing in developing drug delivery and medical devices by showing some interesting videos. Azam Ali (University of Otago, NZ) spoke on translation of biomaterials into devices. George Dias (University of Otago, NZ) gave a stimulating talk on usage of a resorbable keratin-based biopolymer in bone-regeneration scaffolds. The session ended with a motivating presentation from David Powell (Lost Ark Discoveries, NZ) on U.S. medtech innovation and lessons learned from it.

NZCRS president Arlene McDowell awards the NZCRS speaker prize to Sharan Bobbala. The title of Sharan's presentation was "Novel Injectable Pentablock Copolymer Hydrogels for Sustained Release Cancer Vaccines." Photo by Rohit Jain.

The final session of day two comprised oral presentations covering different research areas from postgraduate students and postdoctoral fellows from New Zealand and Australia. After oral presentations, Arlene McDowell (NZCRS President) announced the NZCRS speaker prize winner for 2014: Sharan Bobbala from the School of Pharmacy, University of Otago. ■

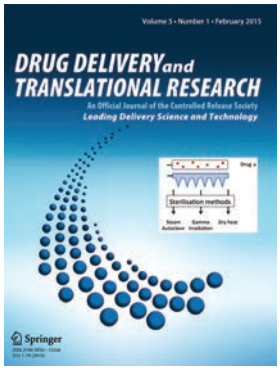
Drug Delivery and Translational Research (DDTR)

Vinod Labhasetwar, Editor-in-Chief, Cleveland Clinic, Cleveland, Ohio, U.S.A.

Vinod Labhasetwar

In the last issue of the *CRS Newsletter*, I highlighted the "impact of negative data" and *DDTR* policy. In the upcoming issue of *DDTR*, you will see an editorial on the same topic. *DDTR* will consider publication of studies that are based on a strong scientific rationale, hypothesis, or technology but resulted in a negative or unexpected finding. Authors are strongly encouraged to discuss in the manuscript the possible reasons why experiments failed and what alternative approaches or changes to the hypothesis or experimental design might be made.

In this regard, I wish to highlight an article published in the current issue of *DDTR* by McConville et al., titled "Lack of *In Vitro–In Vivo* Correlation for a UC781-Releasing Vaginal Ring in Macaques," which falls into the above category. This study describes the preclinical development of a matrix-type silicone elastomer vaginal ring device designed to provide controlled release of UC781, a non-nucleoside reverse transcriptase inhibitor. Testing of both human and macaque-sized rings in a sink condition *in vitro* release model demonstrated continuous UC781 release in quantities considered sufficient to maintain vaginal fluid concentrations at levels 82- to 860-fold higher than the *in vitro* IC_{50} (2.0–10.4 nM) and therefore potentially protect against mucosal transmission of HIV. The 100 mg UC781 rings were well tolerated in pig-tailed macaques, did not induce local inflammation as determined by cytokine analysis, and maintained median concentrations in vaginal fluids of UC781 in the range of 0.27–5.18 mM during the course of the 28-day study. Analysis of residual UC781 content in rings after completion of both the *in vitro* release and macaque pharmacokinetic studies revealed that 57 and 5 mg of UC781 were released, respectively. The pharmacokinetic analysis of a 100 mg UC781 vaginal ring in pig-tailed macaques showed poor *in vivo–in vitro* correlation, attributed to the very poor solubility of UC781 in vaginal fluid and resulting in a dissolution-controlled drug release mechanism rather than the expected diffusion-controlled mechanism.



DDTR Special Issue on Tissue Engineering

DDTR has published 10 high-impact special issues and is currently developing a few more for publication in 2015–2016. If you are interested in developing a special issue in your area of expertise, please contact me (Vinod Labhasetwar, labhasv@ccf.org) with a proposed topic and outline. A special issue on tissue engineering, guest edited by Sing Yian Chew of Nanyang Technological University, Singapore, and Kam W. Leong of Duke University, U.S.A., will be published as the March/April issue of *DDTR*.

Call for Papers

DDTR is currently accepting submissions for three special issues:

- "Microneedles for Drug and Vaccine Delivery and Patient Monitoring," which will showcase emerging pharmaceutical, engineering, and formulation approaches to manufacture of microneedles, while also looking at their applications in drug and vaccine delivery and minimally invasive patient monitoring and diagnosis. Topics include gene/drug delivery systems, vaccine delivery systems, and material design and production, with a strong focus on clinical translation and commercialization. Guest editors are Ryan Donnelly (r.donnelly@qub.ac.uk) and Dennis Douroumis (D.Douroumis@greenwich.ac.uk).
- "Orthopedic Biomaterials and Drug Delivery," which will feature emerging pharmaceutical and regenerative approaches to treat injuries, diseases, and disorders of the musculoskeletal system. Topics include gene/drug delivery systems, cell-based therapies, and biomaterials to support orthopedic tissue regeneration and/or disease modification. Please contact guest editors Blanka Sharma (blanka.sharma@bme.ufl.edu) and Shyni Varghese (svarghese@eng.ucsd.edu).
- "Recent Advances in Dermal Delivery of Therapeutics," which will showcase articles encompassing emerging approaches to delivering therapeutic agents. Topical products have been one of the major conventional modes of delivering pharmaceuticals. The nature of vehicles used in topical delivery of therapeutics has undergone significant evolution. Please contact guest editor S. Narasimha Murthy (murthy@olemiss.edu).

DDTR Outstanding Research Paper Award

Consider submitting your best research for the 2015 *DDTR* Outstanding Research Paper Award. The paper will be selected from the research articles, clinical research, and clinical trials published in *DDTR* during 2015 and will be presented during the 43rd CRS Annual Meeting, July 17–20, 2016, Seattle, Washington, U.S.A. Visit the CRS website for award criteria.

Free Access for CRS Members

Visit the *DDTR* website to glance through research articles, reviews, editorials, and special issues published in *DDTR*. CRS members receive free access to the online journal content as a membership benefit. Login to the CRS website first, and then click the Publications tab to get to the member access link. ■

People in the News

Compiled by Steven Giannos, Independent Consultant

Congratulations to **Robert Langer** of the Massachusetts Institute of Technology on receiving the Queen Elizabeth Prize for Engineering, which includes a £1 million award.

Langer runs one of the largest academic laboratories in the world, is the most cited engineer in history (170,000 times), has more than 800 patents granted or pending, and has co-founded over 20 companies. His connections with CRS include belonging to the CRS College of Fellows, being a past president of CRS (1991–1992), and receiving the Founders Award (1989), and many prominent CRS members are connected in some way to the Langer Lab at MIT.

The award credits him with improving more than 2 billion lives worldwide through disease treatments created in his lab. Langer is known for bringing together researchers from many different disciplines, and this interdisciplinary approach is central to CRS and to our members' work.

Father of PEGylation to Receive Dr. Sol J. Barer Award at Gateway Gala, BioNJ's 22nd Annual Dinner Meeting, Networking Event and Innovation Celebration

Business Wire: January 13, 2015 – TRENTON, NJ, U.S.A. – Abraham Abuchowski, Ph.D., considered the father of PEGylation, the most widely used protein drug delivery system in the world, which has helped save and improve thousands of lives, including many with "bubble boy disease," will be honored with the 2015 Dr. Sol J. Barer Award for Vision, Innovation, and Leadership, at the Gateway Gala, BioNJ's 22nd annual dinner meeting, networking event and innovation celebration on February 5 at the Hilton, East Brunswick, NJ. Dr. Barer will present the award.

PEGylation defines the modification of a protein, peptide, or nonpeptide molecule by the linking of one or more polyethylene glycol (PEG) chains. Medicines developed with a PEGylation delivery system have several advantages, including a prolonged residence in the body, a decreased degradation by metabolic enzymes, and a reduction or elimination of protein immunogenicity. Thanks to these favorable properties, PEGylation plays an important role in drug delivery, enhancing the potentials of peptides and proteins as therapeutic agents.

"Dr. Abuchowski has had a long and lasting impact on biotechnology in New Jersey and beyond," said Sol J. Barer, Ph.D., the former chairman and CEO of Celgene Corporation for whom the award is named. "Based on the innovative technology of PEGylation that he helped pioneer, Abe founded one of the first successful biotech companies in the state. His vision for the industry helped drive the formation of BioNJ as its founding chairman and through his leadership he continues to foster research into areas that have the potential to benefit millions of patients around the world."

Dr. Abuchowski is currently the CEO and CSO of Prolong Pharmaceuticals. Research at Prolong is concentrated on finding treatments for anemias, cancers, and their debilitating comorbidities. A portfolio of hematology and oncology products that use PEGylation technology is in development. Located in South Plainfield, the company announced in December 2014 that it was doubling its manufacturing operations to 24,000 square feet and relocating to a new 12,000 square-foot headquarters.

The development of PEGylation was part of his 1981 doctoral thesis at Rutgers University, which earned him the moniker "the father of PEGylation." In 1983, Dr. Abuchowski left Rutgers to develop PEGylation commercially by founding Enzon, Inc., as a spinout from the university. Enzon was the first biotechnology company in New Jersey to obtain FDA approval of a product. Enzon's first milestone drug was ADAGEN, the uses of which included the treatment of severe combined immunodeficiency (SCID), a rare genetic disease of metabolism that is also known as "bubble boy disease."

In addition to his groundbreaking work with PEGylation, Dr. Abuchowski played a pivotal role in the creation and development of BioNJ, which was formerly known as the Biotechnology Council of New Jersey (BCNJ).

Dr. Abuchowski was among a group of New Jersey life science executives who recognized the need for an advocacy organization to help the then-emerging biotechnology industry realize its potential to discover and develop new medicines and contribute to the economy. He was elected as the organization's first chairman in 1994.

"As our founding chairman, Abe's vision set a direction and tone for this organization that is still having an impact today," said Debbie Hart, president and CEO of BioNJ. "I was fortunate to have been involved with Dr. Abuchowski and his colleagues in the founding of BioNJ, and it has been an honor and pleasure from this vantage point to have the opportunity to learn from and work with him and to watch as he continues to help patients and advance the life sciences industry in New Jersey and around the world."

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People in the News continued from page 21

The Dr. Sol J. Barer Award for Vision, Innovation, and Leadership was established by the BioNJ Board of Trustees in March 2008 in an effort to recognize the outstanding research and business leaders who have made and continue to make significant contributions to the growth of the biosciences in New Jersey and around the world. The honoree is voted on by the BioNJ Board of Trustees from a recommendation based on nominations received by the Nominating Committee. The award is named for Sol J. Barer, Ph.D., who founded the biotechnology group at Celanese that was subsequently spun out to form Celgene, one of the world's largest biotechnology companies.

Past award recipients since 2008 have included Dr. Barer; Dr. Lisa Drakeman, former president and CEO of Genmab; John H. Johnson, then president of global oncology and senior vice president of Eli Lilly and Company; John Crowley, chairman and CEO of Amicus Therapeutics; Paul G. Thomas, founder and CEO of Roka Bioscience; Francois Nader, M.D., president and CEO of NPS Pharma; and Stuart W. Peltz, Ph.D, CEO of PTC Therapeutics.

PixarBio's Dr. Jason Criscione Named Director, Drug Delivery Programs

Business Wire: December 3, 2014 – MEDFORD, MA, U.S.A. – PixarBio Corporation today announced that Jason Criscione, Ph.D., has been named director of drug delivery programs. Dr. Criscione joined PixarBio in March 2014, bringing his immunotherapy drug delivery and materials science experience to design, develop, and clinically translate biomaterials for sustained, local therapeutic intervention in neurological indications.

"Our time-proven R&D model based on concurrent engineering will optimize the speed of development of Dr. Criscione's work."

"PixarBio's founders have translated more products to the clinic than any biomaterials researchers in history. I joined the team to bring immunotherapy approaches to PixarBio, and our early success in pain justifies optimism for the development of novel treatments for a range of acute and chronic neurological conditions such as Parkinson's disease, epilepsy, and spinal cord injury. I've had a great start at PixarBio and now it is time to finish translation to the clinic," said Dr. Criscione.

"Dr. Criscione has been instrumental in developing our postoperative and acute nonopiate pain drug delivery platform. Jason provides PixarBio with new thought leadership around novel approaches to pain and a whole range of immune system disorders," said PixarBio CEO Frank Reynolds. "Our time-proven R&D model based on concurrent engineering will optimize the speed of development of Dr. Criscione's work."

Dr. Criscione received his Ph.D. in biomedical engineering from Yale University. His research focused on designing micro- and nanoparticle platforms to enable intelligent drug delivery and noninvasive, multimodal imaging. His expertise expanded to cover chemistry, polymer and materials science, colloid science, spectroscopy, biophysics, and immunotherapy. He also holds a B.A. in chemistry with a concentration in neuroscience from Oberlin College and an M.S. in physical chemistry from Michigan State University.

PixarBio Corporation is dedicated to developing new therapeutic options for Parkinson's disease, epilepsy, pain, and spinal cord injury. Cofounded by Frank Reynolds, Dr. Robert S. Langer from MIT's Langer Lab, and Katrin Holzhaus, the company is developing novel smart materials to achieve sustained release of agents. Research is focused on a platform for chronic neurological applications. For more information, visit www.pixarbio.com.

PixarBio Cofounder Dr. Robert S. Langer Honored with Prestigious 2014 Kyoto Prize

Business Wire: November 19, 2014 – MEDFORD, MA, U.S.A. – PixarBio Corporation is pleased to announce that its cofounder Dr. Robert S. Langer was honored with the prestigious 2014 Kyoto Prize presented by the Inamori Foundation earlier this month in Kyoto, Japan. The international award is presented to individuals who have contributed significantly to the progress of science, the advancement of civilization, and the enrichment and elevation of the human spirit. Dr. Langer received the advanced technology prize in the field of biotechnology and medical technology for his work as "a founder of the field of tissue engineering and creator of revolutionary drug delivery system (DDS) technologies."

Frank Reynolds, PixarBio's CEO, said, "For almost a decade I've had the honor to collaborate with Bob Langer on important projects, and he just keeps getting better every year. For decades to come, all of our loved ones will benefit from his inventions, and the legions of scientist who follow will marvel at his genius."

Other laureates included theoretical physicist Edward Witten, honored for his "contributions to the development of mathematical sciences through the exploration of superstring theory," and Fukumi Shimura, "an artist in constant pursuit of the fundamental human value of harmonious coexistence with nature."

PixarBio Corporation is dedicated to developing new therapeutic options for Parkinson's disease, epilepsy, pain, and spinal cord injury. Cofounded by Frank Reynolds, Dr. Robert S. Langer from MIT's Langer Lab, and Katrin Holzhaus, the company is developing novel smart materials to achieve sustained release of agents. Research is focused on a platform for chronic neurological applications. For more information, visit www.pixarbio.com.

The Kyoto Prize is Japan's highest private award for global achievement, created by noted philanthropist Dr. Kazuo Inamori. The Kyoto Prize is awarded annually to persons who have made significant contributions in the three categories of advanced technology, basic sciences, and arts and philosophy. Through this prize, the Inamori Foundation seeks not only to recognize outstanding achievements but also to promote academic and cultural development and to contribute to mutual international understanding. For more information, visit www.inamori-f.or.jp/laureates/k30_a_robert/prf_e.html. ■

In the News

Compiled by Steven Giannos, Independent Consultant

January

Depomed to Acquire U.S. Rights to NUCYNTA® (Tapentadol), NUCYNTA® ER (Tapentadol) Extended Release Tablets, and NUCYNTA® (Tapentadol) Oral Solution from Janssen Pharmaceuticals, Inc., for $1.05 Billion

PRNewswire: January 15, 2015 – NEWARK, CA, U.S.A. – Depomed, Inc. (NASDAQ: DEPO) today announced that it has entered into a definitive agreement to acquire the U.S. rights to the NUCYNTA franchise from Janssen Pharmaceuticals, Inc., for $1.05 billion. The NUCYNTA franchise includes NUCYNTA® ER (tapentadol) extended release tablets indicated for the management of pain, including neuropathic pain associated with diabetic peripheral neuropathy (DPN), severe enough to require daily, around-the-clock, long-term opioid treatment, and NUCYNTA® (tapentadol), an immediate release version of tapentadol, for management of moderate to severe acute pain in adults. NUCYNTA (tapentadol) oral solution is an approved oral form of tapentadol that has not been launched. The deal will make NUCYNTA the flagship asset in Depomed's growing portfolio of pain and neurology specialty pharmaceuticals. Please refer to the summary descriptions below for more information on NUCYNTA and NUCYNTA ER. Full product labeling including boxed warnings for NUCYNTA ER and NUCYNTA is available at www.Nucynta.com.

"We believe that NUCYNTA is an ideal strategic fit for Depomed—a rare opportunity to add a proprietary, differentiated drug with a lengthy period of exclusivity that fits precisely into our therapeutic focus," said Jim Schoeneck, president and chief executive officer of Depomed. "NUCYNTA meets all of our criteria for product acquisition that we have laid out over the past two years. The NUCYNTA franchise generated U.S. net sales of approximately $166 million for the 12 months ended September 2014. NUCYNTA has composition of matter patent protection to August 2022, a potential pediatric extension into 2023, and additional patents that could extend beyond that timeframe. Finally, the synergies between NUCYNTA and our existing pain and neurology call points create a number of opportunities to grow not only the NUCYNTA franchise but to enhance the growth of our current business as well."

Needle-Free Transdermal Delivery Startup Prometheon Pharma Opens Platform to Promote Industry Partnerships

Business Wire: January 13, 2015 – GAINESVILLE, FL, U.S.A. – As the biotech industry and investors converge on San Francisco for the JP Morgan Healthcare Conference, University of Florida spinoff Prometheon Pharma announced plans to open its needle-free transdermal patch technology platform to promote industry partnerships.

"We created a simple, de-risked, and success-based process that allows for quick decisions and minimal commitment. This allows partners to respond to changing markets or strategic plans," said Dr. Stephen Hsu, CEO of Prometheon Pharma and inventor of its technology.

The collaboration model is a simple fee-for-service contract designed to de-risk the development process for pharma/biotech partners and provide initial results in as few as four weeks. Prometheon will optimize its proprietary Topicon™ ThermoMatrix™ formulations to deliver target molecules across a robust and validated human skin model to predict if its TruePatch™ product can achieve clinically meaningful bioavailability in patients.

This semi-high throughput model allows the testing of many drugs simultaneously to establish the dose-response range and saturating dose and to conduct tissue toxicology studies. These deliverables will be owned by the collaborator, who can then choose to progress to small animal studies through fee-for-service before pursuing a long-term partnership with Prometheon.

Setting a new industry standard, Prometheon created the first thermosensitive patches that maintain the stability of perishable large-molecule drugs in a solid matrix at room temperature with its Topicon™ ThermoMatrix™ formulation. Upon application to the skin, the formulation melts into a dermoadhesive gel, which serves as a drug reservoir that delivers drugs at a constant and consistent rate.

Prometheon has already used its highly versatile platform technology in small animal models to deliver large-peptide drugs such as insulin and human growth hormone, as well as a hair regrowth formula. ThermoMatrix™ patches could also deliver many other important small-molecule and peptide drugs, as well as subunit vaccines and gene therapies.

Prometheon Pharma is a biotechnology company housed in the globally #1-ranked Sid Martin Biotech Incubator at the University of Florida. Prometheon is dedicated to increasing patient compliance and access as well as reducing healthcare costs with needle-free transdermal, low-refrigeration patches for large peptide and protein drugs. For more information, please visit www.prometheonpharma.com.

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BioLight Announces New Investment in Development of Ophthalmic Drugs

PRNewswire: January 12, 2015 – TEL AVIV, Israel – BioLight Life Sciences Investments Ltd. (OTC: BLGTY, TASE: BOLT), a firm that invests in, manages, and commercializes biomedical innovations in ophthalmology and cancer diagnostics, today announced its investment in a newly formed ophthalmic company that has licensed-in a worldwide drug-delivery platform from the Hebrew University, Israel, that has the potential to enable more efficient and safer delivery of eye drops.

This drug-delivery platform will help address improving patient compliance with eye disease drug regimens and will form the basis for possible drug development by the new company targeting diseases affecting both the front and back of the eye.

BioLight will comanage the new company and will hold 40% equity stake.

Suzana Nahum-Zilberberg, BioLight's chief executive officer, said, "This new investment represents a major step in our goal to expand our ophthalmic portfolio that addresses clear unmet needs in the multibillion dollar ophthalmic drug market. Our experience in the ophthalmic space will definitely contribute to the new company efforts to find the best ways to develop this novel drug delivery technology into a portfolio of new drugs with better efficacy and safety profiles."

ViaCyte Receives Clearance from Health Canada for Diabetes Clinical Trial

PRNewswire: January 8, 2015 – SAN DIEGO, CA, U.S.A. – ViaCyte, Inc., a privately held regenerative medicine company with the first stem cell-derived islet replacement therapy for the treatment of diabetes in clinical trials, has received a No Objection Letter from Health Canada providing clearance to proceed with sites in Canada for the company's phase 1/2 clinical trial of its VC-01™ product candidate. The VC-01 product candidate is currently being evaluated in patients with type 1 diabetes who have minimal to no insulin-producing beta cell function. The location and enrollment start date of the first Canadian clinical trial site have not yet been disclosed.

"The first cohort of patients in this two-cohort dose escalation study of the VC-01 product candidate is currently being assessed at a single site in the United States. Should the product candidate proceed to the second cohort, we intend to expand the trial to multiple sites," said Paul Laikind, Ph.D., president and CEO of ViaCyte. "Health Canada's approval represents further validation of the trial and allows us to expand internationally to one or more sites in Canada."

The Investigational New Drug application for the phase 1/2 trial, called STEP ONE, or Safety, Tolerability, and Efficacy of VC-01 Combination Product in Type 1, was allowed by the U.S. Food and Drug Administration in August 2014. The STEP ONE trial was launched in September 2014 at UC San Diego Health System, with the support of the UC San Diego Sanford Stem Cell Clinical Center and under the direction of principal investigator Robert Henry, M.D. The first implant was performed in October 2014.

In addition to determining the safety of the product candidate in these patients, STEP ONE is designed to evaluate the effectiveness of the VC-01 product candidate in replacing the lost endocrine function that is central to the disease. In an open-label, dose-escalating format, ViaCyte expects to enroll approximately 40 patients in the study at multiple clinical sites.

ViaCyte is a privately held, clinical-stage regenerative medicine company focused on developing a novel cell therapy for the treatment of diabetes. ViaCyte is conducting a phase 1/2 clinical trial, called STEP ONE, of the company's lead product candidate, VC-01, in patients with type 1 diabetes who have minimal to no insulin-producing beta cell function. The VC-01 combination product is based on the production of pancreatic progenitor cells (PEC-01™ cells), which are implanted in a durable and retrievable encapsulation device, known as the Encaptra® drug delivery system. Once implanted and matured, these cells are designed to secrete insulin and other regulatory factors in response to blood glucose levels. The VC-01 combination product is being developed as a potential long-term diabetes treatment without immune suppression and without risk of hypoglycemia or other diabetes-related complications.

ViaCyte is headquartered in San Diego, California, with additional operations in Athens, Georgia. The company is funded in part by the California Institute for Regenerative Medicine and JDRF. For more information, please visit www.viacyte.com.

Covidien's Stellarex™ Drug-Coated Angioplasty Balloon Receives CE Mark to Treat Peripheral Arterial Disease Patients

Business Wire: January 8, 2015 – DUBLIN, Ireland – Covidien plc (NYSE: COV) today announced it has received CE Mark approval for its Stellarex™ drug-coated angioplasty balloon (DCB). The Stellarex™ DCB is used to restore and maintain blood flow to the arteries of the leg in patients with peripheral arterial disease (PAD).

The Stellarex™ DCB is inserted into the diseased artery and inflated to open the vessel and restore blood flow, while a drug called paclitaxel is deposited onto the vessel wall to prevent the reoccurrence of new blockages. The Stellarex™ DCB's proprietary EnduraCoat™ technology provides a durable, uniform coating that reduces drug loss during transit and facilitates efficient drug delivery to the treatment site.

According to *The Lancet*, 40.5 million cases of PAD were reported in Europe in 2010. PAD occurs when arteries in the legs become narrowed or blocked by plaque. These blockages (lesions) can result in severe pain, limited physical mobility, nonhealing leg ulcers, and leg amputation. Patients with PAD

also have an associated higher risk of heart attack, stroke and death.

"PAD is a progressive disease that affects millions of people around the world. DCBs are emerging as an alternative to traditional treatment options, such as angioplasty or stenting, because of their ability to restore blood flow, prevent the reoccurrence of new blockages, and preserve future treatment options," said Dr. Henrik Schröeder, radiologist, Vascular Center–Jewish Hospital, Berlin, Germany, and principal investigator, Illumenate first-in-human (FIH) study. "In clinical trials, the Stellarex™ DCB has demonstrated promising results with strong patency rates and low reoccurrence of target lesions at 24 months."

The 24 month results of the Illumenate FIH study demonstrated a primary patency rate (ability to keep the artery open to restore blood flow) of 80.3%. Additionally, the study showed 87.9% freedom from target lesion revascularization at 12 months and 85.8% at 24 months.

On November 2, 2014, Covidien announced it had entered into a definitive agreement with Spectranetics Corporation under which Spectranetics will acquire Covidien's Stellarex™ DCB platform. The transaction is subject to the closure of the pending acquisition of Covidien by Medtronic, which is expected to occur in early 2015.

Otic Pharma Announces Positive Results from a Phase 2 Trial of FoamOtic Externa

Business Wire: January 7, 2015 – REHOVOT, Israel – Otic Pharma, a privately held biopharmaceutical company focused on the development of innovative retained, localized foam-based products for ear, nose, and throat (ENT) disorders, announced positive clinical results of its lead product, FoamOtic Externa. A single agent, steroid-free product was studied in a phase 2 clinical trial with 220 minor and adult patients with acute otitis externa (AOE). Once-daily dosing of FoamOtic Externa (ciprofloxacin 0.3% otic foam) demonstrated excellent safety and a similar clinical cure rate as twice-daily dosing of Ciprodex® ear drops (0.3% ciprofloxacin and 0.1% dexamethasone otic suspension, Alcon), the world-leading marketed ear drops for AOE.

"We are very pleased with these positive results with once-daily dosing of FoamOtic Externa. Based on these data, we will be initiating a U.S.-based phase 3 trial with FoamOtic Externa during 2015," said Orna Palgi, Ph.D., executive vice president of Otic Pharma. "FoamOtic provides good coverage of the infected ear canal, and the continued release of the drug allows once-daily dosing and better compliance, which is a major advantage for kids. Based on the results the company is developing foam-based products for additional ENT disorders."

The randomized, multicenter, parallel, comparative phase 2 trial enrolled patients aged six months and older. Proportion of subjects that did not require additional antimicrobial therapy at the end of the treatment period, the microbial eradication rate, time-to-end of pain, and the disease recurrence rate, all being efficacy parameters, were found similar between FoamOtic Externa and Ciprodex®, the leading marketed ear drops for AOE. The overall adverse events (AEs) and serious adverse events (SAEs) rates were similar between the two treatment groups, indicating a similar safety profile. "FoamOtic Externa is an effective product, easy to use, and was very well accepted by the patients. It enhances patient compliance since it is conveniently applied once a day. I will definitely recommend using this product based on patients' feedback," said Dr. Shmuel Gur of Clalit Health Services – Pediatric Clinic, Kfar-Saba, Israel, an investigator in the study.

FoamOtic Externa is a proprietary, foam-based extended-release formulation of ciprofloxacin antibiotic that has been designated for self-applied once-daily administration to treat AOE.

The FoamOtic platform addresses the inherent limitations of ear drops. The foam expands, providing good coverage of the infected area; it does not drip out of the ear and while collapsing provides continuous release of the active pharmaceutical ingredients. FoamOtic application is fast and easy, does not require tilting the head or lying on the side, can be self-administered, and provides superior convenience compared with ear drops.

Clinical studies have demonstrated that once-daily administration of FoamOtic Externa provides sustained ciprofloxacin drug concentrations in the external ear canal that can successfully eradicate the pathogenic bacteria as with twice-daily dosing of antibiotic ear drops. The lead indication for FoamOtic is AOE in minor and adult patients. The product candidate completed a phase 2 trial. Otic Pharma is preparing to launch in 2015 a pivotal phase 3 study of FoamOtic Externa to obtain the clinical data required for its approval by the FDA.

Bio-Path Holdings' Liposomal Grb-2 Featured in Peer-Reviewed Journal Expert Opinion on Drug Delivery

Business Wire: January 7, 2015 – HOUSTON, TX, U.S.A. – Bio-Path Holdings, Inc., (NASDAQ: BPTH) ("Bio-Path"), a biotechnology company developing a liposomal delivery technology for nucleic acid cancer drugs, today announced that data from preclinical studies of BP-100-1.01 (liposomal Grb-2) were featured in the peer-reviewed journal *Expert Opinion on Drug Delivery*.

The paper, titled "Liposomal Delivery of Nucleic Acid-Based Anticancer Therapeutics: BP-100-1.01," was authored by Ana Tari, Ph.D., director preclinical operations and research at Bio-Path, and Jorge Cortes, M.D., deputy department chair, Department of Leukemia, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center. The review article can be accessed at www.biopathholdings.com/pdf/ExpertOpinionDrugDelivery.pdf.

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Antisense oligonucleotides, siRNA, and anti-microRNA are designed to selectively bind to target mRNAs and silence disease-causing or associated proteins. The clinical development of nucleic acid drugs has been limited by their poor bioavailability. This review article examined strategies that have been utilized to improve the bioavailability of nucleic acid drugs, particularly the design of cationic and neutral lipid nanoparticles that enable the systemic delivery of nucleic acids *in vivo* and the proof-of-concept evidence that intravenous administration of nucleic acids incorporated into lipid nanoparticles leads to decreased expression of target genes in humans.

The paper featured preclinical studies of liposomal Grb-2 antisense oligonucleotide incorporated into neutral liposomes and concluded that the drug is a specific Grb-2 inhibitor. Grb-2 is an attractive target because, despite not having specific enzymatic activity of its own, it serves as a linker to transduce signals from a number of oncogenic proteins that result in the activation of the Ras signaling pathway. Early results of a phase I trial in leukemia suggest that liposomal Grb-2 effectively reduces Grb-2 protein expression, resulting in inhibition of downstream Ras effectors such as phosphorylated Erk (extracellular signals regulated kinases) at doses that have not resulted in dose-limiting toxicity. Studies with liposomal Grb-2 are continuing and expanding to other indications as well as combinations to fully understand the role liposomal Grb-2 antisense may have in cancer therapy.

"The publication of data from our lead compound, liposomal Grb-2, in this respected peer-reviewed journal emphasizes the potential importance Bio-Path's proprietary neutral liposomal delivery technology may have in oncology," said Peter Nielsen, chief executive officer of Bio-Path Holdings, Inc. "As we move liposomal Grb-2 through the clinic, we will continue to share our findings with the medical community through peer-reviewed publications and conferences, increasing the exposure of our unique technology and drug candidates and expanding our partnering opportunities."

December

Celator® Pharmaceuticals Receives European Patent Allowance on Nanoparticle Delivery Technology

PRNewswire: December 18, 2014 – EWING, NJ, U.S.A. – Celator Pharmaceuticals, Inc. (Nasdaq: CPXX), a biopharmaceutical company transforming the science of combination therapy and developing products to improve patient outcomes in cancer, today announced that the application of European patent number 2,222,278 was allowed by the European Patent Office. The new patent, "Improved Taxane Delivery System," covers the company's proprietary taxane prodrug nanoparticle-delivery technology and CPX-8, a hydrophobic docetaxel prodrug nanoparticle, which is based on this innovative approach to drug delivery. Celator is currently applying its proprietary CombiPlex technology to drug combinations incorporating targeted agents, such as a combination of docetaxel with a heat shock protein (Hsp90) inhibitor where extended and simultaneous exposure of the two agents to solid tumors at the optimized drug ratio is expected to significantly enhance the efficacy of this combination. This should help establish the broad applicability of the CombiPlex platform in the development of combination cancer therapies. This patent provides protection until November 2028.

Celator's nanoparticle-based delivery technology provides versatile control of the pharmacokinetics and tissue accumulation of taxanes such as paclitaxel and docetaxel. The patent covers a pharmaceutical composition comprising nanoparticles or micelles, where the nanoparticles or micelles are formed from associating 1) a conjugate of taxane coupled to a hydrophobic lipid-anchor through a diglycolate linker with 2) a lipid and/or amphiphilic stabilizer. The allowed claims may also provide patent protection for formulations combining docetaxel, and other taxanes, with molecularly targeted agents.

"By connecting a hydrophobic anchor to taxanes in a manner that readily incorporates them into stable nanoparticles, we have been able to reduce early distribution of these drugs to healthy tissues while enhancing and extending their exposure to tumor tissue," said Dr. Lawrence Mayer, president and chief scientific officer of Celator. "The improved tumor drug exposure properties correlated with increased antitumor activity when compared with conventional formulations of docetaxel at equivalent doses, and the reduced toxicity of the nanoparticle formulation in mice led to marked efficacy improvements when it was dosed at the maximum tolerated dose."

Microchips Biotech, Inc., Completes Development and Clinical Demonstration of Proprietary Drug Delivery Platform and Advances Commercialization Efforts in Diabetes, Contraception, and Osteoporosis

Business Wire: December 15, 2014 – WALTHAM, MA, U.S.A. – Microchips Biotech, Inc., formerly MicroCHIPS, Inc., today announced the completion of the development and clinical demonstration of its proprietary drug delivery technology, a microchip-based implant capable of storing and releasing precise doses of a drug on demand or at scheduled intervals for up to 16 years. Unlike traditional drug delivery platforms, Microchips Biotech's implant is capable of responding to wireless signals, which can activate, deactivate, or modify the frequency or dose of the drug without requiring removal. Microchips Biotech is currently pursuing applications of its platform in three key areas: diabetes, female contraception, and osteoporosis, which all require frequent, long-term dosing and high patient compliance. Microchips Biotech published clinical data demonstrating the ability of its platform to deliver a drug to treat osteoporosis in women and is actively advancing development and clinical research programs in diabetes and female contraception, respectively.

"Innovating drug delivery is an integral complement to drug discovery, and Microchips Biotech is uniquely poised to revolutionize the way medicines are administered on a long-term basis," said Cheryl Blanchard, Ph.D., who assumed the role of chief executive officer in July and currently sits on Microchips

Biotech's board of directors. "It's truly an exciting phase in the company's lifecycle as we continue to advance the development of our contraceptive implant and focus our efforts on forming strategic partnerships that leverage our platform to enhance the utility and compliance of new and established therapeutic agents to manage osteoporosis, diabetes, and other chronic conditions that require frequent, long-term dosing."

Microchips was cofounded by renowned MIT researchers Robert Langer, Ph.D., and Michael J. Cima, Ph.D., who designed the novel technology and published the first study on its viability as a long-term drug delivery platform implant in *Nature*. Over the last decade, the safety and viability of the microchip-based implant have been extensively studied in animal models and humans and have been documented in peer-reviewed journals. In 2012, Microchips Biotech conducted a first-in-human study in women with osteoporosis, demonstrating the ability of its platform to deliver the same therapeutic level of a drug to increase bone mass as achieved via daily injections. In the same year, the company received grants to develop a microchip-based, long-term, reversible contraceptive implant for women in developing countries who have limited access to routine medical care and modern contraceptive options.

"The versatility of our platform design lends itself to several clinical applications, and diabetes management is one specific area of tremendous opportunity, a fact that is underscored by our discussions with several potential partners focused on managing that condition," added Dr. Blanchard, who was formerly senior vice president and chief scientific officer of Zimmer, Inc. "For patients with diabetes, compliance is critical and a challenge given the need for frequent, even twice-daily administration of therapeutics, often via injections. Leveraging the microchip-based implant to automate dosing to enhance compliance could be life-changing for the 29 million Americans living with the disease."

Under Dr. Blanchard's leadership, Microchips updated its visual corporate identity with new corporate branding and a revamped corporate website (www.microchipsbiotech.com) that reflects the company's new vision and long-term goals.

€6 Million in New Capital and New CEO for Cristal Therapeutics

Business Wire: December 15, 2014 – MAASTRICHT, The Netherlands – Biopharmaceutical company Cristal Therapeutics has completed a new financing round of over €6 million that includes investments from new and existing investors and a national innovation fund. Venture capital investor Chemelot Ventures joins as a new shareholder, and existing investors Thuja Capital, BioGeneration Ventures, Nedermaas, Utrecht University Holding, and Beheer Innovatiefonds Provincie Limburg also contributed. The financing will be used to launch the first clinical study of Cristal Therapeutics' most advanced therapy, CriPec® docetaxel. Joost Holthuis, cofounder of Cristal Therapeutics and former CEO of OctoPlus, has also been appointed CEO with effect from December 1.

Cristal Therapeutics develops new therapies against cancer and other diseases, such as chronic inflammatory disorders, by using its patented CriPec® technology to entrap existing and new drugs in polymer nanoparticles of 0.0001 mm diameter. These nanoparticles provide better distribution throughout the body and a more selective release of the drugs, such as anticancer drugs in the case of tumors. Therefore, products based on CriPec® may provide improved efficacy and fewer side effects, offering improved treatment of various diseases.

In a range of studies performed since 2011, Cristal Therapeutics has demonstrated the safety and efficacy of various CriPec® nanomedicines in preclinical studies. In the next few years, the first product, CriPec® docetaxel for the treatment of cancer, will be developed further and tested on humans. If successful, this will enable chemotherapy to proceed more selectively and efficiently, with fewer undesirable side effects. Early in 2015, the first clinical study to evaluate CriPec® docetaxel will commence.

Dr. Joost Holthuis, the new CEO of Cristal Therapeutics, comments on this financing round: "Chemelot Ventures joining our group of preeminent investors represents a growing commitment to nanomedicine. The continuing commitment and support of our existing investors is extremely important to our business. That commitment reflects the potential of the drug candidates developed by Cristal Therapeutics on the basis of the CriPec® technology."

Marcel Kloosterman, investment manager of Chemelot Ventures: "We are impressed by the focus, knowledge, and commitment of the Cristal Therapeutics management team. We are pleased to support the company in its efforts to develop a unique new treatment for patients with solid tumors. Cristal Therapeutics' technology is enabling a more effective use of existing medicines with fewer side effects for the patient and also demonstrates its social relevance. Additionally, Cristal Therapeutics is contributing to a substantial increase in high-grade biopharmaceutical knowledge in our Limburg region in the Netherlands. We look forward to the start of the first clinical study with great confidence."

Cofounder Dr. Joost Holthuis has succeeded its founder Dr. Cristianne Rijcken as CEO of the company, effective since December 1, 2014. Dr. Holthuis has an extensive career in the biotech field and founded OctoPlus, which was listed on the Amsterdam stock exchange, and was CEO between 1995 and 2008. In addition to serving on supervisory boards of various highly promising biotech startups, Dr. Holthuis is also a venture partner at biotech venture capital investor BioGeneration in Naarden.

Dr. Rijcken, CEO since its incorporation in 2011, will become chief scientific officer (CSO). Dr. Rijcken, together with Joost Holthuis, launched Cristal Therapeutics as a spinoff of the Department of Pharmaceutics of Utrecht University.

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Joost Holthuis said, "I want to thank Cristianne in particular for her ceaseless commitment to Cristal Therapeutics since our joint start. Her exceptional knowledge and passion for the development of new pharmaceutical therapies will be brought even more to the fore following her appointment as chief scientific officer. I am looking forward to our renewed collaboration in this important period of transformation for Cristal Therapeutics."

Cristal Therapeutics, established in Maastricht, focuses on the development of nanomedicines with improved therapeutic efficacy. The pipeline comprises products based on drugs in development and also on the market, in combination with the patented CriPec® platform, for the treatment of various diseases, including cancer and chronic inflammatory disorders.

CriPec® transforms drugs into polymer nanoparticles via an innovative process. These nanoparticles provide improved distribution throughout the body. The substantial improvement of the efficacy and safety of the drugs entrapped in CriPec® nanoparticles has already been demonstrated in animal studies. Cristal Therapeutics has demonstrated the benefits of CriPec® for various molecules, including peptide drugs (an anticancer drug transported by a protein that is important for the tumor), as well as for applications such as active targeting for more selective treatment. The results to date have contributed to the company's present innovative product portfolio.

Orexo: FDA Approves Two Higher Dosage Strengths of ZUBSOLV®

Business Wire: December 12, 2014 – UPPSALA, SWEDEN – Orexo AB (publ) (STO: ORX) announced today that it has received approval from the U.S. Food and Drug Administration (FDA) of two higher dosage strengths of ZUBSOLV (buprenorphine/naloxone CIII sublingual tablet) for maintenance treatment of opioid dependence. The new dosage strengths are 8.6 mg/2.1 mg and 11.4 mg/2.9 mg buprenorphine/naloxone CIII sublingual tablets. The 8.6 mg/2.1 mg dosage strength is expected to be launched early 2015 and the 11.4 mg/2.9 mg strength later in 2015.

The new dosage strengths complement the existing strengths of 5.7 mg/1.4 mg and 1.4 mg/0.36 mg tablets and enable patients to receive their optimal dose in one tablet. The new strengths are made with the advanced, proprietary sublingual tablet formulation in ZUBSOLV, providing higher bioavailability, a fast dissolve time, small tablet size, and menthol flavor.

"Orexo remains fully committed to advancing the treatment of opioid dependence. During the summer, we received positive data from the largest clinical trials ever conducted in this disease area. Today, we are proud to announce that the FDA has approved two additional dosage strengths of ZUBSOLV. These higher dosage strengths will allow more patients to get the right dosage in only one tablet and thus reduce the need to combine different dosage strengths. This will improve patient convenience and adherence while reducing their out-of-pocket cost, as only one co-pay will be required," said Nikolaj Sørensen, CEO and president of Orexo AB.

The advanced formulation provided by ZUBSOLV meets the needs expressed by patients, such as improved taste and fast dissolve time. Meeting patient needs may have the potential to improve patient adherence, thus reducing relapse rates and improving successful patient outcomes. ZUBSOLV is the only opioid dependence treatment option available in the highest level of child resistant, unit dose, F1 packaging, designed to reduce the chance of unintended pediatric exposure.

Acorda Announces Initiation of Phase 3 Trial of CVT-301 in Parkinson's Disease

Business Wire: December 10, 2014 – ARDSLEY, NY, U.S.A. – Acorda Therapeutics, Inc. (Nasdaq: ACOR) today announced that the first patient has been enrolled in a phase 3 study of CVT-301 for the treatment of OFF episodes in Parkinson's disease (PD). OFF episodes are characterized by a re-emergence of PD symptoms such as tremor, muscle stiffness, and impaired ability to move.

CVT-301 is a novel, self-administered inhaled therapy designed to provide rapid, reliable delivery of a precise dose of levodopa (L-dopa) through the lungs to return people with PD to an ON state. An ON state is when a patient's symptoms are adequately controlled, allowing people with Parkinson's to more readily perform daily activities.

"Parkinson's is a debilitating neurological disease affecting over a million Americans and as many as 10 million people worldwide," said Enrique Carrazana, M.D., Acorda Therapeutics' chief medical officer. "About 350,000 people with PD in the United States experience OFF episodes, which can be exceptionally disruptive, impacting their lives on a daily basis, even multiple times per day. We believe CVT-301 has the potential to be an important treatment for people experiencing OFF episodes."

The multicenter, double blind, randomized trial is expected to enroll approximately 345 participants across three arms: 50 mg, 35 mg, or placebo. These are the same doses used in the phase 2b study. The primary outcome measure is improvement on the Unified Parkinson's Disease Rating Scale (UPDRS) Part III after administration of CVT-301.

More details about the study, including enrollment criteria, can be found at www.acorda.com or http://clinicaltrials.gov/ct2/show/NCT02240030?term=CVT-301&rank=2.

Positive results from the CVT-301 phase 2b study were presented at the 2014 American Academy of Neurology Annual Meeting. In this study, participants receiving CVT-301 showed a statistically significant and clinically important reduction in average UPDRS Part III motor score versus placebo across time points beginning at 10 and up to 60 minutes postadministration ($P < 0.001$). Both doses of CVT-301 were well tolerated, with no increase relative to placebo in troublesome or nontroublesome

dyskinesias during ON periods. There were no serious adverse events in the trial, and the incidence of drug-related adverse events was similar between treatment groups. The CVT-301 inhaler was shown to be easily self-administered in the OFF state.

"Oral L-dopa is the standard of care in reducing the symptoms of PD; however, significant challenges remain in creating an individualized treatment regimen that consistently maintains therapeutic effects as the disease progresses," said Rick Batycky, Ph.D., Acorda Therapeutics' chief technology officer. "CVT-301 uses our proprietary ARCUS technology to deliver L-dopa through the lungs. The ARCUS technology can deliver much larger doses than is possible with standard pulmonary technologies, making it ideal for delivery of medications such as L-dopa."

Acorda's proprietary ARCUS technology platform is a dry-powder pulmonary delivery system that has potential applications in multiple disease areas. This platform allows consistent and precise delivery of significantly larger doses of medication than are possible with conventional pulmonary systems. The ARCUS inhaler is breath-actuated, operated by the user putting their lips to the device and simply breathing in.

The ARCUS technology has been used to successfully deliver more than one million doses to patients in clinical trials of various products. CVT-301 is the most advanced drug candidate using the ARCUS technology. Acorda has an extensive patent portfolio relating to CVT-301 and the ARCUS technology, which covers aspects of the formulated drug product, the inhaler, the method of drug delivery, and manufacturing processes for CVT-301.

CVT-301 is being developed as a self-administered, inhaled L-dopa therapy for treatment of OFF episodes in Parkinson's disease (PD). This is an adjunctive therapy to a patient's individually optimized oral L-dopa regimen. Acorda's proprietary ARCUS® technology provides a precise dose of a dry powder formulation of L-dopa to the lung to enable rapid and predictable absorption. CVT-301 is delivered through a pocket-size, breath-actuated inhaler designed to be patient friendly. In the CVT-301 treatment group, lightheadedness and cough were the most frequently reported adverse events. There were no observed, treatment-associated adverse effects on lung function. Clinical studies conducted to date have been funded in part by grants from the Michael J. Fox Foundation for Parkinson's Research.

Founded in 1995, Acorda Therapeutics is a biotechnology company focused on developing therapies that restore function and improve the lives of people with neurological disorders.

Acorda markets three FDA-approved therapies, including AMPYRA® (dalfampridine) extended release tablets, 10 mg, a treatment to improve walking in patients with multiple sclerosis (MS), as demonstrated by an increase in walking speed. The company has one of the leading pipelines in the industry of novel neurological therapies. Acorda is currently developing a number of clinical and preclinical stage therapies. This pipeline addresses a range of disorders including poststroke walking deficits, Parkinson's disease, epilepsy, neuropathic pain, heart failure, MS, and spinal cord injury. For more information, please visit the company's website at www.acorda.com.

November

Generex Announces Participation in MedCannAccess®–CannScience Partnership on Nonsmoked Forms of Marijuana

PRNewswire: November 17, 2014 – WORCESTER, MA, U.S.A. and TORONTO, Canada – Generex Biotechnology Corporation (www.generex.com) (OTCBB: GNBT) today announced its participation in a MedCannAccess (www.MedCannAccess.com) partnership with CannScience Innovations Inc.

MedCannAccess today announced that it has acquired a substantial minority equity stake in CannScience, a leading cannabinoid drug development firm. This partnership positions MedCannAccess to be a leader in the development of pharmaceutical cannabinoid products.

"Successful companies in the cannabis industry will have three legs to their platform: quality production, an effective patient acquisition and retention strategy, and innovative research and development capabilities," said Rade Kovacevic, vice president of business development at MedCannAccess. "We believe we have strong positions already in the first two legs, and through this investment, we have solidified the R&D piece of our platform, positioning us as a leader in future cannabinoid drug development. Physicians and patients alike have been calling for access to cannabinoid products that do not require smoking or inhalation; this partnership will allow us to take that significant step forward."

CannScience is an R&D biopharmaceutical company established in Toronto, Canada, to conduct research and product development for extracts and formulations related to medical cannabis and its derivatives. CannScience is developing proprietary technologies and owns know-how related to the chemistry and pharmacology of cannabinoids and potentially how they integrate with various medical devices and drug delivery technologies. CannScience intends to develop commercial-ready products and obtain regulatory approval for RapidMist™ in the Canadian and international jurisdictions. The company's founders have a wealth of experience in the life sciences industry and access to laboratories at some of the top research institutions in Canada.

"CannScience is working to develop its product pipeline, which will include proprietary drug, device, and delivery technologies," said Har Grover, the CEO of CannScience. On November 18,

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2014, CannScience entered into a nonbinding letter of intent with Generex to license Generex's proprietary RapidMist™ drug delivery technologies to CannScience for the buccal delivery of cannabis-derived products into the bloodstream.

MedCannAccess was established to provide access to the highest quality of medical cannabis products developed through research and innovation, aiming to improve the quality of life for persons with a wide range of conditions including chronic disabilities and terminal illnesses. MedCannAccess is a proud member of the Canadian Medical Cannabis Industry Association, Toronto Board of Trade, Guelph Chamber of Commerce, and Ontario Chamber of Commerce.

mPhase Technologies' Smart Drug Delivery System Holds Significant Portion of Patentable Claims

Business Wire: November 17, 2014 – CLIFTON, NJ, U.S.A. – mPhase Technologies, Inc. (XDSL) (http://mphasetech.com/), announced an update on the drug delivery system patent application that was originally filed in February 2013. The drug delivery system is based on mPhase Technologies' award-winning advanced battery technology. Frost and Sullivan recognized mPhase with its 2013 North American Advanced Battery Technology Innovation Award for Best Practices.

In December 2013 the patent application for the smart drug delivery system received a first review (Office Action) by the U.S. Patent and Trademark Office. The patent office examiner indicated that a significant portion of the claims were patentable. A response to the office was filed, without amending the claims, but with strong arguments as to why all of the claims are patentable. mPhase is now waiting for a response from the patent office, which is expected no later than in the first quarter of 2015.

mPhase believes the issuance of a patent could lead to licensing opportunities for the novel drug delivery system, possibly creating greater shareholder value. The drug delivery patent, if issued, would enable the automatic dispensing of a preset dosage of a drug agent or medication.

The field of invention relates to a drug delivery system that generally includes a housing having one or more reservoirs, each having a medical agent hermetically sealed therein. A membrane extends across each of the one or more reservoirs, which is adapted to allow the medical agents to pass through in response to external stimuli, such as physical puncturing, melting the membranes through use of heating elements, or electrowetting in response to a voltage pulse. A wicking material extends across the membranes through which the medical agents are dispensed to a patient. Because the housing can be made flat, the overall dispensing device can be reduced in size, allowing the drug delivery device to be located and attached to broader areas of the patient's body for expanded medical applications and treatment.

Under past cooperative research and development agreements with the U.S. Army, mPhase developed a smart nanobattery that made it possible to keep the essential components of a battery, the solid electrode and liquid electrolyte, separated until power is needed. This battery system can be activated electronically, mechanically, or via gravitational pull.

mPhase Technologies Inc. (XDSL) is a 2013 Frost and Sullivan recipient for the North American Advanced Battery Technology Innovation Award. mPhase Technologies is a publicly traded company (XDSL) that is pioneering a revolutionary smart surface technology enabled by breakthroughs in nanotechnology, MEMS processing, and microfluidics. Our smart surface technology has potential applications within drug delivery systems, lab-on-a-chip analytic 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, still in development. More information about the company can be found at www.mPhaseTech.com.

Catalent Acquires Micron Technologies

Business Wire: November 13, 2014 – SOMERSET, NJ, U.S.A. – Catalent, Inc. (NYSE: CTLT), the leading global provider of advanced delivery technologies and development solutions for drugs, biologics, and consumer health products, today announced that it has acquired Micron Technologies, a leading global provider of particle size engineering technologies.

In an important advance in executing its strategy to provide the best drug delivery technologies and the broadest drug development expertise, Catalent will add Micron Technologies' superior particle size engineering capabilities to its industry-leading suite of drug delivery and development solutions. Catalent can now partner with more pharmaceutical innovators at the earliest stages of the drug development process with an unrivaled set of options and expertise. These range from OptiForm® API optimization and Micron Technologies particle size optimization, to expert formulation and final dose form design services, through to leading bioavailability solutions such as RP Scherer Softgel lipid systems and OptiMelt™ hot melt extrusion technologies. Catalent can support its customers all the way through scale-up, clinical, and commercial manufacturing of finished oral and inhaled dose forms around the world, including for highly potent compounds.

"This strategic acquisition allows Catalent to provide an unprecedented set of integrated development solutions and superior drug delivery technologies to the industry, partnering with our customers' R&D teams earlier in the development cycle and helping them deliver better treatments to clinic and to market faster and more efficiently," said John Chiminski, Catalent, Inc., president and CEO. "We are pleased to add Micron Technologies' leading technologies and manufacturing expertise and welcome their highly talented management, scientific, and operations teams to Catalent."

Micron Technologies adds to Catalent's long history of innovation and leadership in the pharmaceutical industry, with

its proven and versatile portfolio of particle size reduction, micronization, and milling technologies used to overcome bioavailability, stability, and manufacturability challenges.

The acquisition is Catalent's second since its IPO in July and follows the acquisition of Redwood Bioscience, with its SMARTag™ antibody-drug conjugate (ADC) technology platform, in October 2014.

Micron Technologies currently operates two state-of-the-art facilities, with excellent quality and regulatory compliance records, in Malvern, Pennsylvania, and in Dartford, United Kingdom, and employs approximately 100 people across both sites. Micron Technologies has over 25 years of experience in air jet milling micronization and is capable of processing R&D and commercial volumes at both of its sites. Micron Technologies currently supports active programs involving over 300 customers from around the world. Both facilities are equipped with advanced systems to ensure the quality, safety, and total containment of highly potent and cytotoxic compounds and to provide integrated analytical services capabilities from early stage development to commercialization.

Joseph Drost, CEO of Micron Technologies, who will continue to lead this business, remarked, "We are excited to become part of Catalent, as there is a natural synergy between our organizations, with the global leader in advanced delivery technologies and development solutions now joining forces with a leading provider of particle size engineering technologies and integrated analytical services. Through access to Catalent's global network, development expertise, and innovative technologies, we can jointly provide end-to-end solutions to accelerate drug development programs and bring better treatments to patients worldwide."

EnGeneIC and Asbestos Diseases Research Institute Initiate MesomiR-1 Phase 1 Trial in Patients with Late Stage Mesothelioma

PRNewswire: November 10, 2014 – SYDNEY, Australia – EnGeneIC, Ltd., an emerging biopharmaceutical company focused on developing its proprietary EDV™ nanocell platform for the targeted delivery of cancer therapeutics and other therapeutic molecules, announced today that, together with the Asbestos Disease Research Institute (ADRI), it has initiated the first clinical trial evaluating its bacterially derived and antibody-guided EDV™ nanocells packaged with microRNA for the treatment of patients with malignant pleural mesothelioma (MPM). The study is the first time a targeted nanotherapeutic approach to microRNA replacement is being tested in patients with MPM.

EnGeneIC's EDV™ nanocells will be packaged with miR-16 microRNAs, which were discovered to be missing in MPM cells by Profs. Glen Reid and Nico van Zandwijk of the ADRI. To deliver the missing microRNAs to the cells, the EDV™ nanocells are designed to specifically target the epidermal growth factor receptor found on MPM cells and have been coined TargomiRs for this study.

The MesomiR-1 trial is an open-label, exploratory phase 1 study of TargomiRs administered in escalating doses by intravenous infusion in patients with MPM who failed to respond to standard of care therapy. The primary study objectives are to establish the optimal dose of TargomiRs and to detect early signs of disease stabilization. Patients will be carefully followed during an eight-week period of experimental treatment including measurement of quality of life, pulmonary function, and changes in immune status.

Participating sites for the trial include the Northern Cancer Institute, Lifehouse at Royal Prince Alfred Hospital, and Concord Repatriation Hospital, all in Sydney.

Dr. Himanshu Brahmbhatt, joint CEO of EnGeneIC, said, "We are excited to commence this trial since we believe that it is the first time a microRNA-based oncology therapeutic will be administered in a thoracic tumor with very limited treatment options and a very poor prognosis. It is also a tremendous opportunity for EnGeneIC to demonstrate the platform nature and versatility of the targeted EDV™ nanocell."

Prof. Nico van Zandwijk, who will be the principal investigator for the MesomiR-1 trial, remarked, "We have previously published that miR-16 expression was severely depleted in all MPM tumor samples tested, which results in tumors growing unchecked. We are extremely pleased to have teamed up with EnGeneIC to use its unique targeted nanocell to restore this functional nucleic acid and to demonstrate the safety of the approach in a group of patients in great need of more effective treatment. "

EnGeneIC's bacterially derived EDV™ nanocells are a powerful nanoparticle drug delivery system designed to directly target and effectively kill tumor cells with minimal toxicity, while at the same time stimulate the immune system's natural antitumor response.

Intravenously injected EDV™ nanocells exit the leaky vascular system only within tumors and attach to cancer cells via a specially designed, targeted bispecific antibody. Once attached, the nanocell is able to enter the tumor cell and deliver a drug payload of up to one million drug molecules per nanocell. In parallel, the bacterial cell wall of the nanocells stimulates key components of the immune system, which are then activated to seek out and destroy cancer cells.

EnGeneIC is an emerging biopharmaceutical company focused on developing its proprietary EDV™ nanocell platform for the targeted delivery of cancer therapeutic and other therapeutic molecules. The company's lead technology platform, EDV™ utilizes antibody-targeted, bacterially derived, nonliving "nanocells" to release high concentrations of chemotherapeutic

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agents, molecularly targeted drugs, and RNA-interference molecules directly into targeted tumor cells. In doing so, EDV™ nanocells enable current cancer treatments to be more potent and far less toxic, while also offering a potential new means for treating drug-resistant cancers. EnGeneIC is currently preparing an IND for FDA submission, with plans to launch a phase 1/2a clinical trial in recurrent glioblastoma patients in early 2015. Trials are also in planning stages for non-small cell lung cancer. For more information, please visit www.engeneic.com.

STENTYS Expands Product Offering to All Coronary Stent Indications Through Exclusive Agreement with Micell to Distribute Its Novel Drug-Eluting Stent

Business Wire: November 3, 2014 – PRINCETON, NJ, U.S.A., and PARIS, France – STENTYS (Paris: STNT) (FR0010949404—STNT), a medical technology company commercializing the world's first and only Self-Apposing® coronary stent, today announced it has entered into a five year agreement with Micell Technologies Inc. to be the exclusive distributor of the MiStent coronary stent worldwide (excluding the United States, Canada, China, South Korea, and Japan).

Gonzague Issenmann, chief executive officer and cofounder of STENTYS, explains: "We are thrilled to launch this exciting new product that is designed to outperform the market-leading workhorse stents thanks to a unique coating technology. Our customers will now have the opportunity to use MiStent for routine procedures and STENTYS Self-Apposing stent for complex vessel anatomy that requires optimal apposition, both of which are designed for safe vessel healing and improved patient outcomes."

"This long-term partnership is one more building block of the company's growth strategy. With two CE marked sirolimus-eluting stents covering all coronary indications and commercialized through our fast increasing sales network, we will strengthen our market position, increase access to our target audience, as well as create an opportunity for even greater revenue growth," concluded Gonzague Issenmann.

The MiStent sirolimus-eluting absorbable polymer coronary stent system (MiStent SES®) is a balloon-expandable stent designed for rapid healing and slow progression of coronary artery disease. The bioabsorbable coating of MiStent SES disappears within three months of implantation to promote fast vessel healing. However, sirolimus elution is precisely and consistently controlled up to nine months after implantation, thereby inhibiting vessel renarrowing. These unique properties of both fast polymer absorption and sustained drug release are made possible by an innovative proprietary coating technology that allows sirolimus to be encapsulated as tiny crystals; once the polymer is gone, the crystals slowly dissolve into the tissue surrounding the stent, providing a continued local antiproliferative and anti-inflammatory effect for several months.

MiStent SES has been studied clinically in the DESSOLVE I and II trials. The first trial on 30 patients showed no reduction in artery lumen diameter between 8 and 18 months (late lumen loss of 0.09 mm). The second trial of 184 patients, which compared MiStent SES and Medtronic Endeavor® DES, showed lower MACE at three years in the MiStent SES arm (8.3 vs. 15.3%, $P = 0.2$), with a very low rate of reintervention for MiStent SES (TLR of 2.5% at three years) and no definite or probable stent thrombosis.

MiStent SES has received CE Marking and has not yet been marketed. STENTYS plans to launch the product in H1 2015 in Europe, to be followed by the many geographies where STENTYS has built a commercial network. STENTYS and Micell will partner to conduct MiStent's postmarket study, DESSOLVE III.

October

CeloNova's Super-Selective Embolic Microsphere with Drug Loading Capabilities Could Mean Improved Quality of Life and Overall Survival for Liver Cancer Patients

Business Wire: October 30, 2014 – SAN ANTONIO, TX, U.S.A. – CeloNova BioSciences, Inc. (CeloNova), today announced that the U.S. Food and Drug Administration (FDA) has granted approval to start an investigational device exemption (IDE) clinical trial for its novel ONCOZENE™ embolic microspheres, loaded with doxorubicin, a chemotherapy drug used in the treatment of hepatocellular carcinoma (HCC). HCC is the most common primary liver cancer and accounts for approximately 600,000 deaths annually on a worldwide basis. Untreated HCC patients have a median survival time of less than 12 months.

CeloNova's ONCOZENE™ microspheres' small sizes and precise calibration allow for super-selective embolization combined with distal penetration, which may greatly increase the chemotherapeutic impact at the tumor site while lowering the toxicity in other parts of the body, thereby potentially improving the patient's tolerance of the treatment. CeloNova's TANDEM™ microspheres are available in Europe and bear the European Union's CE mark since it was granted in 2012 for embolization of HCC, with or without delivery of doxorubicin.

"Our ONCOZENE™ microspheres platform, when combined with its precise drug delivery capability, presents a potentially improved treatment option for liver cancer patients," said Jane Ren, Ph.D., CeloNova's chief technology officer. "We are very pleased to be working with the leading HCC experts in the world to alleviate the pain of our patients."

"We are excited to move ONCOZENE™ microspheres into a pivotal phase 3 trial," said Dr. Ghassan Abou-Alfa at Memorial Sloan-Kettering Cancer Center. "Early studies have shown that liver-directed therapies utilizing drug-eluting microspheres such as ONCOZENE™ microspheres provide an excellent treatment option for locally advanced HCC patients."

"This IDE trial is designed to develop an evidence-based treatment plan for late-stage HCC patients and will enroll patients in

multiple cancer centers across the United States, Europe, and Asia," said Dr. Riccardo Lencioni, professor at the Pisa University School of Medicine in Italy and chairman of the World Conference on Interventional Oncology (WCIO).

CeloNova CEO Martin Landon commented, "The recent expanded indication for our ONCOZENE™ and EMBOZENE™ microspheres, to include embolization of hepatoma, combined with this IDE trial approval for ONCOZENE™ microspheres loaded with doxorubicin, represent two more 'industry first' examples of how we are executing on our vision to bring unique and disruptive solutions to physicians, patients, and payers that improve patient care and add significant clinical and economic value to the healthcare community."

The company announced on September 3, 2014, that the FDA had issued 510(k) clearance expanding the indication of its ONCOZENE™ and EMBOZENE™ microspheres products to include the treatment of hepatoma, also known as HCC. That approval provides support for another treatment option for physicians and patients in their battle against primary liver cancer.

CeloNova BioSciences, Inc., headquartered in San Antonio, Texas, is a global medical device company that develops, manufactures, and markets a family of interventional cardiology and endovascular products. Our products are developed and manufactured in Carlsbad, California, U.S.A., and Ulm, Germany. The company's regional offices are located in Germany, France, the United Kingdom, the Netherlands, and Austria. For additional information about CeloNova BioSciences, see the company website at www.celonova.com.

BioDelivery Sciences to Develop a Long-Acting Injectable Depot Formulation of Buprenorphine with Evonik for Use in Opioid Dependence and Pain

PRNewswire: October 28, 2014 – RALEIGH, NC, U.S.A. – BioDelivery Sciences International, Inc. (BDSI) (NASDAQ: BDSI), has entered into an exclusive agreement with Evonik Corporation to develop and commercialize a proprietary, injectable microparticle formulation of buprenorphine potentially capable of providing 30 days of continuous therapy following a single subcutaneous injection.

While BDSI plans to pursue an indication for the maintenance treatment of opioid dependence, the company has also secured the rights and plans to develop a product for the treatment of chronic pain in patients requiring continuous opioid therapy. BDSI has also secured options to license Evonik-owned intellectual property related to these products.

It is estimated that approximately 2.5 million people in the United States are dependent on prescription opioids or heroin. Despite the availability of effective treatments, including Bunavail (buprenorphine and naloxone) buccal film, challenges remain regarding patient adherence to long-term buprenorphine treatment, which is critical to successfully manage opioid dependence.

"Given our significant experience with buprenorphine in both opioid dependence and chronic pain, we believe this is an ideal opportunity for BDSI to extend our franchise in both of these areas, as the need remains high," said Dr. Andrew Finn, executive vice president of product development for BDSI. "We look forward to working closely with Evonik to expeditiously complete formulation development work and move the product into the clinic late next year. Since this will be a 505(b)(2) development program, we believe there may be an opportunity to move toward an NDA submission for opioid dependence in approximately three years time."

"Evonik is pleased to work with BDSI on the development of this novel long-acting buprenorphine product," said Dr. Jean-Luc Herbeaux, head of Evonik's global health care business line. "With its broad range of competencies in API and drug delivery systems, Evonik strives to support customers in the development and launch of novel medical treatments. Using our proprietary FormEZE® microparticle technology and Resomer® biomaterials, this pharmaceutical will be manufactured at our state-of-the-art facility in Birmingham, Alabama."

"The potential availability of a long-acting formulation of buprenorphine has the opportunity to significantly advance the treatment of opioid dependence and furthers our commitment to this underserved treatment area," said Dr. Mark A. Sirgo, president and chief executive officer. "Not only would a single monthly injection provide an opportunity to substantially improve adherence to buprenorphine treatment, which is a formidable problem for many patients, it could also help to eliminate the problem of diversion. We also believe this will be an outstanding companion product to Bunavail and, if approved, provides another product for our existing sales team."

As part of the agreement, BDSI will have the right to license the product(s) following the attainment of phase I ready formulations. At that point, Evonik could receive downstream payments for milestones related to regulatory filings and subsequent NDA approvals as well as product royalties. Evonik has the exclusive rights to develop the formulation and manufacture the product(s). ■

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Calendar of Events

2015

Global Health & Innovation Conference
March 28–29
New Haven, CT, U.S.A.
www.uniteforsight.org/conference

Society for Biomaterials
April 15–18
Charlotte, NC, U.S.A.
http://2015.biomaterials.org

Controlled Release Conference
April 20–21
London, U.K.
www.smi-online.co.uk/2015controlledrelease45.asp

2015 CC-CRS/CSPS Joint Conference
Sponsored by CRS
May 26–28
Toronto, Canada
http://cc-crs.com/CRS

1st International Congress of the Controlled Release Society – Greek Local Chapter
Sponsored by CRS
May 27–28
Athens, Greece
www.afea.gr/event.asp?pid=146&lng=1

Controlled Release Technology: Delivery Systems for Pharmaceuticals, Proteins, and Other Agents
June 8–12
Cambridge, MA, U.S.A.
http://web.mit.edu/professional/short-programs/courses/controlled_release_technology.html

42nd Annual Meeting & Exposition of the Controlled Release Society
July 26–29
Edinburgh, Scotland, U.K.
controlledreleasesociety.org