CRS Leading Delivery Science and Technology

Newsletter

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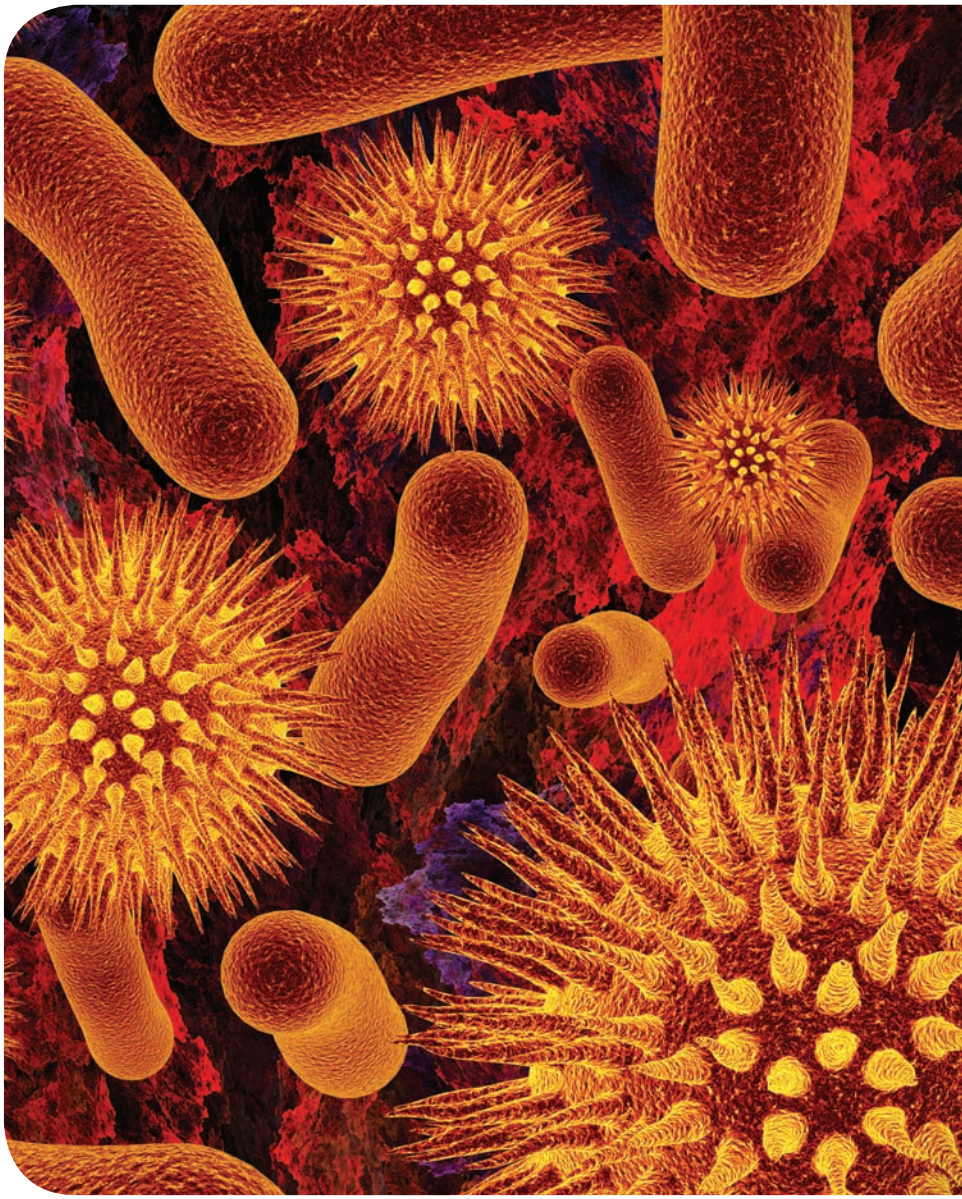


What's Inside

For Sale

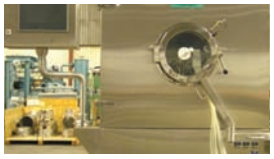
Transdermal Patches & Other Pharmaceutical Equipment

Featured Item

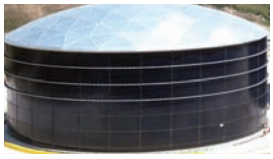
Hirano 24” wide, web coater, for the application of a thin film onto a web of backing materials.

Key Features: Web Speeds up to 4m/min • “Doctor Blade” type coating head • Fife web steering • Slurry Viscosity 2,000 to 15,000 CPS • Intermittent coating control • Steam heated, two zone continuous drying oven up to 130°C

Flow Layout: Unwind station; “Doctor Blade” coating station; continuous drying ovens; out-feed control and rewind station.



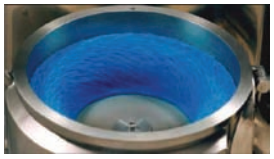
O’Hara, pilot size, automatic tablet coater LCIII, interchangeable pans



Never installed 250,000 gallon, bolted, stainless steel storage tank
35' diameter × 40' high

Elizabeth Hata 3 layer, 55 station, B tooling rotary tablet press

2-Munters 32,000 cfm, unused desiccant dehumidifiers,
Model ICA-3000-100



LCI Marumerizer granule former, produces smooth uniform spheres, 20 liter batch capacity

Mizuho, lab size, emulsifier/ dispersion triple action mixer, vacuum & jacketed

Please see our website for more information and pictures of these and many more items of pharmaceutical equipment.

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CRS Newsletter

Leading Delivery Science and Technology

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

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Arlene McDowell
University of Otago
New Zealand

Happy New Year!

I heard a great quote the other day by a New Zealand satirist and writer, Te Radar. "The best thing about family is that they are always there. The worst thing about family is that they are always there." Many of us will have spent time with family over the holiday season and can probably relate to this quote on some level. Family now has a new meaning to me because in June last year I became a mum to a lovely baby boy, Jack. On page 21 of this issue, you will find the names of those who recently joined as members of CRS. We welcome these new additions to the CRS family and look forward to getting to know them.

You may have noticed changes to the look of the *CRS Newsletter* cover. These changes are consistent with our lovely new website (www.controlledreleasesociety.org) and are part of the updated style as CRS continues to establish itself as the premier society for delivery science and technology. And what a stunning cover image too. Inside this issue, read about how to create a clear writing style in the article on Plain English by Linda Richardson. Our local chapters form the siblings of the CRS family, and they are certainly a vibrant group. The China Chapter had its first meeting in 2011, and the Canadian chapter held a networking event. Nanomedicine was the topic of discussion at the meeting of the Italian Chapter in Rome and at a joint Indo–U.S. symposium in India. As this issue goes to print, the New Zealand Chapter is preparing to co-host a workshop with the Australian CRS Chapter, followed by the annual Formulation and Delivery of Bioactives (FDB) conference at the University of Otago in New Zealand. We are very fortunate that CRS President Martyn Davies will be an invited speaker at the FDB conference this year.

Baby Jack's arrival meant that I missed the CRS Annual Meeting & Exposition in Maryland, so I am looking forward to the 2012 one in Québec City, Canada. While many of us catch up throughout the year by email, Skype, or phone, nothing beats talking face-to-face, and Québec City will provide a beautiful venue to catch up with colleagues and to meet new ones.

On behalf of the editorial team of the *CRS Newsletter*, I wish you a happy, healthy, and successful 2012.

Best wishes,

Arlene McDowell ■

Martyn C. Davies
University of Nottingham
Nottingham, United Kingdom

Even More to Discover in 2012

Dear Members,

As this is the first *CRS Newsletter* for 2012, I would like to extend my welcome to the New Year! As CRS is truly an international organization, I also can't help but recognize the Chinese New Year, held at the end of January. The year 2012 is the year of the dragon. I hope it has been a pleasant year thus far, full of new discoveries, and in the spirit of the dragon, I am confident CRS can "roar" ahead into this year.

It is difficult to say the words "new discoveries" without thinking about the CRS Annual Meeting & Exposition, to be held in Québec City, Canada, July 15–18 of this year. There are always countless new discoveries, breakthroughs, and innovative technologies to be found, along with endless new connections to be made, at a CRS Annual Meeting & Exposition. In addition, this year CRS gets to "discover" Québec City for the first time. While the CRS Annual Meeting & Exposition has been previously held in Canada, we have not met in Québec City. I am very excited to explore beautiful, historic Québec City. This beautiful walled city holds many opportunities to take in its European charm and exciting history, along with some of the best cuisine in North America. Registration for this year's meeting will be open in mid-March. I encourage you to register early and sincerely look forward to seeing you in July.

Still in the vein of "new"—did you notice the wonderful new *CRS Newsletter* cover? Or the new tagline? CRS leadership has been working to update the vision and mission statements and the tagline to more accurately reflect the work of our members and the direction of our society. The new statements read:

CRS vision statement: Visionary leadership in delivery science and technology.

CRS mission statement: CRS is an international, multidisciplinary society dedicated to delivery science and technology.

Tagline: Leading Delivery Science and Technology

A lot of consideration went into crafting these new statements. With help from volunteer members, the Board, and staff, we feel that these new statements will help better drive our society into a future that is encompassing of all areas of delivery science and that maintains a distinct leading edge in the science.
In "delivering" delivery science to all corners of the world, our unique chapter structure allows CRS to reach many scientists. The Board has recently approved chapter funding that supports the activities that occur in more than twenty countries. Membership in CRS chapters is free, and it offers delivery scientists the opportunity to get a taste of what CRS can offer. I encourage you to support your local chapter and to share the value of CRS membership with your fellow chapter members. You can find links to each chapter's information from the Community tab on the CRS website.

Another opportunity to share delivery science is the satellite meetings. You have the chance to share your knowledge and lead a meeting or workshop in your specialized area. These meetings can be educational as well as opinion leading and can be held throughout the year. This is a great chance to disseminate our science to delivery scientists, or to share our research and knowledge with those less familiar but able to benefit from our science. Please feel free to contact me if you have ideas for a satellite meeting.

Finally, I would like to invite each and every member of CRS to become involved. I can easily tell you how much CRS has helped develop me professionally and personally. I owe (much of) my career to the contacts I have made through my membership and involvement in CRS. We are always looking for fresh ideas and energy. I highly encourage you to serve the society that serves delivery science. Contact me or CRS Headquarters to get involved.

Again, Happy (belated) New Year! I hope CRS plays a major part in all your new discoveries this year.

Martyn C. Davies ■

As the 2012 CRS Annual Meeting & Exposition approaches, the CRS Newsletter *will highlight some of the top science from the meeting. Below read a preview of what to expect from the Bioactive Materials track during this year's meeting in Québec City, Canada. Watch for the next issue for a preview of the research to be presented in the other tracks.*

Bioactive Materials Sessions at the 2012 CRS Annual Meeting & Exposition, Québec City, Canada

Co-Chairs: Hamid Ghandehari, University of Utah, U.S.A. and Dusica Maysinger, McGill University, Canada

The Bioactive Materials sessions of the 2012 Controlled Release Society Annual Meeting & Exposition in Québec City promise an exciting line-up of world-class scientists that will represent the continuum of materials science and engineering, the cellular and biological responses to materials, and related translational considerations, with a common focus on the controlled delivery of bioactive agents. The topics to be discussed during scientific sessions will include inorganic nanosystems, theranostics and cancer nanotechnologies, stem cell and regenerative medicines, polymeric biomaterials for controlled release, DNA and RNAi delivery, oral delivery systems, translational nanomedicine, intracellular processes, oncology and tumor targeting, and transdermal delivery.

In addition to the scientific sessions, four mini-symposia on hot topics such as active versus passive targeting, new chemistries for design of novel biomaterials, evaluation of the influence of nanoparticle morphology on cellular response, and use of recombinant polymers for controlled release are being organized. During these sessions, a palette of experts who are developing new biomaterials and applying them for delivery and/or diagnosis of different diseases including neurological disorders will show their findings and invite you to their discussion. There will be a variety of synthetic approaches and elegant methods to construct and characterize these and other biomaterials.

Examples of applications of various innovative and bioresponsive materials will be presented and related to the biological questions and unmet needs in controlled release. In addition, the issues related to the structural features of the blood-brain barrier and problems of drug delivery to the nervous system and solid tumors will be discussed. Mechanisms of nanodelivery systems during their odyssey from outside to the interior of the cells will also be presented. Both the scientific sessions and mini-symposia will be presented by world-class invited speakers. Visit the CRS Annual Meeting & Exposition website at www.controlledreleasesociety.org/meeting for a complete listing of sessions and invited speakers.

The plenary sessions will be devoted to multifunctional nanocarriers for drug delivery, dendritic constructs, their origins and use in controlled delivery, and design of novel biomaterials for tissue engineering applications.

Finally, ample opportunities will be available for poster presentations and interaction among colleagues. ■

Plenary Speakers Announced for 39th CRS Annual Meeting & Exposition

Plenary speakers offer unique insights into many of the innovative and thought-provoking subjects in delivery science, often highlighting new areas and technologies or sharing outside perspectives on the science. This year's selection of plenary speakers promises to deliver new understanding into different areas of delivery science and technology.

Molly Shoichet

Plenary speaker **Molly Shoichet** is a professor of chemical engineering and applied chemistry, chemistry and biomaterials, and biomedical engineering at the University of Toronto, Canada. Shoichet holds the Tier 1 Canada Research Chair in tissue engineering and is an expert in the study of polymers for drug delivery and regeneration, which are materials that promote healing in the body. Shoichet has published close to 400 papers, patents, and abstracts and has given over 250 lectures worldwide. Her plenary session, titled "Drug and Cell Delivery Strategies to the Central Nervous System," describes three regenerative medicine strategies in the central nervous system for treatment of spinal cord injury, stroke, and blindness. These strategies are being pursued through both stem cell transplantation and endogenous stem cell stimulation.

Donald A. Tomalia

CEO and founder of NanoSynthons LLC **Donald A. Tomalia** is the pioneering scientist and inventor associated with the discovery of dendrimers and polyoxazolines. He is an inventor with over 120 U.S. patents, author of over 240 peer-reviewed publications, and serves as the director of the National Dendrimer and Nanotechnology Center, in addition to his work on several editorial boards. "Dendrimer-Based Nanomedicine—The Present and Future" will offer his unique

experiences with the science, including the current use of abiotic dendrimers in a variety of nanomedical applications, among them nanodiagnostics, drug delivery, imaging, and nanopharmaceuticals, and will explore the future of many new dendrimer-based nanomedical applications.

Speaker **Vladimir P. Torchilin** is a distinguished professor and director at the Center for Pharmaceutical Biotechnology and Nanomedicine, Northeastern University, U.S.A. This past president of CRS has published more than 350 original papers and more than 150 reviews and book chapters, written and edited 10 books, and holds more than 40 patents. He is editor-in-chief of *Current Drug Discovery Technologies* and of *Drug Delivery* and is on the editorial boards of many journals, including *Journal of Controlled Release* (review editor). Join Torchilin as he speaks on "Targeting Cell Organelles." Research

Vladimir P. Torchilin

shows that there are already enough means to deliver drugs inside cells, bypassing the lysosomal degradation. Torchilin explains that intracellular drug delivery with subsequent organelle targeting opens new opportunities in overcoming problems associated with multiple pathologies, including lysosomal storage diseases and multidrug resistance (MDR) tumors.

Full descriptions of the speakers and their subjects can be found at www.controlledreleasesociety.org/meeting. Plan now to join these outstanding scientists and gain their insights into delivery science at the CRS Annual Meeting & Exposition. ■

See These Exhibitors at the 39th CRS Annual Meeting & Exposition

July 15–18, 2012 • Québec City, Canada

Exhibiting companies that have reserved space at the 39th Annual Meeting & Exposition of the Controlled Release Society, as of press time, are listed below. For ongoing updates, visit www.controlledreleasesociety.org.

3M Drug Delivery Systems
Adhesives Research
Advanced Polymer Materials Inc.
Agere Pharmaceuticals
Agilent
Akina Inc.
Alkermes Pharma Ireland Ltd.
Apricus Bio/NexMed U.S.A.
Aptalis Pharmaceutical Technologies
Aptuit Inc.
Asahi Kasei America, Inc.
Avanti Polar Lipids
Aveva Drug Delivery Systems
Banner
BASF
BETATEK, Inc.
Bio-Images Research & Drug Delivery International
Buchi
Catalent Pharma Solutions
Celanese EVA Performance Polymers
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Croda Inc.
Delta Industrial Services
Dissolution Technologies
Distek, Inc.
Dow Water & Process Solutions
DURECT Corp./Lactel Absorbable Polymers
Elsevier
EMD Millipore Corp.
Evonik Degussa/Pharma Polymers
Fluid Imaging Technologies
Gateway Analytical, LLC
Gattefossé
Gaylord Chemical Company
Giltech Ltd.
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Lipoid LLC
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Styrene-co-maleic Acid (SMA) Telomeric Micelles Encapsulated-Zinc Protoporphyrin (SMA-ZnPP) and Other Drugs: Stability Study

Gahininath Y. Bharate,[1,2] Hideaki Nakamura,[1] Jun Fang,[1] Seiji Shinkai,[2] and Hiroshi Maeda[1,2]

A number of natural or synthetic polymers are used as micelle-forming agents. Among them we developed styrene-maleic acid copolymer (SMA) for this purpose. SMA has been used as a car and flour polishing agent and for seizing in the paper industry. Recently, it was approved as a food additive by the U.S. Food and Drug Administration. Use of SMA for pharmaceutical purposes was first started by Maeda's group. Namely, SMA was conjugated with neocarzinostatin (NCS) to make the macromolecular anticancer drug SMANCS.[1,2]

SMA is soluble in organic solvents as well as water. The anhydride group is reactive toward primary amino groups and forms a maleyl amide linkage. In the case of SMANCS, SMA confers high lipophilicity so that SMANCS becomes lymphotropic, a preferred character for the control of lymphatic metastasis. SMA also confers an albumin-binding character.[3,4,5] A lipophilic nature had the advantage of forming an oily formulation in a lipid contrast agent (Lipiodol®).[4] This method led to a new strategy for most tumor-targeting drug delivery using SMANCS/Lipiodol that is administered into the tumor-feeding artery with a catheter, yielding remarkable tumor regression in the most difficult-to-treat cancers, such as primary metastatic liver cancers and renal cancer.[6]

In the past several years, we found that SMA is one of the most versatile micelle-forming agents in that the procedure is simple with reasonable biocompatibility. Another unique aspect of SMA micelles is their stability upon lyophilization and complete recovery of the micelles by adding water, or stability *in vivo*. We found that the micelles only undergo disruption under severe conditions in alkaline or with detergents. More importantly, the drug is released upon internalization into the cells.[7] Recently, SMA micelles of photosensitizers such as Rose Bengal and methylene blue were found to be reasonably stable, to exhibit the enhanced permeability and retention (EPR) effect *in vivo*, and to be applicable for imaging (*unpublished data*).

Experimentals

In this newsletter, we present the stability of SMA micelles containing ZnPP (SMA-ZnPP) and other low-molecular-weight drug candidates. The SMA-ZnPP micelles were prepared very simply by adjusting the pH to >8.0 and then precipitating by acid, followed by dialysis.[8] In this study, two types of SMA, maleylcarboxylated and partially butylated, were used. The nanomicelles thus formed were characterized by UV absorption, fluorescence spectroscopy, Fourier transform infrared spectroscopy (FTIR), dynamic light scattering, zeta potential, and Sephadex G-100 chromatography, as well as biological evaluation.

Stability experiments were based on fluorescence spectroscopy of SMA-ZnPP micelles under different conditions. A release study of ZnPP from SMA micelles was performed by placing the micelle solution (0.5 mg/mL) in dialysis tubes with cut-off molecular mass of 10 kDa against 0.1 M phosphate buffered saline ranging from pH 6.0 to 9.0 at 37°C under stirring.

Results and Discussion

The characterization of two types of SMA-ZnPP micelles is summarized in Table 1.

Free ZnPP in dimethylsulfoxide (DMSO) or in alkaline solution showed the strongest fluorescence in the 580–610 nm range upon excitation at 420.0 nm. However, when SMA-ZnPP was dissolved in aqueous solutions, it was quenched completely, and it appears to exist as a densely stacked form (Figure 1). This suggests that SMA-ZnPP behaves as an encapsulated micellar structure, having π–π interaction of the stacked up state of the tetrapyrrole ring, which suppresses fluorescence due to energy transfer in aqueous solution. Similar phenomena were observed for the micellar drugs using SMA containing doxorubicin and pirarubicin and other fluorescent probes (e.g., Rose Bengal and methylene blue).

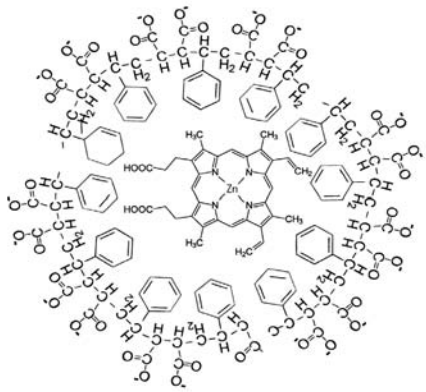

Figure 1. *Schematic representation of SMA-ZnPP micelle.*

Using fluorescence spectroscopy, we investigated the stability of SMA-ZnPP micelles at different pH (6.0–11.0). As shown in Figure 2A and B, weak fluorescence was seen below pH 6.0, which starts to emerge at higher pH, indicating the disintegration of the micelle structure (Figure 2A). A similar phenomenon is seen in the presence of a high concentration of urea and detergent (sodium dodecyl sulfate [SDS]) (Figure 2C

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Table 1. Characterization of SMA-ZnPP

SMA Micelle	% Yield (based on ZnPP)	% ZnPP Loading	Mean Particle Size (nm)	Mean Mw by Sephadex G-100	Zeta Potential (ζ, mV)[a]
Carboxy SMA-ZnPP	85	43.5	26.6	115	–46.85
Butyl SMA-ZnPP	92	34.3	29.3	128	–29.13

[a] Zeta potential was determined by Photal model ELSZ (Otsuka Electronics, Osaka, Japan) in 0.1 M phosphate buffer (pH 7.5).

and D), suggesting the disruption of micelle structure by hydrogen bond breakage or by counter ions.

Adequate disintegration of the micelle drugs is an important character, so as to provide the active ingredient access to the molecular target in the cells. SMA micelles were found to undergo disintegration in the presence of lecithin similar to SDS.[7] More importantly, we found SMA-ZnPP micelles were

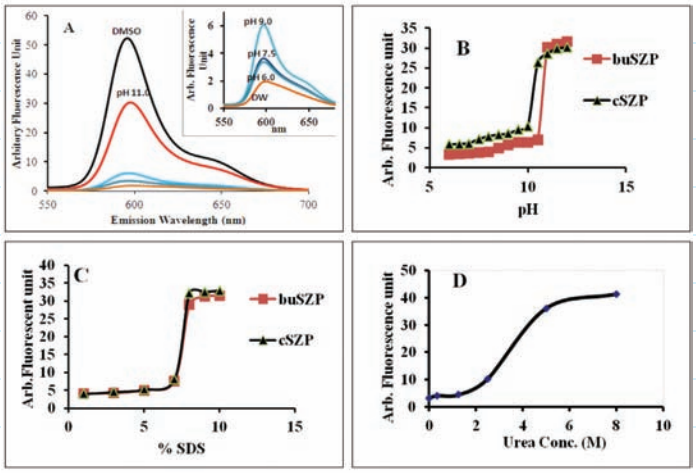

Figure 2. *Fluorescence spectrums of free ZnPP and SMA-ZnPP were recorded on F-4500 spectrofluorometer (Hitachi, Tokyo). (A) The fluorescence spectra of free ZnPP in DMSO and SMA-ZnPP in different pHs; the concentration of ZnPP and SMA-ZnPP was 1 μM (ZnPP equivalent) each. (B) Disintegration of SMA-ZnPP micelles is seen by abrupt increase of fluorescence intensity (at 595 nm) at or above pH 10.5. Stability of the SMA-ZnPP micelles in SDS (C) and Urea (D) is shown.*

disintegrated upon endocytotic uptake, a similar result to exposure to lecithin.[7] This means SMA micelles have ideal drug-release properties, predominantly in the cell after cellular uptake.

The inflection point for butyl SMA-ZnPP micelles was pH 10.5, whereas carboxy SMA-ZnPP was pH 10.0, indicating that butylated SMA was more stable than carboxy SMA. Moreover, Sephadex G-100 chromatography of carboxy SMA-ZnPP showed the apparent molecular size in an aqueous system was about 115 kDa. However, in the presence of albumin, it exhibited 152 kDa, indicating that albumin could bind to SMA-ZnPP micelles.

Zero-order release rate of free ZnPP from its SMA micelles was observed in the pH range of 6.0–9.0 (data not shown). The release rate was found to be a little higher at pH 9.0 (3.0%/day) than at the lower pH 6.0 (2.25%/day).

Conclusion

SMA was found to have a versatile nanomicelle-forming capacity. The micelles can be prepared simply, encapsulating various agents, just by changing pH, consisting of primarily SMA and the drug. All the SMA-drug micelles were proven to be stable during lyophilization and showed a very slow drug-release rate at a wide range of pH. More importantly, it exhibited drug release upon internalization into the cells.[7]

Acknowledgements

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References

1. Maeda, H, Takeshita, J, Kanamaru, R. A lipophilic derivative of neocarzinostatin, a polymer conjugation of an antitumor protein antibiotic, Int. J. Pept. Protein Res. 14: 81-87 (1979).
2. Maeda, H, Ueda, M, Morinaga, T, Matsumoto, T. Conjugation of poly(styrene-co-maleic acid) derivatives to the antitumor protein neocarzinostatin: Pronounced improvements in pharmacological properties, J. Med. Chem. 28: 455-461 (1985).
3. Takeshita, J, Maeda, H, Kanamaru, R. *In vitro* mode of action, pharmacokinetics, and organ specificity of poly(maleic acid-styrene)-conjugated neocarzinostatin, SMANCS, Gann Jpn. J. Cancer Sci. 73: 278-284 (1982).
4. Oka, K, Miyamoto, Y, Matsumura, Y, Tanaka, S, Oda, T, Suzuki, F, Maeda, H. Enhanced intestinal absorption of a hydrophobic polymer-conjugated protein drug, SMANCS, in an oily formulation, Pharm. Res. 7: 852-855 (1990).
5. Kobayashi, A, Oda, T, Maeda, H. Protein binding of macromolecular anticancer agent SMANCS: Characterization of poly(styrene-co-maleic acid) derivatives as an albumin binding ligand, J. Bioact. Compat. Polym. 3: 319-332 (1988).
6. Nagamitsu, A, Greish, K, Maeda, H. Elevating blood pressure as a strategy to increase tumor-targeted delivery of macromolecular drug SMANCS: Cases of advanced solid tumors, Jpn. J. Clin. Oncol. 39: 756-766 (2009).
7. Nakamura, H, Fang, J, Gahininath, B, Tsukigawa, K, Maeda, H. Intracellular uptake and behavior of two types zinc protoporphyrin (ZnPP) micelles, SMA-ZnPP and PEG-ZnPP as anticancer agents; unique intracellular disintegration of SMA micelles, J. Controlled Release 155: 367-375 (2011).
8. Iyer, AK, Greish, K, Fang, J, Murakami, R, Maeda, H. High-loading nanosized micelles of copoly(styrene-maleic acid)-zinc protoporphyrin for targeted delivery of a potent heme oxygenase inhibitor, Biomaterials 28: 1871-1881 (2007). ■

Plain English Leads to Savings and Safety Compliance

Linda Richardson, All Clear Translations

Plain English is a form of writing that has been utilized since the 1970s. The format and style of this article is written using the guidelines for Plain English. You will notice the use of bullets, short sentences, and graphics. These tools enhance the learning experience for the reader and increase understanding and retention of the information. Including Plain English in your safety training can make a difference. I hope you, the targeted reader, have an enjoyable experience learning new methods to increase your reader's comprehension level.

The purpose of this article is to educate you on the benefits of Plain English and why there is movement toward Plain English writing in government and business. It will enhance your message, reduce confusion, increase your perceived value, and save money for your company. Safety consultants and technical writers who use Plain English are writing reader-centric communications to increase comprehension and retention of safety procedures and operating manuals.

Creating documents with less content **increases** communication. Using Plain English impacts the bottom line. Often, writers are valued for the amount of content they deliver. After all, we were taught that to communicate well means more words, so offer detailed descriptions and more technical information, right? To creatively write less, producing less content, may seem less educational. Plain English enables better communication, reduced costs, and better memory retention of safety rules for all employees. English is a complex language.

Brief history of the Plain Language (English) movement in the United States:

1970s President Nixon decreed that the Federal Register be written in "layman's terms."

Citibank converted promissory notes to Plain English to improve consumer relations.

President Carter issued executive orders to make government regulations more cost-effective and easy to understand.

1980s President Reagan rescinded those orders.

1991 Eight states passed statutes related to plain language.

1998 President Clinton issued a memorandum to the heads of U.S. federal executive departments and agencies directing them to begin using plain language.

2010 President Obama signed into law the Plain Writing Act of 2010, which stated that writing with Plain English can reduce agency costs.

Listed in the Oxford (U.K.) and Webster's (U.S.) English dictionaries are about 1.5 million words. In comparison, the French dictionary word count is about 100,000. Discussed in this article are the history of Plain English, its impact to industries, and who utilizes this form of communication.

What is a Plain English document?

- Reader-centered writing
- Short sentences and paragraphs free of clichés
- Consistent terms, no jargon or acronyms
- Economical use of words, making more understandable content
- Formatting using bullets and small paragraphs.

What are some things that make a document hard to read?

- **Bold font in long sentences**
- ALL CAPITAL LETTERS MAKE A DOCUMENT HARDER TO READ
- Use of passive voice
- Use of verbs like nouns: for example, don't say "come to a conclusion," instead say "conclude"
- Cultural references
- Run-on text and long sentences
- Abbreviations and dashes
- Centered text: which example do you find easier to read?

Example 1

Summarizing the evidence on plain language as a promising strategy for clearly communicating safety information and improving safety literacy.

Example 2

Summarizing the evidence on plain language as a promising strategy for clearly communicating safety information and improving safety literacy.

Why Plain English?

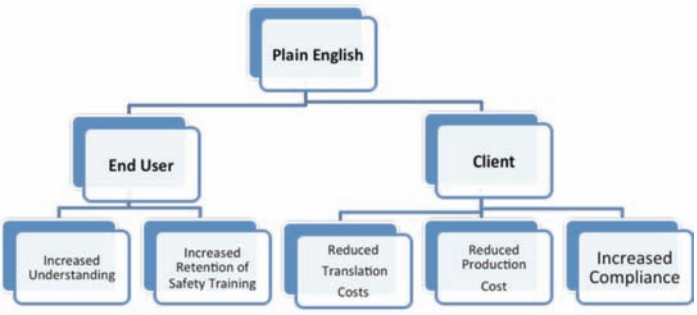
- Streamline manuals, processes, and paperwork
- More easily train staff of all language skills and backgrounds, including staff and consumers who speak English as a second language
  - *14% of the workforce* is Latino
  - Asians are the biggest gainers in workforce demographics
- Increase productivity
- Reduce confusion and claims
- Increase memory retention
- Increase compliance
- Decrease injuries
- Save money.

Who uses Plain English?

- Many companies and agencies; some are:
  - American Council of Life Insurance

- Shell Oil
- Caterpillar
- Boeing
- Target Stores
- General Motors.

- OSHA and all government agencies. "If we want to prevent regulation then we need to improve our safety record," said Federated Farmers health and safety spokesman Donald Aubrey.
- The Securities and Exchange Commission (SEC) requires Plain English.



Communication has been cited as the biggest stumbling block to compliance. There are several reasons why communication is not working. One is jargon (confusing terms, lack of understanding). Utilizing Plain English increases understanding and increases the value of the consultation. No longer is a long, wordy safety manual considered more informative and comprehensive. The manual is not evaluated on the volume of content created but on the ability to enhance training and retention and to save companies money. How can Plain English help Environmental Health and Safety, Human Resources, and management? We have found that companies are reaching out for help in creating a document that better communicates to **all** of their employees. We consultants must rethink our communication methods and include the client on how they communicate their safety and operating requirements. In conclusion, the benefits are great when using Plain English training manuals, safety manuals, and operating manuals. Readers strongly prefer a Plain Language document because it is faster to read, easier to use, and better understood. Companies strongly prefer Plain English because it increases compliance, improves safety, decreases injuries, and saves money.

From 1992 to 1995, a consultant worked with the technical writers at Federal Express to reorganize and revise the company's ground-operations manuals. The team took all the steps: they did a field study of users, tested the old manuals for usability, and compared the manuals to benchmark standards. The team identified the following needs (among others):

- An organization based on user tasks rather than formal job titles
- A more accessible and readable format
- Better tables of contents and indexes
- Improvements in the readability of the text through font changes and writing style
- Substantially increased use of graphics and tables.

Examples of Plain English in Action

Coast Guard Boating Information

CO Detector Update: 72 words

The Coast Guard has conducted an investigation to determine what carbon monoxide (CO) detection devices are available to recreational boaters, such that, when installed and activated could reduce the risk of being exposed to high levels of CO—THAT SILENT KILLER. A variety of technologies is available for detecting the presence of CO on boats and should be considered by recreational boaters to reduce their risk of injury or death while boating.

CO Detector Update (Revised): 39 words

Carbon monoxide is a silent killer. The Coast Guard recommends that you use a carbon monoxide detection device on your boat to reduce the risk of being exposed to high levels of CO. You may choose from a variety of devices.

Company Operating Manual

Freeing a Stuck Vehicle

Before: 36 words

When the process of freeing a vehicle that has been stuck results in ruts or holes, the operator will fill the rut or hole created by such activity before removing the vehicle from the immediate area.

Revised: 19 words

If you make a hole while freeing a stuck vehicle, you must fill the hole before you drive away.

Resources:
www.plainlanguage.gov
Howto.gov
Plain Writing Act of 2010
U.S. General Services Administration

In the testing, readers of the old manuals searched for an average of 5 minutes to find information and found the correct answer only 53% of the time. With the new manuals, the average search time dropped to 3.6 minutes, and the success rate improved to 80%. With some further improvements to the index, the team estimated—very conservatively—that the new manuals would save the company $400,000 in the first year, just in the time that employees spend searching for information. That's not counting costs that flow from getting wrong answers.

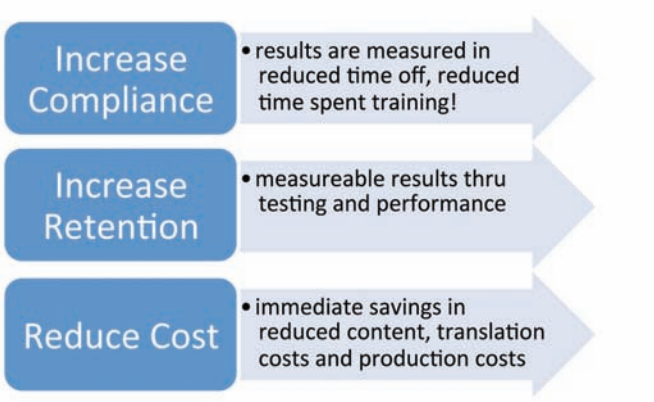
Now imagine using a Plain English resource to help you create your safety manuals! What can you offer in savings and

Plain English continued on page 10

Plain English continued from page 9

compliance to your client? Using Plain English provides your client with a safety manual that will save them money. Safety can be looked at as a savings measure more than a necessary cost. Your client realizes savings and better cash flow through better compliance and through decreased accidents and work-related injury time off. Plain English provides you with a strong tool to build your value and brand.

Increase the value of your manuals by offering Plain English communications. How do you measure success for your client, company, or department?



Engaging in new, innovative solutions like Plain English will impact your company's bottom line; you will win loyal customers, referrals, and increased sales. Plain English is an innovative solution and will be an integral part of your process to new and better training systems. Plain English will eliminate miscommunication. Engage supporting services for Plain English that help you communicate in a clear, concise method to your reader. If you are a safety consultant, increase your value as a proactive, innovative consultant and increase your competitive advantage.

> Workplaces with successful safety and health management systems reduce injury and illness costs 20%–40%. OSHA standards require that an employer instruct its employees using understandable language.
>
> Source: OSHA.gov

A company will minimize risk by offering a comprehensive safety package that probably includes a variety of training methods, including:

- Manuals
- In class training
- Online training
- On the job training.

Today's business climate is all about decreasing costs while increasing profitability. Proactively including Plain English writing in your training will positively impact your bottom line and cash flow. By increasing comprehension and retention of training, you will make a difference in your company's survival.

Offering another component to a successful safety plan can

- Increase your perceived value
- Eliminate the competition
- Create your "Blue Ocean" (uncontested market space).

According to the U.S. Small Business Association, 82% of businesses fail because of poor cash flow. One good way to sell your safety program to management is to tie it into their cash flow. You have increased the value proposition of being a resource to help complete their mission by saving costs while increasing understanding. A winning proposition! Do you communicate outstanding value?

Linda Richardson is the President of All Clear Translations and partner in All Clear Communication. Contact Linda at 412.496.5105, linda@allclearcommunication.com, or Linda@allcleartranslations.com ■

Your Membership:

Your Access to the Future of Delivery Science and Technology

Test tubes and shampoo images courtesy of istock.com. Eye drops courtesy of Comstock.

Your membership is your all-access pass to leading research and the delivery science community.

Access: Innovative Research

From the research presented in the journals *Drug Delivery and Translational Research* and the *Journal of Controlled Release*, to the science presented at the CRS Annual Meeting & Exposition, to books and online webcasts, CRS is your source for the best delivery science and technology research.

Access: Targeted Networking

The CRS Annual Meeting & Exposition is just the beginning of the great opportunities to connect with delivery scientists. Utilize the online community through the website, find experts through the new LATTE database, join a committee, connect on LinkedIn, or join your local chapter, and access one of the most valuable resources – each other.

Access: Career Advancement

Advance your professional skills through volunteering, participating in the mentoring program, and more. CRS offers fellowship programs and recognition through awards. The new online career center is one more chance to develop your career in delivery science.

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Jorge Heller Postdoctoral Fellowship Year Reflections 2010–2011

Qun Wang, Ph.D.
Postdoctoral Fellow, Langer Laboratory
Harvard—MIT Division of Health Science and Technology, Harvard Medical School

Qun Wang

In 2005, I entered the Department of Chemical and Petroleum Engineering at the University of Kansas as a Ph.D. student. I chose Dr. Cory Berkland, a joint professor in the Department of Chemical and Petroleum Engineering and the Department of Pharmaceutical Chemistry, as my advisor. I believe that a different but related discipline can help expand my academic knowledge and analytical skills and enable me to apply the theoretical methodology to a broader practice. The multidisciplinary background can make me fit and manage different projects easily. It turns out that I made the right choice.

Under the guidance of Dr. Berkland, my research focused on the interface of engineering and pharmaceutics. I have developed solid skills and knowledge in the areas of polymer science and engineering, drug delivery systems, biomaterials, and nanotechnology and built a breadth of analytical skills to characterize materials. I have created many materials for drug delivery systems, including drug-loaded films, fibers, self-assembling colloids, gels, and nano- and microparticles. I have published 19 papers in well-known refereed journals and hold six patents in the United States and China.

Postdoctoral Fellowship

In 2010, before my graduation, I was very lucky to receive the Jorge Heller Postdoctoral Fellowship from the Controlled Release Society Foundation. CRS is the premier society worldwide for drug delivery science and technology. CRS Foundation fellowships are designed to identify and acknowledge the future leaders of CRS, while honoring individuals who have made notable contributions to the society and delivery technologies. It's my great honor to receive this award. I have passion for doing research and want to pursue my career in academia. With this fellowship, I plan during my postdoctoral period to get top-level training for my future career from a top-level school, such as Massachusetts Institute of Technology (MIT) and Harvard Medical School.

Using Intestinal Stem Cells to Treat Colorectal Cancer Through Regenerative Medicine

I contacted Prof. Robert Langer, the David H. Koch Institute Professor at MIT, whose lab is the largest biomedical engineering lab in the world. He entrusted me with a leading role in a very challenging project to use intestinal stem cells to treat colorectal cancer through regenerative medicine. The intestine can be thought of as both a catalytic and absorptive surface where most of the chemical digestion and nutrient absorption in the gastrointestinal (GI) tract takes place. The mucosa is composed of a monolayer of epithelium organized into circular folds and further organized into crypts and fingerlike projections known as villi. This combination of macroscale and microscale patterning increases the surface area of the small intestine 600-fold over that of a cylindrical tube of the same diameter.

Cancer is a major healthcare issue for many countries around the world, including the United States. Colorectal cancer is the third most common cancer and the second leading cause of cancer death in the United States. Worldwide, more than one million cases of colorectal cancer are clinically diagnosed annually, and more than half of those who are diagnosed die every year. The current treatments, such as intestinal transplantation and chemotherapy, are limited by a lack of donors, high degree of implant failure, massive side effects, and the need for heavy immunosuppression.

Regenerative medicine seeks to replace or facilitate the regeneration of damaged or diseased tissue by applying a biomaterial support system or scaffold, or a combination of cells and bioactive molecules. The fundamental principle of regenerative medicine is that the engineered biomaterials can facilitate regeneration of structures that resemble the original tissue and organ. Drug delivery and regenerative medicine are closely related fields. Actually, regenerative medicine can be recognized as a special case of drug delivery, since the goal of regenerative medicine is to accomplish accurate controlled delivery of cells and tissue. Controlled release of therapeutic factors has been shown to promote the regeneration of tissue. From the point of view of materials science, both drug delivery systems and tissue engineering scaffolds should be biocompatible and biodegradable. The medical functions of encapsulated drugs and cells could be dramatically improved by designing materials with controlled structures at the appropriate scale. Intestinal tissue engineering is a systemic research that requires combined knowledge from different areas. My multidisciplinary background makes me fit the project very well.

Significance of Research

In the Langer Lab, my research is the first to target topical delivery of intestinal stem cells to the damaged site of the intestine to treat colorectal cancer. Significantly, intestinal stem cells have the fascinating ability to efficiently generate all the intestinal epithelial cell types and heal the damaged or ulcerated area of the intestine. Furthermore, with this innovative approach, intestinal stem cells could be acquired from the patients themselves and easily expanded *in vitro* to avoid heavy immunosuppression. For this groundbreaking method, I created

a thin layer of an epithelial patch that could immediately adhere to the intestinal surface, especially to the damaged surface when delivered *in vivo*. The materials used in this patch can support the initial survival and proliferation of the delivered cells and greatly increase the delivery efficiency. Through delivery of cell-encapsulated patches, this original method can achieve rapid regeneration of the epithelial barrier and enable the remission and cure of the disease. The delivery route can be performed easily; thus, we expect that this therapeutic strategy can be rapidly translated to clinical use as an effective and convenient therapeutic method for colorectal cancer. Moreover, the stem cell-engineered epithelial patch could provide a platform for high-throughput testing of prospective drugs and inflammatory modulators, which may lead to the development of new drug and therapeutic agents useful for the treatment of patients with other intestinal diseases.

In the future, I will further expand my research in this area. I hope my work could relieve the pain of patients. Actually, we were recently approached by a group at Harvard Medical School to collaborate on a translational research project to adapt our method for clinical use. ■

Sung Wan Kim Postdoctoral Fellowship Applications Accepted Through March 12, 2012

Sung Wan Kim

Through generous donations totaling more than $100,000, postdoctoral fellowships have been awarded to three outstanding scientists to expand their perspectives, networks, research, and collaborations in delivery science. A new fellowship for 2012 is named in honor of Sung Wan Kim, University of Utah, for his pioneering career in delivery science.

The Sung Wan Kim Postdoctoral Fellowship Recipient Will:

- Receive a one-year $30,000 postdoctoral fellowship
- Relocate to a research laboratory in a new environment
- Receive a complimentary registration to the 39th CRS Annual Meeting & Exposition in Québec City, Canada, July 15–18, 2012
- Participate with an abstract and poster in the 2012 CRS Annual Meeting & Exposition
- Serve as an invited speaker at the 2013 CRS Annual Meeting & Exposition to present outcomes of the research

Selection Criteria:

- Candidate must be a graduate student who has completed his or her Ph.D. by July 2012 or a recent postdoctoral individual
- Candidate's research must be in delivery science or an associated field
- Candidate may be from academia, government, or industry
- Candidate will demonstrate excellence in scientific research and strong leadership potential

Support the CRS Foundation
The Sung Wan Kim Postdoctoral Fellowship and the building of the CRS Foundation Endowment for future awards are made possible only through individual and corporate support. Please give to support the future leadership of CRS and delivery science.

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By telephone, fax, or e-mail to:
Cheryl Kruchten, CRS staff
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CRS FOUNDATION

The CRS Foundation's Jorge Heller Postdoctoral Fellowship was presented to Qun Wang at the 37th Annual Meeting & Exposition of the Controlled Release Society in Portland, Oregon, U.S.A., July 2010. The research was conducted in 2010 and 2011. Many thanks to the CRS Foundation donors who made this fellowship possible. ■

Interview with Dr. Rohit Jain, a Recent Ph.D. Graduate in the Veterinary Field

Arlene McDowell, University of Otago, New Zealand
Veterinary Editor

Dr. Rohit Jain's Ph.D. studies were completed at the Mastitis Research Group, School of Pharmacy, University of Otago, New Zealand. His Ph.D. supervisors were Dr. Olaf Bork and Prof. Ian Tucker. His current position is Postdoctoral Fellow, Bomac Laboratories Limited, New Zealand.

Q *What attracted you to study for a Ph.D. in the area of veterinary therapeutics?*

A I chose the project on veterinary therapeutics as it is a vast but slightly underexplored area of research, especially with regard to new formulation development. Also, veterinary therapeutics is of particular interest in countries like New Zealand where the economy is based on dairy farming. I have always been interested in research. This Ph.D. in pharmaceutical sciences enabled me to pursue my research interests, such as chemical stability of drugs and formulation development.

Q *Could you briefly outline your research in the area of controlled release?*

A Antibiotics are used to treat bovine mastitis, which is a common inflammation of the mammary gland (udder) that results in decreased milk production and losses that make it a costly disease in dairy farming. The antibiotics for mastitis treatment are commonly available as a dry powder ready for reconstitution with diluents for intramuscular injection. This is a formulation limitation, as the reconstituted product has a short shelf life (two days at 15–20°C) due to poor chemical stability. This short shelf life leads to discarding of unused product, making it unsuitable for use in farm conditions, as it is practically and economically not suitable for the treatment of a large group of animals. The aims of my Ph.D. thesis were to understand the chemical stability of an antibiotic commonly used in treatment of bovine mastitis, to develop a chemically stable formulation, and to test this formulation in the target animals (cows).

Q *What was your most significant research finding?*

A The chemical stability for antibiotic formulations was enhanced significantly compared with the existing marketed product of the same antibiotic. The results from an *in vivo* study in the target animals (cows) for the antibiotic formulations were comparable with the existing marketed product.

Q *What is your favorite part of research?*

A Spreading the knowledge (in terms of publications and conference presentations) gained during the research to the wider scientific community.

Q *Has CRS had an influence on your career?*

A CRS has been very helpful in providing a platform by the way of conferences and workshops that enabled me to share knowledge and make contacts with fellow researchers.

Q *What are your future plans?*

A Currently, I am working for Bomac Laboratories Limited, a Bayer Company, in New Zealand on a postdoctoral fellowship sponsored by the Ministry of Science and Innovation, New Zealand. My future plans include searching for the right postdoc or industry position opportunity. I would like to gain more experience in the fields of drug stability, controlled release systems, and formulation development.

Q *What would be the best piece of advice you could give a fellow student doing a Ph.D.?*

A In my opinion, hard work, attention to detail, and critical evaluation of data are key for a successful Ph.D.

Q *And finally, what's your favourite animal?*

A Personally, a dog, but professionally, considering my Ph.D. project, my favourite animal is a COW.

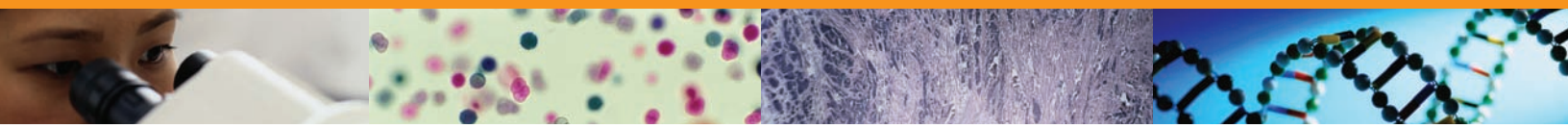
Read more about Rohit's research in the following publications:

Jain, R, Wu, Z, Tucker, IG. A stability-indicating HPLC assay with diode array detection for the determination of a benzylpenicillin prodrug in aqueous solutions, J. Pharm. Biomed. Anal. 50(5): 841-846 (2009).

Jain, R, Wu, Z, Olaf, B, Tucker, IG. Pre-formulation and chemical stability studies of penethamate, a benzylpenicillin ester prodrug in aqueous vehicles, Drug Dev. Ind. Pharm. 38(1): 55-63 (2011).

Contact: rohit.jain@otago.ac.nz.

Are you a recent graduate, or have you had a student recently complete their studies? We would like to hear from you and find out about your research. Contact Arlene McDowell (arlene.mcdowell@otago.ac.nz). ■



Barrett K. Green—The Father of Microencapsulation

Ronald J. Versic, Ronald T. Dodge Company

B. K. Green, circa 1956

Barrett K. Green (September 11, 1906–August 29, 1997) was an American scientist, innovator, and industry pioneer who is best known as the inventor of microencapsulation, a term applied broadly to processes that create microcapsules of a payload material. Green was a longtime NCR employee (1933–1973), held 197 patents, and was highly respected and honored as both a scientist and a leader in the development of practical, real-world products. Today, virtually thousands of controlled release products (and others) are possible because of his ability to translate his science into practical, usable, real-world products. His story offers inspiration regarding not only the potential value of our current research efforts but also the broader scope of this value as it extends into many other areas of need.

The purpose of this article is to share information about Green's background, time at NCR, and the impact he has had on the controlled release industry.

Early Years

Barrett Green developed a strong interest in science and chemistry during high school in the early 1920s. This interest took him to Cornell University in Ithaca, New York. Cornell was well-known (even in the early 20th century) for diversity in all fields of knowledge, with emphasis on both learning a discipline and applying it in the "real" world. Green focused his attention on colloids and colloid science in his undergraduate years and received a B.S. degree in chemistry in 1928. He continued his work in colloid chemistry an additional four years as a graduate student at Cornell. His keen interest in this area and Cornell's emphasis on applied technology formed a foundation for his inventive interests.

NCR

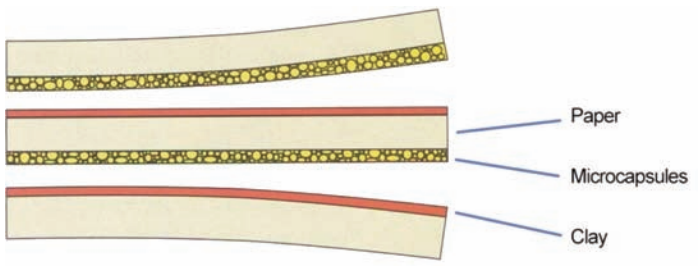
Green's career at NCR Corporation began as a research scientist (one of the first hired by NCR) in 1933 and ended in 1973 when he retired as Assistant Vice President of Central Research. During his long, celebrated career at NCR (previously known as National Cash Register), Green pioneered modern-day coacervation techniques that led to the development of carbonless paper, scratch-and-sniff products, and time-release capsules, among many other uses.

Carbonless paper—Green's major breakthrough product—emerged from research efforts extending from the late 1930s into the 1950s. By 1942, Green had developed a working method of microencapsulating ink and a prototype carbonless paper. Over the next decade, he refined his methods and scaled the process to production levels. He worked closely with Thomas Busch of Appleton Papers on the difficult process of applying the microcapsules to paper in a thin, flexible layer.

Microencapsulation

Definition	A means of packaging, separating, and storing materials in microscopic capsules for later release under controlled conditions
1902	Observation of process by Viennese chemist Wolfgang Pauli
1939	Barrett K. Green began research at NCR
1942	H. G. Bungenberg de Jong of The Netherlands suggested coacervation could be used to make microcapsules for drugs
1942	Barrett K. Green developed a working method of microencapsulating ink and a prototype carbonless paper
1954	NCR introduced the first successful carbonless paper to the business world
1955	Green received a patent for microencapsulation
1955 to present	Industry applications include xerography, scratch-and-sniff, and time-release capsules

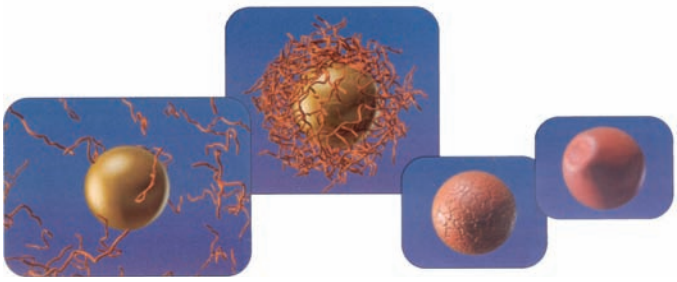
Carbonless paper had three layers: the paper, a film of acid-sensitive dye packaged in microcapsules, and a layer of acidic clay to develop the dye from transparent to dark blue or black. Pressure from a writing implement (pen or pencil) broke the microcapsules of dye on the underside of each sheet (except the last one). When the dye was released, it reacted with the acidic layer on the surface of the next sheet. Considerable effort went into designing capsule walls that were sturdy enough to withstand processing but would rupture under the pressure of a pencil.



Barrett K. Green continued on page 16

Barrett K. Green continued from page 15

Scientists had long been intrigued by the possibilities of controlling the release of an active ingredient by encapsulating it. What was theoretically possible proved difficult in practice. Green's research, partly based on his studies as a graduate student at Cornell, involved enclosing a liquid in a solid. Essentially, he solved the pressure-triggered release problem by chemically "hardening" the outer layer of the capsule using gelatin. When gelatin is treated with a reactive chemical such as formaldehyde, chemical bonds form between the gelatin chains, resulting in a three-dimensional network of cross-linked gelatin. Cross-linked gelatin is harder and less soluble than regular gelatin, yielding a tougher and more durable microcapsule.



NCR introduced the first successful carbonless paper to the business world in 1954. Green received a patent for microencapsulation on July 5, 1955.

In an article written at the time of his retirement, Green reflected on his discovery:

> I can remember very well the day we found what we had been looking for with encapsulation and paper. We had developed a process earlier, but it wasn't good enough. We used an emulsion on the paper, and in a warm room, the emulsion melted and the paper was ruined.
>
> What we had visualized before we could actually do it, was to leave the oil in the clay, which was coated on the paper—leave it there isolated and insulated, but colorless.
>
> I remember the afternoon I applied the clay toluene test after I'd made some capsules by the coacervation process, and the test was successful. I knew right away that we had what we'd been looking for.

As a result of Green's discovery, NCR (no carbon required) paper became a major cutting-edge product that was manufactured by NCR around the globe and was widely used by tens of thousands of customers. It provided a much-improved business forms medium at a time when the business forms industry was growing dramatically.

Prior to his discovery, no major products had been developed using the science of encapsulation. Again, Green reflected on his breakthrough: "The science of encapsulation had been established, but no one had put it to work—to do a job. When I was a student at Cornell, the professors had very little to say about the idea of a liquid being dispersed in a solid."

Applied Technology

A few years after NCR introduced carbonless paper, another first-of-its-kind product—based on Green's research—was delivered to the marketplace. Chester Carlson, an inventor, enlisted the aid of the Haloid Company of Rochester, New York, to help commercialize his new copying process known as xerography. Xerography was a dry photocopy process that used toner consisting of microencapsulated dyes. The Xerox 914, released in 1959, was the first machine that faithfully produced copies of virtually any document without resorting to less-desirable and messy wet processes.

An unexpected path that this versatile technology took was the development of fragrance ads used in advertising scented products. Commonly known as scratch-and-sniff, these ads consisted of small capsules filled with a solution, typically perfume. Scratching the surface ruptured the capsules, and the scent was released.

The microencapsulation work of Barrett Green provided a foundation for applications in many diverse industries, including pharmaceuticals, foods, cosmetics, nutritional supplements, personal care, pet care, household, agriculture, detergents, paints, adhesives, and sealants. The real-world applications of Green's technology developed over a half-century ago may be limited only by the imagination today.

Recognition

Barrett K. Green was well known and highly acclaimed for his work during his lifetime. He was honored by his colleagues at NCR and other professionals, recognized by his community, received numerous awards for his research and product developments, and was inducted into the prestigious Engineering and Science Hall of Fame after his retirement.

During National Engineers Week in early 1965, Green was honored for his 1964 work on the photochromic microimaging concept. He was also acknowledged at that time as the author of the "Coacervation" section in the *New Encyclopedia of Chemistry*, as co-author of a paper titled "New Principle of Emulsion Stabilization" presented to the American Chemical Society, and as co-author of a paper titled "Chemical Switches" presented at the International Symposium on the Theory of Switching presented at Harvard University.

Later in 1965, Green and a fellow researcher from NCR, Lowell Schleicher, were acknowledged for their work in microencapsulation and colloid chemistry, receiving the "Modern Pioneers in Creative Industry" award from the National Association of Manufacturers.

On October 17, 1991, Barrett Green received one of his most prestigious awards from the Engineers Club of Dayton: he was enshrined into the Engineering and Science Hall of Fame as the "developer of the process of microencapsulation." Others honored at that ceremony included Dr. Leland Clark, inventor of the

heart-lung machine, and Chester Carlson, the developer of xerography. Other well-known inductees include Orville and Wilbur Wright, Thomas Edison, Enrico Fermi, and Jonas Salk.

Green was also honored by the community in which he worked and lived, with his name and accomplishments immortalized in granite on the Dayton Walk of Fame in 2004. Scientists, entertainers, philanthropists, corporate and business leaders, and others have been recognized on the Walk of Fame for their "outstanding and enduring personal or professional contributions to the community, nation, and the world." Green was honored as an inventor and acknowledged as the "father of microencapsulation."

Photo taken at the Dayton Walk of Fame, where famous Daytonians and their major accomplishments are immortalized in granite.

Perhaps Barrett Green's greatest legacy can be found in the hundreds of products that have been developed as a result of his work. Green could easily be considered one of the original "green" thinkers. He believed in using resources to their best advantage. Over seven decades ago—with the invention of carbonless paper—he was "going green." Green's life was all about maximizing resources, finding solutions to real-world problems, and turning pure science into economically viable and useful products.

Acknowledgements
Charles Frey was very helpful in editing the text into a shorter form from the original manuscript. For access to the full original manuscript and related information, consult the References.

References

1. The Donald D. Emrick Memorial Library and Information Center (www.controlled-release.com) is useful on the broader subject of controlled release and the early development of related technologies.
2. See www.microencapsulation.net for an overview of the technologies of microencapsulation for achieving controlled release.
3. The full original manuscript at www.coacervation.net contains considerably more material on Barrett K. Green and the development of coacervation.
4. The Ronald T. Dodge Company is a global supplier of microcapsules. It is a privately owned company founded in 1979. Dr. Ronald J. Versic is president, founder, and Chief Scientific Officer. Products include fragrance inks and coatings, peroxide catalysts, and custom products. ■

IN MEMORIAM

In Memory of Dr. Johann Wiechers

Jamileh Lakkis, Lipofoods

Dr. Johann Wiechers was an accomplished scientist, an inspiring educator, and a very dear friend to many people who had the good fortune of knowing or working with him. He passed away on November 5, 2011, after contracting a dangerous form of pneumonia, in a Kuala Lumpur hospital where he was surrounded by his family. His invited presentation for the Consumer & Diversified Products track of the 2011 CRS Annual Meeting & Exposition in Washington, D.C., was one of his last contributions to the field of skin delivery and to the personal care industry.

A pharmacist by training, Johann received his Ph.D. from the University of Groningen in 1989 for his work on skin penetration enhancement. He started out his career in the dermal delivery industry at Unilever in the United Kingdom, followed by almost 12 years as a technical director at Uniqema in The Netherlands. He later joined Dataderm International GmbH as a managing director for two years and eventually founded his own consulting company, JW Solutions, in 2007. He was president of the International Federation of Societies of Cosmetic Chemists (IFSCC), a technical advisor for Allured Publishing, a board member of the Dutch Society of Cosmetic Chemists (NVCC), a visiting professor in pharmaceutical chemistry and drug delivery at the University of London, and an adjunct professor in the School of Medicine at the University of Queensland in Brisbane, Australia. Johann was a very prolific presenter and author, with more than 450 papers, book chapters, columns, and podium presentations.

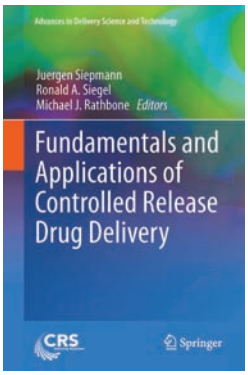
His thorough understanding of cosmetic formulations was best articulated in his vision of skin delivery in the novel concept of the Formulation for Efficacy (FFE) system and the subsequent 2011 launch of specialized software that was described as a great tool to help formulators navigate through the maze of skin delivery. His long-lasting legacy will be his skillful incorporation of real science into the field of cosmetics.

Johann was a constant presence at major conferences and seminars in the cosmetics and personal care industry. He was a very engaging speaker whose unmatched passion for science was coupled with a clear willingness to share his knowledge and to listen to opposing views. His peers, however, will mostly remember his grace, great sense of humor, zeal for life, and down-to-earth gentleman qualities.

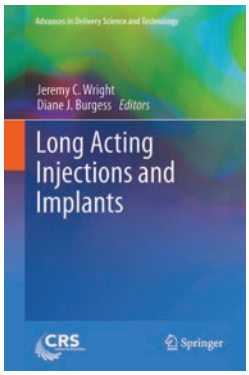
Johann will be deeply missed by his friends and colleagues.

Two New CRS Books Published in December 2011

The new CRS book series *Advances in Delivery Science* doubled in size in December 2011, now with four volumes highlighting major aspects of delivery science and technology. Each volume has been edited by established leaders in the field, with each of the chapters written by experts in delivery science and technology. The newest additions include *Fundamentals and Applications of Controlled Release Drug Delivery* and *Long Acting Injections and Implants*.



Fundamentals and Applications of Controlled Release Drug Delivery covers the fundamentals of the science and technology of drug delivery, and is intended for those who are entering the field of delivery science and are not familiar with the terms. Created by editors **Juergen Siepmann, Ronald A. Siegel, and Michael J. Rathbone**, this book covers the value of drug delivery, polymeric delivery materials, temporal delivery systems and mechanisms, spatial delivery systems and mechanisms, applications of controlled drug delivery, and the future outlook of the science. This book is ideal for those crossing into the area of delivery science or as a student text.



Long-acting injections and implants improve therapy, enhance patient compliance, improve dosing convenience, and are the most appropriate formulation choice for drugs that undergo extensive first-pass metabolism or that exhibit poor oral bioavailability. An intriguing variety of technologies have been developed to provide long-acting injections and implants. Many considerations need to go into the design of these systems to translate a concept from the lab bench to actual therapy for a patient. *Long Acting Injections and Implants* surveys and summarizes the field. Editors **Clive G. Wilson and Patrick J. Crowley** provide essential information for experienced development professionals, but the book was also written to be useful for scientists just beginning work in the field.

According to CRS book series editor Michael Rathbone, other books are in the pipeline on topics such as sRNA, animal health applications, and vaginal drug delivery. If you are interested in editing a book in the series, which serves as a forum for the dissemination of knowledge relating to delivery science, technology, and innovation, contact Rathbone at michael_rathbone@imu.edu.my for more information. ■

New CRS Board Nomination Process

Following the new CRS bylaws approved in 2011, the CRS Board nominations process has been updated. Beginning this year, each Controlled Release Society member has the opportunity to participate in the nominating process and help shape the selection of future CRS leadership. According to Nominating Committee Chair and Past President Mark Tracy, "Under the new CRS bylaws, the size of the Board of Directors has increased from eight to eleven members, and our nomination process now includes a call for nominations to CRS membership. The goal of both of these bylaw updates is to promote enhanced diversity in leadership at the Board level."

The call for nominations was sent to members in January. Nominations were sought for Secretary, Treasurer, and Directors-at-Large for the 2012 CRS Board election. The Secretary and Treasurer each have a one-year term of service, while Directors-at-Large serve for up to three years. A description of each of these positions can be found in the CRS bylaws at www.controlledreleasesociety.org/about/leadership/Pages/bylaws.aspx. The nominating period ended February 6, 2012.

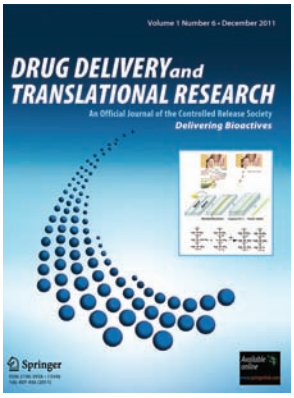
Now that the nomination period has closed, the Nominating Committee will review the candidates suggested by both the committee members and the membership at large and will select final candidates. A ballot will be posted with each finalist's name and biographical information. CRS members will then have the opportunity to review the ballot and may petition to add a candidate directly to the ballot, with the sponsorship of at least 30 members. The ballot will then be finalized, and the election will be held in May, with the new officers taking their positions in July.

"We look forward to completing this new nomination process and presenting a ballot of strong candidates to the CRS membership for election in May," said Tracy. CRS members will receive communications from CRS Headquarters for future opportunities to help shape the CRS leadership team.

CRS Nominating Committee
Mark Tracy, Chair
Terry Allen
David Brayden
Doug Dale
Ken Howard
Kazunori Kataoka
Julia Rashba-Step
Ron Siegel ■

Drug Delivery and Translational Research

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



I hope you had a good New Year celebration. I am pleased to report that *Drug Delivery and Translational Research* (*DDTR*), an official journal of CRS, has successfully compiled its first full volume. All issues were published on time, with papers reporting results of high-quality translational drug delivery research, from preclinical data in rodents and primates to human clinical data. We have reached about 1,000 downloads per issue, an indication of the growing interest of the scientific community in the studies chosen for publication in *DDTR*. This achievement is a team effort, and I want to thank all of you for your contributions to the success of *DDTR*.

Editor's Pick

I am pleased to announce the paper published by Professor Ram Mahato's group in issue no. 6 of DDTR as the editor's pick. The study describes the combination of drug delivery to overcome drug resistance in cancer therapy. In my editorial in the same issue, I described how cancer develops drug resistance and commented on different drug delivery strategies that hold great potential for preventing tumors from developing drug resistance or for treating drug-resistant tumors.

Paclitaxel- and lapatinib-loaded lipopolymer micelles overcome multidrug resistance in prostate cancer

By Feng Li, Michael Danquah, Saurabh Singh, Hao Wu, and Ram I. Mahato

Professor Mahato's group from the University of Tennessee has shown that lapatinib, which interacts with and inhibits p-glycoprotein (P-gp) activity, when used in combination with paclitaxel, can synergistically treat resistant prostate cancer. P-gp is a membrane-associated efflux transporter, which influences the intracellular retention of anticancer drugs in resistant cells. In a xenograft athymic nude mouse tumor model, the group has shown significant inhibition of tumor growth when the lapatinib–paclitaxel combination was given twice a week intravenously using a micellar formulation. The combination therapy strongly inhibited tumor angiogenesis. Read more about this paper at www.springerlink.com/content/2190-393x/1/6/.

First Issue in 2012

A *DDTR* Special Focus Issue on "Advances in Image-Guided Drug Delivery," with Arash Hatefi and Tamara Minko as Guest Editors

Image-guided drug delivery (IGDD) is a form of therapy in which imaging methods are used for guidance and monitoring of disease location, drug targeting levels, drug localization, and release kinetics before and during treatment. The goal of IGDD is to optimize therapeutic efficacy and minimize unwanted toxicity through personalized image-guided treatments. A major challenge in developing such therapies is in overcoming the extra- and intracellular barriers to the delivery of therapeutics into target cells. The reviews and research articles in this theme issue review recent advances in the synthesis, characterization, and biological evaluation of different image-guided delivery systems, with a focus on solving complex drug delivery problems.

About the Guest Editors

Arash Hatefi, Ph.D., received his Ph.D. in pharmaceutics from the University of Alberta, Canada, in 2002. He then moved to the United States for a three-year postdoctoral fellowship at the Center for Nanomedicine and Cellular Delivery at the University of Maryland. During this period, he worked on recombinant engineering of highly cationic fusion biopolymers in *E. coli* with potential application in targeted gene therapy. In 2006, he became an assistant professor of pharmaceutical sciences at Washington State University, where he developed several multifunctional fusion vectors that could target and transfer genes into cancer cells. In 2010, he joined the Department of Pharmaceutics at Rutgers University and is currently working on the development of image-guided gene delivery systems for cancer gene therapy.

Tamara Minko, Ph.D., is a Professor II and Chair of the Department of Pharmaceutics, Rutgers University. Her current research interests include nanoscale-based targeted delivery of drugs, peptides, siRNA, and antisense oligonucleotides. Professor Minko is the author or co-author of more than 400 publications, including peer-reviewed papers, books, textbook chapters, and conference proceedings. She is a member-at-large and member of the Board of Scientific Advisors of the Controlled Release Society, a fellow of the American Association

of Pharmaceutical Scientists, a recipient of numerous awards, an editor of *Pharmaceutical Research*, a member of the editorial boards of nine scientific journals, and a member of study sections at the U.S. National Institutes of Health (NIH), Department of Defense (DoD), and other review panels. Her research is supported by grants from NIH, DoD, the National Science Foundation, and other national and international sources.

Submit Your Research to *DDTR*

DDTR is an official journal of the CRS, providing a unique forum for publication of high-quality research that focuses exclusively on translational aspects of the science and technology of delivery of bioactives. Join the leading scientists who are publishing their work in *DDTR*. Consider submitting reports of your best translational drug delivery research to compete for the new Outstanding Paper award. The first such award will be given during the 2012 CRS Annual Meeting & Exposition, July 15–18, 2012, in Québec City, Canada. The awardee will be selected from the research articles published in *DDTR* during 2011. More information can be found at www.controlledreleasesociety.org/about/Awards. ■

Welcome New Members

Emmanual O. Akala
F. N. U. Arnida
Shivani Chilampalli
Thomas Cilmi
Jeffrey T. DePinto
Jospeh M. DeSimone
Maureen Donovan
Jaime M. Ferreira
Doris Gabriel
Elisabeth V. Giger
Dylan M. Glatt-Dowd
Navid Goodarzi
Michael Guarnieri
David R. K. Harding
Basma M. Ibrahim
Hamsa Jaganathan
Arvind K. Jain
Song Li
Amey V. Mahajan
Samantha A. Meenach
Jean-Antoine Meiners
Fred Monsuur
Defang Ouyang
Kanlaya Prapainop
Hitoshi Sasaki
Alex Schwarz
Elena Maria Varoni
Randy Wald
Hywel D. Williams
Wei Zhang

CRS
Leading Delivery Science and Technology

Indo–U.S. Joint Symposium "Nanomedicine: Prospects and Challenges"

Co-organizers: Padma V. Devarajan[1] and Vinod Labhasetwar[2]

The Indo–U.S. joint symposium Nanomedicine: Prospects and Challenges was held November 14–15, 2011, at the Institute of Chemical Technology (ICT), Mumbai, India. The well-attended symposium was sponsored by the Indo-US Science and Technology Forum (IUSSTF, www.indousstf.org). The forum was established in 2000 under an agreement between the governments of India and the United States. Prof. Padma Devarajan of ICT and Prof. Vinod Labhasetwar of Cleveland Clinic, U.S.A., were the coordinators of the joint symposium. Prof. Vandana Patravale of ICT chaired the symposium's Scientific and Organizing Committee.

Prof. K. G. Akamanchi, Dean of Research of ICT, welcomed the delegates. Prof. M. M. Sharma, former director of ICT, an internationally renowned chemical engineer, fellow of the Royal Society, and recipient of the Padmavibhushan—a prestigious civilian honor bestowed by the President of India—was the chief guest. Prof. Sharma pointed out that India's ancient Ayurvedic system of medicine includes a subdivision called *Bhasma,* dealing with colloidal metal nanoparticles used in the treatment of various ailments. In fact, *Bhasma* could be considered an application of some of the earliest "nanomedicine." Prof. G. D. Yadav, director and R. T. Mody Professor of Chemical Technology at ICT, in his inaugural address reviewed various nanotechnologies and their biomedical applications. Dr. Rajiv Sharma, executive director of IUSSTF and the guest of honour, stated in his presentation that the forum acts as a catalyst for Indo–U.S. cooperation in science and technology and announced that the IUSSTF is accepting proposals to establish collaborative centers between Indian and U.S. institutions. Prof. Padma Devarajan highlighted the strengths of the Department of Pharmaceutical Sciences and Technology of ICT, specifically in nano drug delivery.

In his inaugural comments, Prof. Labhasetwar reiterated that there are many aspects of nanotechnology applied to biology and medicine that make it exciting: "Nanomedicine" is about *innovation*, such as synthesis of new nanomaterials for imaging, drug delivery, and diagnosis. It is about *translational research*, moving laboratory discoveries to the bedside. It is about *better health outcomes*; it can directly affect human health (especially when nanoparticle-mediated drug delivery proves more effective and less toxic than conventional therapy). It is also about *economics* as new technologies are being developed and commercialized.

The symposium featured 17 plenary and invited talks by scientists from both India and United States, covering a wide array of innovative and translational aspects of nanotechnology. The first day began with a plenary talk by Prof. Labhasetwar, who described the results of a nanoparticle-based, localized vascular delivery mechanism to prevent postangioplasty restenosis. He suggested that this approach could overcome some long-term complications associated with stents, such as the risk of in-stent restenosis and late thrombosis.

Prof. V. Labhasetwar giving a plenary talk on a nonstent approach to inhibition of restenosis.

Dr. Amit Misra of the Central Drug Research Institute, India, described an inhalable particle-based delivery system for the treatment of tuberculosis. Dr. Shantikumar Nair of Amrita Vishwa Vidyapeetham, India, described various types of multifunctional nanomedicine and their potential applications in diagnosis and therapy. Various synthetic and biopolymers are being explored for drug delivery applications. In this regard, Prof. Ashutosh Chilkoti of Duke University, Durham, North Carolina, U.S.A., described polypeptide-based biopolymers that self-assemble into nanoparticles and can release conjugated drugs in response to acidic environment in solid tumors, thus achieving targeted delivery. Prof. Chandra P. Sharma of Sree Chitra Tirunal Institute of Medical Science and Technology, India, described polyplex-based gene delivery systems, particularly the significance of polymer structures and unpacking of polyplex-DNA complex inside cells for efficient gene transfection. Prof. Pradeep R. Vavia

Release of abstract book for the joint Indo–U.S. symposium "Nanomedicine: Prospects and Challenges." Left to right: Prof. P. V. Devarajan, Prof. V. Labhasetwar, Dr. R. S. Sharma, Prof. M. M. Sharma, Prof. G. D. Yadav, Prof. K. G. Akamanchi, and Prof. V. B. Patravale.

[1] Institute of Chemical Technology, Mumbai, India.
[2] Lerner Research Institute, Cleveland Clinic, Cleveland, Ohio, U.S.A.

of ICT described cyclodextrin-based nanosponges and their use to improve oral bioavailability of poorly water-soluble drugs. Prof. Suresh P. Vyas of Dr. H. S. Gour University, India, spoke on targeted delivery of liposomes, particularly their intracellular processing and application for vaccine delivery. The last talk of the day was by Dr. Harish C. Joshi of Emory University School of Medicine, Atlanta, Georgia, U.S.A., on discovery of new anticancer agents (noscapine and others) targeted toward microtubules.

The second day of the symposium began with an invited talk by Prof. James Basilion of Case Western Reserve University, Cleveland, Ohio, U.S.A., who described application of gold nanoparticles to deliver photosensitizers for photodynamic therapy to combat brain tumors. Continuing with a cancer-related presentation, Prof. Maciej Zborowski of Cleveland Clinic, Cleveland, Ohio, U.S.A., presented data on the use of magnetic nanoparticles to determine circulating tumor cells, which could potentially be used as a prognostic marker to assess the effectiveness of anticancer treatment. Dr. Vandana B. Patravale of ICT then described the use of lipid nanoparticles for delivery of antimalarial drugs, particularly for the treatment of severe malaria.

Prof. D. Burgess giving an invited talk on siRNA delivery.

Forms of siRNA have the potential to treat many diseases, but their safe and efficient delivery remains a challenge. Prof. Diane J. Burgess of the University of Connecticut, Storrs, Connecticut, U.S.A., described an anionic lipid-based delivery mechanism for siRNA. Dr. Mark Tracy from Alnylam Pharmaceuticals, Cambridge, Massachusetts, U.S.A., presented clinical data regarding siRNA lipid-based nanoparticles and suggested that RNAi is a technology that could provide a new class of pharmaceuticals for the treatment of a variety of diseases.

In the first of two presentations by industrial representatives, Dr. Manoj Kharkar of Dow Wolff Cellulosics (Horgen, Switzerland) spoke on nanomaterials and safety. This is an important topic, as the use of nanomaterials in commercial products is on the rise. Dr. Purnima Parkhi of Agilent Technologies described spectroscopic imaging techniques for biomedical applications, particularly for identifying abnormal tissue composition in various disease conditions (e.g., discriminating between cancerous and normal cells).

In recent years, significant interest has developed in determining the effects of nanoparticle shape on biodistribution and exploring nanoparticles of particular shapes for targeting of therapeutics to particular organs where they show greater accumulation. There were two talks on this topic. Prof. Samir Mitragotri of the University of California, Santa Barbara, California, U.S.A.,

Prof. M. M. Sharma inaugurating the symposium. Accompanying him are Prof. G. D. Yadav, director of ICT, and Prof. P. Devarajan, co-organizer of the symposium.

described the technique of fabricating nano- and microparticles of different shapes and sizes and presented data on how these structures interact with their biological environment, such as their adhesion to vascular walls, the process of phagocytosis of nanomaterials as a function of their shape, and how these factors influence the circulation time and targeting of nanomaterials to different body compartments. Next, Prof. Devarajan of ICT demonstrated how irregularly shaped nanoparticles are trapped in the spleen. This tendency is significant, as the spleen acts as a reservoir for many pathogens. Her data demonstrate that these irregularly shaped nanoparticles can be effectively used to deliver drugs to treat infections of the spleen.

In addition to invited talks, there were 74 abstracts for poster presentation, with several abstracts selected for podium presentation. In all, various aspects of nanotechnology—synthesis of different nanomaterials, various approaches to targeting nanomaterials, delivery of different types of therapeutics for the treatment of various types of cancers, cardiovascular conditions, and infectious diseases, and many other applications—were covered during this highly interactive two-day symposium.

In concluding comments, Prof. Labhasetwar reiterated that nanotechnology is at a crossroad as we think of the investment in this technology, our expectations for it, and the array of potential outcomes, particularly in the field of medicine. The question he addressed was, have we met the expectations originally outlined since the Nanotechnology Initiative was launched about a decade ago? The initiative certainly has galvanized new thinking, collaborations, and innovation. We have a better understanding of nanomaterials and the challenges that we face in translating these for biomedical applications than a decade ago. It gives us confidence as we see the entry of the first nanomaterial-based pharmaceuticals into the marketplace. It is an indication that the field of nanomedicine has matured, and there is more to come. Prof. Devarajan announced that a special issue based on the theme of the symposium is planned for publication in *Drug Delivery and Translational Research*, an official journal of the Controlled Release Society. ■

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Drug Delivery Science in Italy and Beyond: Annual CRS Italy Chapter Workshop

Paola Mura, University of Florence

The annual CRS Italy Chapter workshop, "Nanostructured Devices for Drug Delivery: From Small Molecules to Biotech Drugs," was held in Rome on November 17–19, 2011. The workshop was financed by CRS U.S.A. and some industries, which allowed us to invite outstanding foreign scientists as well as to support the participation of young researchers.

Over the years, the annual workshop has become an important milestone for the Italian pharmaceutical and drug delivery community. The number of attendees is constantly increasing (130 participants in 2011), and the multidisciplinary nature of the workshop attracts people from different disciplines and work interests.

Prof. Alhaique, University Sapienza of Rome, opened the workshop by welcoming the participants. The CRS Italy Chapter president, Prof. Caliceti of the University of Padua, illustrated in detail the upcoming international activities of CRS and the opportunities offered to CRS members. The attendees were invited to join the annual international CRS Meeting & Exposition, "Smart Materials—From Innovation to Translation" (Québec City, Canada, July 15–18, 2012).

The workshop program started with the excellent opening lecture, "Nanomedicine Today," delivered by Prof. Moghimi, Copenhagen University.

Prof. Caraglia, Federico II University of Naples, opened the session dedicated to "Nanotechnologies and Cancer: Therapeutic and Diagnostic Opportunities," reporting about the clinical implications of nanotechnologies in cancer therapy. Dr. De Rosa, Federico II University of Naples, described new self-assembling nanoparticles for biphosphonate delivery. Dr. Mastrotto, University of Padua, reported on novel pH-sensitive polymeric micelles for controlled anticancer drug delivery. Dr. Barbieri, University of Parma, presented lecitin–chitosan nanoparticles for tamoxifen oral delivery, and Dr. Scialabba, University of Palermo, discussed superparamagnetic polymeric nanoparticles for anticancer drug delivery. Dr. Perkins, Novozymes, presented the applications of human serum albumin in drug delivery and targeting. Dr. Gasco, Nanovector, described the use of solid lipid nanoparticles for cancer therapy. Dr. Valbusa, Bracco, presented the dynamic contrast-enhanced MRI methods for characterization of nano-sized drug delivery systems, and Dr. de Santis, Sigma Tau, reported on the use of AvidinOX for tissue-targeted delivery of biotinylated therapeutics.

After dinner, Prof. Alhaique lectured on "Drug Delivery: History and Translation," offering a brief overview on the history of pharmacy. Finally, in a very familiar atmosphere, Dr. Blasi and Dr. Salmaso chaired a roundtable on the innovation perspectives in the field of drug delivery technologies and the possibilities of attracting industrial support from the investor's point of view.

Left to right: Francesca Mastrotto, Paolo Blasi, and Gennara Cavallaro

The invited lectures of Prof. Grassi, University of Trieste, and Prof. Ogris, Ludwig Maximilian University of Munich, opened the "Nanotechnologies and Nucleic Acid Delivery" session by describing the state-of-the-art of nucleic acid based drugs and the combinatorial gene therapy with targeted synthetic vectors. Dr. Castagner, ETH, Zurich, and Prof. Conese, University of Foggia, presented overviews on alkylmethacrylic acid copolymer nanocarriers and nanocomplexes and polyplexes for gene delivery in respiratory diseases. Followed by this, lectures on cationic lipid carriers for nucleic acids and applications of light-scattering techniques for the characterization of nanostructured devices were delivered by Prof. Cortesi, University of Ferrara, Dr. Vighi, University of Modena, and Dr. Brun, Alfatest.

Prof. Göpferich, University of Regensburg, opened the session dedicated to "Nanodevices and Their Interaction with Cells" with an invited talk focused on the art of controlling nanoparticle interactions with cells. The session featured Dr. Badiali, University of Modena, Dr. Ungaro, University of Naples, Dr. Marianecci, Sapienza University of Rome, and Dr. Blasi, University of Perugia, who delivered talks on the use of leptin-conjugated nanoparticles as a drug delivery system to the brain, respirable nano-embedded microparticles for prolonged delivery of antibiotics, *in vivo* evaluation on mice oedema of nonionic surfactant vesicles for ammonium glycyrrhizinate delivery, and *in vitro* and *in vivo* characterization of lipid nanoparticles for brain drug targeting. Dr. Giordano, Buchi, presented the technological innovations in microencapsulation of API in polymeric matrixes.

The "Nanotechnologies in Drug Delivery: New Challenges" session featured Prof. Masserini, Bicocca University of Milan,

Dr. Van der Walle, University of Strathclyde, and Prof. Haas, University of Mainz, with opening remarks on nanoparticle use for therapy and diagnosis of Alzheimer's disease, mesoporous silica particles for oral delivery of cyclosporine A, and pharmaceutical development of liposomal drug delivery formulations at the nanoscopic scale, respectively. Dr. Palumbo, University of Palermo, discussed the dexamethasone dipropionate loaded Elastin-g-PLGA nanoparticles for restenosis treatment, and Dr. Ciocca, Accelera, described new tools for early drug development in the field of nanotechnologies.

The day ended with the social dinner, a traditional event of all CRS workshops. This year, the social dinner took place at Nobile Collegio Chimico Farmaceutico Universitas Aromatariorum Urbis, an ancient private university located in the core of the historical centre of Rome, in the middle of the Roman Forum, which was a Roman temple of 142 BC. Good food and wine, tasted in the ancient rooms of the complex dedicated to a Museum of Pharmaceutical Art and Pharmacy History, left unforgettable memories with all the participants.

On the last day, Dr. Maio, Merck-Serono, updated on new inorganic carriers for poorly soluble drugs based on a "nano from inside" approach, and Prof. Uccello-Barretta, University of Pisa, presented on NMR methods in the characterization of cyclodextrin-capped gold nanoparticles. Dr. Pasut, University of Padua, delivered a talk on hyaluronic acid–salmon calcitonin conjugate for the treatment of osteoarthritis. Prof. Cavalli, University of Turin, discussed the development of new cyclodextrin-based lipid nanocapsules for the delivery of amphotericin B. Dr. Nicoli, University of Parma, discussed the use of iontophoresis on the release of BSA from agarose hydrogels for ophthalmic application. Dr. Dorati, University of Pavia, delivered a talk on a novel three-dimensional biodegradable scaffold based on functionalised polylactic acid for tissue engineering. Dr. Corace, University of Bologna, presented on tacrine HCl nasal delivery to the central nervous system using antioxidant liposomes. Dr. Manet, ISOF-CNR Bologna, described the use of optical spectroscopic methods to understand the binding of poorly water soluble drugs, doxorubicin and artemisinin, to a pb-cyclodextrin polymer, and Dr. Di Meo described gellan-prednisolone nanogels as a new tool for drug delivery applications. Dr. Coletti, TA Instruments, illustrated the applications of isothermal titration calorimetry for analysis of binding of organic compounds to nanoparticles, and Dr. Cossi, QI Technologies, described the quantitative analysis of submicron particles.

All the chairmen powerfully conducted the different sessions, contributing to the general success of the workshop, by effectively stimulating the discussion and the audience involvement in active participation.

The concluding remarks of Dr. van der Walle underlined once again the multidisciplinary nature of the workshop and the efforts of the organisation to involve young scientists with a view to shaping the future, and this is well reflected by their role in chairing sessions and podium presentations. ■

CRS Canadian Local Chapter Presents the 2011 Networking Event

It was with great pleasure that the Canadian Chapter of the CRS, CSPS, and Biotech Montreal welcomed 115 Montrealers to the 2011 Networking Event at the St. Paul Hotel in the Old Port in Montreal on November 9, and welcome to our new members who joined that evening! Their presence and interest created the true spirit of the event, where research and industry liaised in a relaxing setting and were informed by excellent speakers.

Captivated audience.

Again, many thanks to the two speakers who instructed the participants during the evening. Everyone's attention was captured when Prof. Masad José Damha presented his research about "Making Sense out of Antisense and siRNAs." Prof. Damha's talk not only provided insights into the development of novel endogenous targets for anticancer applications but also gave us the opportunity to appreciate in which direction research is now moving in the development of delivery strategies.

Prof. Denis deBlois's talk illustrated how the traditional models of drug development are being challenged by all stakeholders, and new partnerships of knowledge creation are needed to face the major unmet medical needs of the 21st century. Following several requests from attendees, Prof. deBlois has graciously allowed us to make his slides available to you, and they are available on the CCCRS webpage.

Additionally, special thanks goes to our sponsors, Biomomentum (www.biomomentum.com) and Goudreau Gage Debuc (GGD) (www.ggd.com/en/Judicious-Advice), who made the event

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CRS Canadian Chapter continued from page 25

possible. Last but not least, a sincere thanks goes to all the volunteers and May Shawi of Biotech Montreal, of CSPS, Lory Boudjikanian, Sylvie Marlow, Gregoire Leclaire, and particularly to Barb Scollick and Bev Berekoff for taking care of the logistical aspects of the event. This was the first event organised by our new Meeting Coordinator, Marc Thibault. Hats off to Marc for a job well done.

Professor Damha in action.

Professor deBlois talking pharma and the movies.

In addition to small local events, take note that the 39th Annual Meeting & Exposition of the Controlled Release Society is coming to Québec City in 2012. We will keep you posted on any special local event that will take place inside the main event. We hope to see you soon, and thanks again. ■

CRS China Chapter Holds Its First Annual Meeting

CRS China Chapter held its first annual meeting on October 14, 2011, in Shanghai, China. Six professors, from China and overseas, were invited to give keynote presentations in the morning, and 17 others gave presentations in two afternoon sessions. About 450 people participated in the event. After the annual meeting, in the evening, the CRS China Chapter had a member meeting, and Professor Weiyue Lu from the School of Pharmacy, Fudan University, was elected the new president of the CRS China Chapter. Professor Zhirong Zhang from West China School of Pharmacy, Sichuan University, became the president elect. So the committee of the CRS China Chapter is now governed under President Weiyue Lu, President Elect Zhirong Zhang, and Immediate Past President Qiang Zhang. ■

In the News

Compiled by Steven Giannos, Chrono Therapeutics Inc.
Industrial Editor

January 2012

FDA Advisory Committee Declines to Recommend Approval of Progesterone Vaginal Gel 8% for the Reduction of Risk of Preterm Birth in Women with Short Uterine Cervical Length

PRNewswire: January 20, 2012 – LIVINGSTON & PARSIPPANY, NJ, U.S.A. – Columbia Laboratories, Inc. (Nasdaq: CBRX), and Watson Pharmaceuticals, Inc. (NYSE: WPI), today confirmed that the Advisory Committee for Reproductive Health Drugs of the U.S. Food and Drug Administration (FDA) did not recommend approval of progesterone vaginal gel 8% for the reduction of risk of preterm birth in women with short uterine cervical length at the mid-trimester of pregnancy. While panel members generally agreed that progesterone vaginal gel 8% is safe, the panel stated that more information is needed to support approval.

While the FDA will consider recommendations of the Committee, the final decision regarding the approval of the product rests solely with the FDA. The FDA's Division of Reproductive and Urologic Products is expected to take action on Columbia's New Drug Application (NDA) by February 26, 2012.

"We will work with the FDA to address the Advisory Committee's comments as the Agency finalizes its review of our NDA. We remain confident in the PREGNANT study results that showed the administration of progesterone vaginal gel 8% is a safe and effective treatment for patients at risk for preterm birth due to short uterine cervical length in the mid-trimester of pregnancy. We hope the agency's final decision will acknowledge the clear unmet medical need in this patient population," said Frank Condella, President and CEO of Columbia Laboratories, Inc.

"As was highlighted today, there are currently no products approved to reduce the risk of preterm birth in women with premature cervical shortening—an established strong predictor of preterm birth risk," said Fred Wilkinson, Watson's Executive Vice President, Global Brands. "The availability of a safe and effective product, with a demonstrated ability to reduce the risk of preterm birth in women with short uterine cervical length in the mid-trimester of pregnancy, would represent a significant advance in the prevention of early preterm birth and its associated complications."

The Committee evaluated data submitted by Columbia to the FDA in its New Drug Application (NDA 22-139), which includes data from two Phase III clinical trials. One of these trials, the PREGNANT study, showed that women with a short uterine cervical length as measured by transvaginal ultrasound between 19 and <24 weeks of gestation who were treated with progesterone vaginal gel 8% had a significantly lower risk of preterm birth before 33 weeks gestation compared to those who were treated with placebo (p = 0.022). This study included women with and without a prior history of preterm birth. Progesterone vaginal gel 8% was also associated with a significant reduction in the risk of preterm birth before 35 weeks gestation (p = 0.012).

In the PREGNANT study, the frequency of maternal treatment-emergent adverse events both overall and by individual event was comparable between the placebo and progesterone vaginal gel treatment groups. The most frequent events in the progesterone vaginal gel group were expected complications of a high-risk pregnancy and included "premature baby" (19%), "uterine contractions abnormal" (14%), and "premature labor" (7%). "Cervical disorder" (10%), "nausea" (10%), "headache" (7%), and "vulvo vaginal mycotic infection" (7%) were also reported.

The Advisory Committee for Reproductive Health Drugs is an independent panel of experts that evaluates data concerning the efficacy and safety of marketed and investigational products for use in the treatment of reproductive conditions and makes non-binding recommendations to the FDA.

NovaDel Announces Termination of License Agreements for Ondansetron Oral Spray Product

Business Wire: January 20, 2012 – BRIDGEWATER, NJ, U.S.A. – NovaDel Pharma Inc. (OTCBB: NVDL), a specialty pharmaceutical company that develops oral spray formulations of marketed pharmaceutical products, today announced the termination of certain license agreements with Talon Therapeutics, Inc. and Par Pharmaceutical Companies, Inc., relating to the development and commercialization of the Company's ondansetron HCl oral spray product, effective as of January 16, 2012.

Pursuant to the agreements terminating the Talon and Par license agreements, all rights to develop and commercialize the product were returned to the Company in exchange for Talon's right to receive certain royalty payments in connection with the product. The Company believes the termination of these license agreements better positions the Company for a potential strategic transaction by returning control of the product within the United States and Canada to the Company. Further details regarding the terms of the termination agreements can be found in the Company's Current Report on Form 8-K filed in connection herewith.

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APR Applied Pharma Research s.a., Labtec GmbH and Norgine BV Announce the Signature of an Exclusive Licensing Agreement under which Norgine Will Market and Distribute Setofilm™

Business Wire: January 18, 2012 – BALERNA, Switzerland – APR Applied Pharma Research s.a. ("APR"), Labtec GmbH ("Labtec"), and Norgine BV ("Norgine") announce the signature of an exclusive licensing agreement under which Norgine will market and distribute Setofilm™ Ondansetron Oral Dispersible Film ("ODF"), in Europe and selected non-European countries.

Norgine and APR, together with its joint venture partner Labtec, today announced that they have entered into an exclusive licensing agreement under which Norgine has acquired the commercialization rights in Europe and selected non-European countries in Middle East, Africa, and Australasia, of Setofilm™ the ondansetron orally dispersible film strip developed by APR and Labtec. Financial terms of the deal were not disclosed.

"We are very pleased to announce that Setofilm™ will be marketed in Europe and also in other countries in Middle East, Africa, and Australasia by Norgine, a company with recognized marketing and commercial strengths across the territory. We believe that Setofilm™ nicely fits with Norgine's therapeutic focus in supportive care," said Paolo Galfetti, CEO of APR. "APR is proud to provide patients with a unique product that will help them in the management of these debilitating conditions."

Peter Stein, Norgine's CEO said "We are delighted to have acquired the rights to Setofilm across all the markets in which Norgine has a direct presence and to have entered this relationship with APR and Labtec. We believe the product offers real benefits to patients and as such is an excellent addition to our existing products in supportive care."

Setofilm™ is already registered in 16 European countries. Setofilm™ is the first prescription product developed as an "orodispersible film" form to be registered in Europe and has been developed by APR and Labtec in collaboration with Monosol RX, the developer of Zuplenz® ondansetron film for the U.S.

Setofilm™ is indicated for the prevention and treatment of Chemotherapy and Radiotherapy Induced Nausea and Vomiting ("CINV" and "RINV") in adults as well as children aged equal or above 6 months, and the prevention and treatment of Post-Operative Nausea and Vomiting (PONV) in adults and children aged equal or above 4 years. The dosage form is especially useful for patients who have difficulties swallowing, such as children or elderly patients.

This formulation is based on a novel and proprietary oral drug delivery technology platform and consists of a very thin polymeric film strip containing Ondansetron. The product has the size of 3 cm^2 and 6 cm^2 for the 4 mg and 8 mg dosage, respectively. Once placed in the mouth, it dissolves in a few seconds and is swallowed with the saliva without the need of water. The Ondansetron film strip improves patient compliance by reducing swallowing difficulties experienced by many patients taking other oral Ondansetron formulations currently available.

CINV and PONV alone are affecting about 2.3 million people in the 7 major EU markets. This number is expected to grow in the coming years. Children are more likely to develop CINV and PONV than mature patients. Ondansetron is the leader product in the management of severe conditions of nausea and vomiting.

NovaDel Continuing to Explore Strategic Alternatives

Business Wire: January 18, 2012 – BRIDGEWATER, NJ, U.S.A. – NovaDel Pharma Inc. (OTCBB: NVDL), a specialty pharmaceutical company that develops oral spray formulations of marketed pharmaceutical products, today announced that, as previously disclosed, it is continuing to explore various strategic alternatives for the Company, including selling the Company or some or all of its pharmaceutical products or license rights, or raising capital for the Company through a financing transaction.

The Company has estimated the timing and amounts of cash receipts and disbursements over the next month and believes it will not have adequate cash to meet its working capital needs after the end of January 2012. If the Company is unsuccessful in promptly implementing a transaction to sell the Company or some or all of its assets or in obtaining additional financing, the Company intends to file for bankruptcy protection.

On January 12, 2012, the following directors of the Company resigned: Mark Baric, Thomas Bonney, and Charles Nemeroff. Mr. Steven B. Ratoff continues to remain as Chairman and Chief Executive Officer and is continuing the pursuit of strategic alternatives.

Bioject Retains Financial Advisor to Explore Strategic Alternatives

Business Wire: January 17, 2012 – PORTLAND, OR, U.S.A. – Bioject Medical Technologies Inc. (OCTBB: BJCT), a leading developer of needle-free drug delivery systems, today announced that it has retained the services of Mr. Snehal Patel, an experienced life science professional and financial advisor, to assist the company as it explores strategic alternatives, including the sale of the company. A sale of the company may not result in proceeds to the common shareholders, given the liquidation preferences of the preferred shareholders. Inquiries should be made to Mr. Patel at spatel@bioject.com or 203-434-3290.

In addition, the holders of the company's $225,000 convertible notes due December 29, 2011, have unilaterally extended the maturity date of the notes until February 28, 2012. The note holders include certain members of the Board of Directors and former President and CEO. The notes will continue to accrue interest.

Bioject Medical Technologies Inc., based in Portland, Oregon, is an innovative developer and manufacturer of needle-free drug delivery systems. Needle-free injection works by forcing medication at high speed through a tiny orifice held against the skin. This creates a fine stream of high-pressure fluid, penetrating the skin and depositing medication in the tissue beneath. The Company is focused on developing mutually beneficial agreements with leading pharmaceutical, biotechnology, and veterinary companies.

Genentech Announces First Milestone Payment to Device-Maker ForSight VISION4, Inc. in Development of Sustained Delivery Lucentis

Business Wire: January 13, 2012 – SOUTH SAN FRANCISCO, CA, U.S.A. – Genentech, a member of the Roche Group (SIX: RO, ROG; OTCQX: RHHBY), today announced it will make its first milestone payment to ForSight VISION4, Inc. as part of an exclusive license agreement to develop the company's investigational drug delivery device, designed to provide sustained delivery of Lucentis® (ranibizumab).

Genentech and Roche entered into an agreement with ForSight VISION4 in December 2010 for exclusive worldwide rights to the company's proprietary implantable ocular device in the development and commercialization of anti-VEGF-A targeted ophthalmic therapies. This first undisclosed milestone payment is based on Genentech's decision to submit an Investigational New Drug (IND) application for clinical testing of the device in combination with Lucentis. Currently, Lucentis, which is indicated for treatment of certain eye diseases, is recommended to be administered by monthly injections to the eye.

"This development reflects Genentech's commitment to ophthalmology and investigating new technologies that may potentially provide sustained delivery of Lucentis and reduce the frequency of injections," said Hal Barron, M.D., chief medical officer and head, Global Product Development. "The license agreement with ForSight VISION4 represents part of our ongoing strategy to support the retinal community by innovating and discovering new ways to help people with sight-threatening illnesses."

The agreement provides Genentech with the opportunity to apply the device to other select targets for treatment of ophthalmic diseases. Genentech is responsible for clinical development and commercialization and is currently collaborating with ForSight VISION4 in the manufacturing and engineering of the device. ForSight VISION4 is entitled to undisclosed milestone payments and royalties on potential future sales.

"The ForSight VISION4 technology has the potential to revolutionize the way we treat ophthalmic disease," said Eugene de Juan, Jr., M.D., founder of ForSight VISION4, Inc. "Genentech is an ideal partner given their long-term clinical experience with Lucentis and pioneering work in the anti-VEGF therapeutic space." The device is a refillable drug port delivery system (PDS) designed to release Lucentis over a period of months.

Lucentis is currently FDA-approved to treat two eye conditions that can potentially lead to vision loss and blindness: neovascular (wet) age-related macular degeneration (AMD), which affects an estimated 1.6 million U.S. adults over the age of 50, and macular edema following retinal vein occlusion (RVO), which affects more than 1 million people in the U.S.

Kedem Pharmaceuticals Initiates Development of Sublingual Anti-Cancer Drug, Gleevec®

PRNewswire: January 12, 2012 – PHOENIX, AZ, U.S.A. – Kedem Pharmaceuticals Inc. (OTCBB: KDMP), a specialty pharmaceutical company with focus on sublingual drug delivery system is pleased to announce that it has initiated the development of Gleevec®. Gleevec® is an important anti-cancer drug for the treatment of several blood related cancers in children and adults. In children the drug has demonstrated a powerful action against Chronic Myeloid Leukemia, possibly one of the most prescribed drugs for this condition. The drug is administered orally and in children there is a significant issue in getting the drug swallowed, due to size of the pill and bad taste. Our sublingual formulation with taste masking features makes the drug acceptable and pleasant in taste for the children with chronic dosage requirements. For more information, visit www.kedempharmaceuticals.com.

Tris Pharma Announces US Patent Grant Covering Platform Technology

PRNewswire: January 6, 2012 – MONMOUTH JUNCTION, NJ, U.S.A. – Tris Pharma, an emerging specialty pharmaceutical company, announced the US grant of its core technology patent for its OralXR+™ platform. This is the first patent grant of a substantial estate filed by Tris Pharma and covers a multitude of actives having modified release formulations comprising drug-ion exchange resin complexes.

"This patent grant further validates Tris' breakthrough in commercializing modified release formulation involving unique dosage forms such as a 24-hour ER liquid suspension. The patent covers our unique, high tensile, aqueous coating compositions and combined with our patent-pending/trade-secret manufacturing process and special design apparatus provides for efficient and scalable manufacturing capabilities. This has resulted in launch of several new, first-in-the-category products that were heretofore not capable of being developed," said Ketan Mehta, President and CEO of Tris Pharma.

While the benefits of modified release are well understood, these benefits were largely limited to patients who can swallow traditional solid dosage forms. The OralXR+ technology bridges the gap for patients who have difficulty swallowing "pills" and thereby helps extend the market for modified release products. Tris is working with multiple pharma partners to develop

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products based on this patented technology in the areas of CNS, respiratory, pain, cardiovascular, and OTC cough/cold.

Pulmatrix Announces Grant of Patent Supporting Its Novel Pulmonary Drug Therapies

Business Wire: January 5, 2012 – LEXINGTON, MA, U.S.A. – Pulmatrix, a clinical stage biotechnology company discovering and developing a new class of therapies for the prevention, treatment, and control of respiratory diseases, announced that the European Patent Office has granted Pulmatrix's patent number EP 2315580 B1 entitled "Pharmaceutical formulations and methods for treating respiratory tract infections," a patent relating to compositions and uses of the company's inhaled drug therapies. The newly granted patent describes both dry powder and liquid formulations with optimized ranges of the formulation components, and also describes methods for treating respiratory infections and diseases as well as methods for treating acute exacerbations of asthma, chronic obstructive pulmonary disease (COPD), or cystic fibrosis (CF). The granted patent also specifically contains composition of matter claims covering Pulmatrix's lead dry powder iCALM formulation, PUR118, which is being evaluated in ongoing clinical trials, including two ongoing Phase 1b studies in patients with COPD, which includes patients with emphysema and chronic bronchitis.

"We are pleased that our proprietary technology has been recognized by the European Patent Office, both for its unique formulations as well as its methods of use in treating respiratory diseases and infections," said Robert Connelly, Chief Executive Officer of Pulmatrix. "With composition of matter claims from this grant and other granted patents, we are very confident that our full intellectual property portfolio will protect our iCALM and iSPERSE platforms for delivering both standalone and combination therapies that could offer significant unique benefits to patients."

Pulmatrix has built a comprehensive intellectual property portfolio to support the advancement of the company's novel inhaled drug platforms, iCALM and iSPERSE. Pulmatrix's intellectual property estate includes 7 granted patents and over 100 pending applications worldwide. This broad intellectual property covers compositions of both iCALM and iSPERSE formulations, including multi-drug formulations, as well as the specific application of iCALM and iSPERSE products to a number of chronic and serious respiratory diseases, such as COPD, CF, asthma, respiratory infections, bronchiectasis, and other respiratory diseases. Relevant multi-drug combinations covered in the intellectual property include, but are not limited to, one or more of the following classes of inhaled therapeutics: long-acting muscarinic antagonists (LAMAs), long-acting beta-2 agonists (LABAs), short acting beta agonists (SABAs), inhaled corticosteroids (ICS), and antibiotics. For additional information about Pulmatrix, please visit http://www.pulmatrix.com.

Midatech Secures £6.3 Million Financing to Strengthen Product Development Portfolio

Business Wire: January 5, 2012 – OXFORD, England – Midatech Ltd., a global leader for the design, development, synthesis, and manufacture of nanomedicines, announced today it has raised £6.3 million through a private investment round. This financing will be used to strengthen and diversify Midatech's product development portfolio, especially in oncology. It will be used to support clinical development of chemotherapeutic gold nanoparticles designed to target ovarian, lung, and breast carcinoma and to support development of therapeutic cancer vaccines in SynTara, a joint venture with Immunotope Inc. The funding will also be used to expand the capacity of Midatech's resources to accommodate its expanding development portfolio. In November 2011, Midatech received regulatory approval for a first-in-human study of MidaForm™ insulin delivered transbuccally. Phase I results are expected in Q1 2012.

"This funding reflects on the excellent work that Midatech has achieved in advancing its programs through preclinical development and targeting specific compounds for drug delivery by gold nanoparticles," commented Prof. Thomas Rademacher, CEO and Chairman of Midatech, adding, "In addition to its advanced diabetes program currently being commercialized in MidaSol Therapeutics LP, a joint venture with MonoSol Rx, Midatech is now well funded to expand its activities to encompass other disease indications, by initiating several programmes in oncology."

Midatech is a world leader in the design, synthesis, and manufacture of biocompatible nanoparticles. These nanoparticles can be used to create a wide variety of products with novel characteristics, functions, and applications for a number of industry segments including life sciences, electronics, and fine chemicals. For further company information, see www.midatechgroup.com.

Ikaria® Commences Global Registration Trial for Bioabsorbable Cardiac Matrix

PRNewswire: January 3, 2012 – HAMPTON, NJ, U.S.A. – Ikaria, Inc., a critical care company focused on developing and commercializing innovative therapies for critically ill patients in the hospital and ICU settings, today announced that it has commenced its global development program, the PRESERVATION I clinical trial, for its Bioabsorbable Cardiac Matrix (BCM). The CE Mark registration trial has commenced in Australia, and will be followed in Europe. The trial also is expected to commence in other countries, including Israel.

PRESERVATION stands for a placebo-controlled, multicenter, randomized, double-blind trial to evaluate the safety and effectiveness of IK-5001 for the prevention of remodeling of the ventricle and congestive heart failure after acute myocardial infarction.

BCM, also known as IK-5001, is being investigated to prevent ventricular remodeling and subsequent congestive heart failure (CHF) following acute myocardial infarction (AMI). Ventricular remodeling is the structural alteration of the damaged heart muscle that occurs following an acute heart attack. Once this damage occurs, the weakened heart muscle forces the rest of the heart to compensate. Under this extra workload, the heart muscle dilates, the walls of the heart thin, and the heart further remodels, thereby causing another cycle of dilation and overcompensation. The extra workload to the heart causes further structural damage and can lead to congestive heart failure.

BCM, an aqueous mixture of sodium alginate and calcium gluconate, will be delivered in a bolus injection via the coronary artery during catheterization and flows into the damaged heart muscle, where it forms a flexible scaffold, or "matrix," that provides physical support of the heart muscle during recovery and repair. Once the heart tissue heals, BCM gradually dissipates and is excreted through the kidneys.

"Due to the novel self-assembling and self-disassembling nature of BCM, as well as the fact that it provides structural support to the heart without any metabolic effect on the body, we believe the medical device pathway is the most appropriate regulatory approval pathway," stated Douglas Greene, MD, Executive Vice President of Research & Development of Ikaria.

PRESERVATION I is a placebo-controlled, multi-center, randomized, double-blind clinical trial involving approximately 300 patients which evaluates the safety and effectiveness of BCM when administered to patients who had successful percutaneous coronary intervention (PCI) following acute ST-segment elevation myocardial infarction (STEMI).

The major endpoints for the PRESERVATION I trial are: 1) Left ventricular end diastolic volume index (anatomic measurement of left ventricular end diastolic volume index will be assessed through echocardiogram); 2) a validated, disease-specific, self-administered questionnaire to quantify symptoms, function, and the quality-of-life of subjects, and; 3) an exercise tolerance test to measure the response to treatment in subjects with moderate to severe heart disease.

The trial aims to recruit patients across 45 sites. Approximately 50 Australian patients will be recruited at 11 clinical trial sites. Ikaria acquired the exclusive worldwide license to develop and commercialize BCM from BioLineRx Ltd. in 2009. More information on the PRESERVATION I trial can be found at www.clinicaltrials.gov.

December 2011

Alnylam Announces Publication of Pre-clinical Results with ALN-HTT, an RNAi Therapeutic for the Treatment of Huntington's Disease, in Experimental Neurology

Business Wire: December 28, 2011 – CAMBRIDGE, MA, U.S.A. – Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), a leading RNAi therapeutics company, announced today the publication of promising pre-clinical results in Experimental Neurology (doi:10.1016/j.expneurol.2011.11.020) related to its ALN-HTT program, an RNAi therapeutic drug-device combination for the treatment of Huntington's disease. The findings—the result of a research partnership between Alnylam and Medtronic, Inc., and supported by CHDI—demonstrate that a small interfering RNA (siRNA) targeting the huntingtin gene, when administered by intrastriatal infusion with convection-enhanced delivery (CED), results in widespread distribution of the siRNA and significant silencing of the huntingtin mRNA throughout the striatum. Furthermore, administration of the RNAi therapeutic was well tolerated in these studies. The authors of the paper include researchers from Alnylam, Medtronic, and the University of Kentucky, where the work was conducted.

"These published data represent important advancements in our Huntington's disease program across multiple dimensions. Indeed, these pre-clinical results extend our earlier reported data on siRNA biodistribution in the central nervous system and the degree and scope of therapeutic huntingtin gene silencing. We are also encouraged by the safety results following continuous intrastriatal infusion over approximately one month in this pre-clinical model," said Dinah Sah, Ph.D., Vice President, Research, at Alnylam. "In aggregate, these studies, which were performed in collaboration with the University of Kentucky, support our continued and combined efforts with Medtronic and CHDI to advance this important research effort."

The new pre-clinical studies employed direct delivery of the huntingtin-specific siRNA to the striatum using an implantable infusion system and CED. Direct delivery to the central nervous system (CNS) by intrastriatal CED for seven days resulted in broad distribution of the siRNA across the striatum and surrounding brain regions. This level of distribution of the siRNA resulted in the silencing of the huntingtin gene throughout the putamen by an average of approximately 45 percent, as well as reductions in the levels of huntingtin protein when evaluated by immunohistochemistry. This silencing of huntingtin occurred in a manner dependent on infusion rate and siRNA concentration.

A new pre-clinical model developed from these findings suggests that continuous CED of an siRNA targeting huntingtin has the potential to achieve physiologically significant coverage of the striatum of Huntington's disease patients with therapeutically relevant drug levels.

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"We are very pleased with these early results in our research collaboration, which continues to represent an exciting opportunity to combine an innovative therapeutic strategy with state-of-the-art drug device delivery technology for Huntington's disease. A highlight of this study is that the pre-clinical results suggest scalability of RNAi therapeutic delivery to the striatum of Huntington's patients," said Gregory Stewart, Ph.D., Distinguished Scientist, CNS Drug Therapy R&D at Medtronic. "The collaboration between Alnylam, Medtronic, and CHDI marks an important effort to develop a novel treatment strategy for this devastating neurodegenerative disease." This research was done in collaboration with the laboratory of Professor Don M. Gash, Ph.D., at the University of Kentucky College of Medicine in Lexington, Kentucky. Some of these findings have been previously presented at the 2009 World Congress on Huntington's Disease.

"These findings demonstrate the potential of RNAi therapeutics for the treatment of neurodegenerative diseases, and in particular, intraparenchymal CNS delivery of therapeutics as an important approach to drug delivery," said Professor Gash. "We look forward to the continued efforts in advancing this therapeutic approach to patients with Huntington's disease."

Silk Microneedles Deliver Controlled-Release Drugs Painlessly

PRNewswire: December 22, 2011 – MEDFORD and SOMERVILLE, MA, U.S.A. – Bioengineers at Tufts University School of Engineering have developed a new silk-based microneedle system able to deliver precise amounts of drugs over time and without need for refrigeration. The tiny needles can be fabricated under normal temperature and pressure and from water, so they can be loaded with sensitive biochemical compounds and maintain their activity prior to use. They are also biodegradable and biocompatible. The research paper "Fabrication of Silk Microneedles for Controlled-Release Drug Delivery" appeared in *Advanced Functional Materials*.

The Tufts researchers successfully demonstrated the ability of the silk microneedles to deliver a large-molecule, enzymatic model drug, horseradish peroxidase (HRP), at controlled rates while maintaining bioactivity. In addition, silk microneedles loaded with tetracycline were found to inhibit the growth of *Staphylococcus aureus*, demonstrating the potential of the microneedles to prevent local infections while also delivering therapeutics.

"By adjusting the post-processing conditions of the silk protein and varying the drying time of the silk protein, we were able to precisely control the drug release rates in laboratory experiments," said Fiorenzo Omenetto, Ph.D., senior author on the paper. "The new system addresses long-standing drug delivery challenges, and we believe that the technology could also be applied to other biological storage applications."

While some drugs can be swallowed, others can't survive the gastrointestinal tract. Hypodermic injections can be painful and don't allow a slow release of medication. Only a limited number of small-molecule drugs can be transmitted through transdermal patches. Microneedles—no more than a micron in size and able to penetrate the upper layer of the skin without reaching nerves—are emerging as a painless new drug delivery mechanism. But their development has been limited by constraints ranging from harsh manufacturing requirements that destroy sensitive biochemicals, to the inability to precisely control drug release or deliver sufficient drug volume, to problems with infections due to the small skin punctures.

The process developed by the Tufts bioengineers addresses all of these limitations. The process involves ambient pressure and temperature and aqueous processing. Aluminum microneedle molding masters were fabricated into needle arrays of about 500 mm needle height and tip radii of less than 10 mm. The elastomer polydimethylsiloxane (PDMS) was cast over the master to create a negative mold; a drug-loaded silk protein solution was then cast over the mold. When the silk was dry, the drug-impregnated silk microneedles were removed. Further processing through water vapor annealing and various temperature, mechanical, and electronic exposures provided control over the diffusity of the silk microneedles and drug release kinetics.

"Changing the structure of the secondary silk protein enables us to 'pre-program' the properties of the microneedles with great precision," said David L. Kaplan, Ph.D., coauthor of the study, chair of biomedical engineering at Tufts, and a leading researcher on silk and other novel biomaterials. "This is a very flexible technology that can be scaled up or down, shipped and stored without refrigeration, and administered as easily as a patch or bandage. We believe the potential is enormous."

Other co-authors on the paper, all associated with the Department of Biomedical Engineering, are Konstantinos Tsioris, doctoral student; Waseem Raja, post-doctoral associate; Eleanor Pritchard, post-doctoral associate; and Bruce Panilaitis, research assistant professor. The research was based on work supported in part by the U.S. Army Research Laboratory, the U.S. Army Research Office, the Defense Advanced Research Projects Agency–Defense Sciences Office and the Air Force Office of Scientific Research.

Tsioris, K., Raja, W. K., Pritchard, E. M., Panilaitis, B., Kaplan, D. L. and Omenetto, F. G. (2011), Fabrication of Silk Microneedles for Controlled-Release Drug Delivery. Advanced Functional Materials. doi: 10.1002/adfm.201102012.

Abbott Initiates Clinical Trial to Study Drug Eluting Bioresorbable Therapy

PRNewswire: December 22, 2011 – ABBOTT PARK, IL, U.S.A. – Abbott (NYSE: ABT) today announced the initiation of ESPRIT I, a first-of-its-kind clinical trial in Europe evaluating the safety and performance of the novel Esprit™ drug eluting bioresorbable vascular scaffold (BVS) for the treatment of blockages in the superficial femoral arteries (SFA) and iliac

arteries that have resulted in claudication (leg pain upon walking). Claudication is the most common symptom in patients with peripheral artery disease (PAD), and is associated with diminished physical activity and poor quality of life for patients. The SFA and iliac arteries, located in the upper leg and pelvis, are common areas of blockage in patients with PAD. The first patient was treated with an Esprit BVS as part of the trial by Marc Bosiers, M.D., head of the Department of Vascular Surgery at St. Blasius Hospital in Dendermonde, Belgium. The Esprit drug eluting BVS is designed specifically for use in peripheral arteries and is made of polylactide, the same proven biocompatible material used in the company's Absorb™ drug eluting BVS for coronary artery disease. Absorb is authorized for sale in Europe and is investigational in the United States. Esprit is designed to restore blood flow by opening a blocked vessel and providing support until it is healed. Once the vessel can remain open without the extra support, the scaffold is designed to dissolve, leaving the vessel free of a permanent metallic implant. Because a permanent implant is not left behind, clinical outcomes may be improved and options for retreatment of the vessel preserved.

"Treating blockages in the SFA is a clinical challenge, as there are unique biomechanical forces exerted on the SFA during normal leg movement, which can lead to restenosis or re-narrowing of the vessel," said Johannes Lammer, M.D., professor of radiology at the Medical University of Vienna, Austria, and principal investigator for the ESPRIT I trial. "Current endovascular therapies, such as self-expanding stents and angioplasty balloons, have limitations and have not solved the problem of restenosis. A bioresorbable drug eluting device, designed to act as a temporary scaffold to support the vessel and then fully dissolve, may change the way we treat peripheral artery disease."

"ESPRIT I is the first clinical trial to evaluate our bioresorbable technology in patients with disease in the SFA and iliac arteries," said Charles A. Simonton, M.D., FACC, FSCAI, divisional vice president, Medical Affairs, and chief medical officer, Abbott Vascular. "In addition to ESPRIT I, we also are investigating our bioresorbable therapy for the treatment of below-the-knee critical limb ischemia—a severe form of PAD—in the ABSORB BTK trial. We've seen promising long-term clinical data with our bioresorbable therapy in coronary patients, and we believe there is potential for this technology in the treatment of PAD."

Noven Announces Phase 3 Results for Investigational Non-Hormonal Therapy for Vasomotor Symptoms

Business Wire: December 22, 2011 – MIAMI, FL & NEW YORK, NY, U.S.A. – Noven Pharmaceuticals, Inc., a wholly owned subsidiary of Hisamitsu Pharmaceutical Co., Inc., today announced top-line results from the first of two planned Phase 3 clinical studies evaluating low-dose mesylate salt of paroxetine (LDMP, formerly referred to as Mesafem) for the treatment of vasomotor symptoms (VMS) associated with menopause (hot flashes).

This first study, sponsored by Noven, was a 24 week, multi-center, double-blind, randomized, placebo-controlled Phase 3 efficacy and safety study of LDMP for the treatment of VMS associated with menopause. The primary objective of the study was to assess the safety and efficacy of LDMP for the treatment of menopausal VMS. The primary outcome measures were mean changes in frequency and severity of moderate-to-severe hot flashes from baseline to the fourth and twelfth weeks of the study, as well as maintenance of therapeutic effect at week 24. All primary outcome measures in the study were achieved with statistical significance. The most frequent adverse events observed in the study were nasopharyngitis, upper respiratory tract infection, headache, nausea, and fatigue.

A second, 12 week study of LDMP is underway. If that study meets its primary endpoints, Noven expects to submit a New Drug Application for LDMP to the U.S. Food & Drug Administration in 2012.

Moberg Derma Terminates Collaboration in Canada

Business Wire: December 22, 2011 – STOCKHOLM, Sweden – Moberg Derma AB (STO:MOB) and Medical Futures Inc. have agreed that the distribution agreement between the parties shall cease, and that cooperation ends. The agreement gave the distributor the exclusive right to market and sell Emtrix® in Canada. Moberg Derma regains all rights to Emtrix® in Canada. The distributor has the right to sell off its stock for a period.

"Sales in Canada have not met expectations, and we have therefore agreed to terminate the agreement. We aim to select a new distributor with strong consumer marketing capabilities," says Peter Wolpert, CEO of Moberg Derma. For further information, please visit: www.mobergderma.se.

Fuse Science Announces the Launch of its Analgesic and Diabetic Oral Fuse Delivery (OFD) Research Project Platforms

PRNewswire: December 20, 2011 – AVENTURA, FL, U.S.A. – Double Eagle Holdings, Ltd. (OTCQB: DROP), the parent company of Fuse Science, Inc. (www.fusescience.com), announced today the formal launch of its Hypoglycemic, Hyperglycemic, and Analgesic project platforms for the advancement of its OTC and pharmaceutical licensing efforts.

Some of the proprietary science platforms that Fuse Science deals with are oral fuse delivery technologies (OFDs). These OFDs are placed under the tongue or in the inner cheek of the patient where they are absorbed and release the applicable active or nutrient into the blood stream. OFDs do not require water and may be more convenient to take than liquids or injections. OFDs are especially designed to be very useful with pediatric and geriatric patients or anyone in need of faster absorption of a given active into the blood stream that bypasses the GI track, providing an alternative to the more traditional invasive drug delivery systems.

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"Today we announce the further advancement of the true core of our Powered by Fuse™ technology," said Brian Tuffin, Fuse Science Chief Executive Officer. "It is with high confidence that we advance our OFD Analgesic, Hypoglycemic, and Hyperglycemic project platforms with the objective of completing our pediatric and adult formulations to provide an effective sublingual and/or Buccal delivery alternative for the respective drugs."

The business opportunities from these project platforms are as follows:

- The side effects of aspirin on the stomach include bleeding of the abdomen and deterioration of the stomach lining. By bypassing the GI track with our drop technology we intend to improve performance and usage in the $2.5 billion adult analgesic category.
- The largest disease state globally is diabetes with an estimated 285 million people, corresponding to 6.4% of the world's adult population living with diabetes in 2010. The number is expected to grow to 438 million by 2030, or 7.8% of the adult population. One major issue associated with the treatment of diabetes is lack of compliance. The ease of use associated with the OFD will help address the major compliance issues in this $25 billion dollar treatment category worldwide.

"We are extremely passionate about our work in this area," said Ed Maliski, Ph.D. & Lead Scientist. "Our work is born out of diabetes sufferers on staff who are committed to advancing these platforms with a sense of urgency. We have produced significant results with our OFD work and feel very confident at this stage with our ability to advance these project platforms."

"We continue to be very deliberate and focused with every step we take as a company, and our efforts in the OTC and Pharmaceutical space represents the foundation to our long term focus," added Tuffin. "These actions in combination with the long awaited, Powered by Fuse™ EnerJel™ launch on December 30th, 2011, at www.poweredbyfuse.com are calculated steps in our effort to create long term shareholder value."

Alexza Retains Lazard to Explore Strategic Options

PRNewswire: December 16, 2011 – MOUNTAIN VIEW, CA, U.S.A. – Alexza Pharmaceuticals, Inc. (Nasdaq: ALXA) announced today that that it has retained Lazard to assist in exploring strategic options to enhance stockholder value, including a possible sale or disposition of one or more corporate assets, a strategic business combination, partnership, or other transactions.

In order to conserve cash to support operations, Alexza also announced that it has provided to all of its employees a 60-day notice of layoffs under the California WARN Act. Alexza expects to significantly reduce its work force as it continues the actions necessary to pursue FDA approval of ADASUVE and continues its Marketing Authorization Application work with the European Medicines Agency.

On Monday, December 12, 2011, the Psychopharmacologic Drugs Advisory Committee (PDAC) of the U.S. Food and Drug Administration (FDA) voted to recommend that ADASUVE™ (Staccato® loxapine) be approved for use as a single dose in 24 hours in conjunction with the FDA recommended Risk Evaluation and Mitigation Strategy (REMS), for the treatment of agitation in patients with schizophrenia or bipolar mania. The vote on this question was 9/8/1 (yes/no/abstain).

The PDAC also concluded that the product had been shown to be effective (vote of 17/1/0; yes/no/abstain), and that the product would be acceptably safe for use as a single dose in 24 hours, when used in conjunction with the REMS proposed by the FDA (vote was 11/5/2; yes/no/abstain). The PDAC also voted on additional questions as previously reported by the Company.

ADASUVE is Alexza's lead program and the ADASUVE NDA has a Prescription Drug User Fee Act (PDUFA) goal date of February 4, 2012. In Europe, a Marketing Authorization Application (MAA) for ADASUVE is currently under review by the European Medicines Agency (EMA) and the application will follow the Centralized Procedure.

$60M Later, Biotech Altea Calls It Quits

Atlanta Business Chronicle, by Urvaksh Karkaria: December 9, 2011 – ATLANTA, GA, U.S.A. – A life sciences company that raised more than $60 million in venture capital, and once contemplated going public, has flamed out.

Atlanta-based Altea Therapeutics Corp. was developing a proprietary, noninvasive method to deliver therapeutic proteins, conventional drugs, and vaccines through the skin by creating "micropores" on the skin's surface. Like some of its peers, Altea ran out of money before it could get there.

"The product was doing great, the technology was doing great, the company was doing great," said Altea's former chief executive, Eric Tomlinson.

The problem, he said, was that the company's commercialization partners—Eli Lilly and Co., Amylin Pharmaceuticals Inc., and Hospira Inc.—chose to halt funding, leaving the company strapped for cash. The collapse of the two partnerships cost Altea $10 million to $12 million in anticipated funding for 2011, said Tomlinson, a former chair of industry trade association Georgia Bio.

At its peak, Altea employed as many as 75, including pharmaceutical scientists and engineers. Now, the company has left its 40,000-square-foot facility at Georgia Tech and sold its technology and intellectual property to an out-of-state life sciences company.

Altea was launched in 1998, based on the research of a group of Atlanta engineers. Altea was the first tenant in the 128,000-square-foot Technology Enterprise Park, headquartered at Georgia Tech. Tomlinson, former CEO of Woodlands,

Texas-based Gene Medicine Inc., helped the company raise money from a phalanx of investors including Aperture Venture Partners LLC, Domain Associates LLC, Venrock Associates, KBC Group, The Quilvest Group, and Rockport Ventures.

Altea considered going public in 2008, but abandoned the idea in the wake of the financial meltdown. In 2008, Altea struck a partnership with Hospira for the development and commercialization of a transdermal patch that delivers enoxaparin, an anti-coagulant used in preventing blood clots during joint replacement surgery. Hospira was to fund product development, manufacturing, and commercialization. Hospira decided to exit the anti-coagulant drug business using enoxaparin, because it was unable to source enough of the medication, Tomlinson said.

A year later, Altea inked a similar deal with Eli Lilly and Amylin to develop a skin patch to deliver exenatide, a drug used to manage Type 2 diabetes. The deal included an undisclosed amount of equity investment in Altea. Amylin and Lilly were, at the same time, developing a weekly injectable form of exenatide. In 2010, that product encountered "considerable delays" in getting FDA approval and required additional clinical trails, Tomlinson said. Amylin and Lilly decided to focus their money on the injectable product, Tomlinson said, rather than Altea's patch technology, which would have taken longer to develop.

Ampio Pharmaceuticals Announces Agreement to Acquire Key Drug Delivery Technology

PRNewswire: December 5, 2011 – GREENWOOD VILLAGE, CO, U.S.A. – Ampio Pharmaceuticals, Inc. (NASDAQ: AMPE) ("Ampio" or the "Company"), a company that discovers and develops new uses for previously approved drugs and new molecular entities ("NMEs"), today announced it has signed an agreement to acquire certain rights relating to a patented orally disintegrating tablet (ODT) drug delivery technology that can be used worldwide to elevate the market acceptance of Ampio's Zertane™ product for premature ejaculation. The Zertane™ ODT formulation allows for rapid oral absorption, ease of use without the need for liquids, and avoids unpleasant bitter taste. This acquisition provides additional intellectual property to protect Zertane™ ODT's unique formulation, over and above the many method of use claims for Zertane™ contained in patents Ampio already owns. The Company indicated that acquisition of the rights to this technology is expected to speed and facilitate Ampio's filing of marketing authorization applications for product regulatory approvals of Zertane™ worldwide and is important for the additional planned licensing and pricing agreements currently in negotiations. The completion of the transaction is subject to customary conditions, including a certain third party consent and successful completion of a technology and materials transfer plan more fully described in a Form 8-K to be filed shortly.

"This acquisition of this technology is an important step in the manufacturing and commercialization plan for Zertane™. This agreement demonstrates our commitment to the fast and successful launch of a unique dosage and formulation of Zertane™. The Zertane™ commercialization plan is on course as outlined in the previous press releases and securities filings. We are committed to complete the development of a combination product of Zertane™ with a PDE5 inhibitor to simultaneously treat both premature ejaculation and erectile dysfunction. Our strategy with this line of products is to expeditiously pursue multiple
licensing partners worldwide," stated Don Wingerter, Ampio's CEO. For more information about Ampio, please visit our website, www.ampiopharma.com.

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Quest PharmaTech Announces Development of Second Generation Photodynamic Therapy Products for the Treatment of Cancer Based on Nanotechnology

PRNewswire: November 29, 2011 – EDMONTON, AB, Canada – Quest PharmaTech Inc. (TSX-V: QPT) ("Quest" or the "Company"), a biotechnology company developing and commercializing products for the treatment of cancer, today announced the acceptance for publication of a research paper entitled "Antitumor Efficacy of Photodynamic Therapy Using Novel Nanoformulations of Hypocrellin Photosensitizer SL052," in the *Journal of Photochemistry and Photobiology*. The paper highlighted the results from a research study conducted by scientists from the University of Saskatchewan in Saskatoon and the BC Cancer Agency in Vancouver, comparing the antitumor effect of Quest's photosensitizer, SL052, in a novel nano-formulation with other previously developed formulations for photodynamic therapy. The results demonstrated the superior antitumor effect of the new nanoparticle formulation over another nano-formulation which was previously developed by the Company in collaboration with IntelligentNano, an Edmonton based private company. The results from that study were previously published in the journal *Nanomedicine* titled "Water-Soluble and Biocompatible Sono/Photosensitizer Nanoparticles for Enhanced Cancer Therapy."

The Company has filed patent applications for both of these formulations, and has initiated a preclinical program to explore their utility for intravenous delivery of Quest's proprietary SL052 photosensitizer for the treatment of gastrointestinal cancer. This second generation photodynamic therapy product will complement the Company's ongoing prostate cancer treatment program that utilizes SL052 with a novel intra-arterial drug delivery system.

In another study completed by University of Alberta scientists, the mechanism of action of the Company's novel hypocrellin based photo/sono-sensitizer was examined and published in a paper titled "Sonodynamic and Photodynamic Mechanisms of Action of the Novel Hypocrellin Sonosensitizer; SL017: Mitochondrial Cell Death is Attenuated by 11, 12-Epoxyeicosatrienoic Acid" in the journal *Investigational New Drugs*.

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"These new studies conducted by external researchers and published in peer reviewed scientific journals show that this new nanoparticle formulation of SL052 enhances the delivery of our photosensitizer to the target area and can be utilized for various indications thereby expanding the potential application of our proprietary drug and formulations to treat a variety of cancers," said Thomas Woo, Vice President of Product Development at Quest.

Femina Pharma Announces ALJ's Denial of Merck's Motion for Summary Determination on Domestic Industry in ITC Patent Dispute Concerning NuvaRing®

PRNewswire: November 28, 2011 – MIAMI, FL, U.S.A. – Femina Pharma Incorporated announces the issuance of Order 24 in Investigation No. 337-TA-768 (In the matter of Certain Vaginal Ring Birth Control Devices) by the Administrative Law Judge at the United States International Trade Commission ("ITC") denying the Merck Respondents' Motion for Summary Determination on the basis of lack of Domestic Industry. The issuance of Order 24 follows the prior issuance on July 15, 2011, of Order 14 denying Merck's Motion for Summary Determination of Invalidity of U.S. Patent No. 6,086,909.

On February 11, 2011, Femina Pharma Incorporated filed a complaint with the ITC for infringement of the '909 patent through importation of certain vaginal ring birth control devices, including NuvaRing® against Merck & Co., Inc., Schering Plough Corporation, Organon USA, Inc., N.V. Organon, Wal-Mart Stores, Inc., CVS Pharmacy, Inc., Walgreen Co., and several Canadian On-Line Pharmacies. The Canadian On-Line Pharmacies have been held in default. NuvaRing® was acquired by Merck through its 2009 acquisition of Schering Plough.

Separately, Femina Pharma Incorporated announces the November 15, 2011, filing of a patent infringement lawsuit in federal district court in the Eastern District of Virginia against Merck & Co., Inc., Schering Plough Corporation, Organon USA, Inc., Wal-Mart Stores, Inc., CVS Pharmacy, Inc., and Walgreen Co. alleging infringement of the '909 patent by the NuvaRing® (C.A. no. 1:11cv1248) (the "District Action"). The District Action seeks monetary damages and injunctive relief.

Joseph Matus Fuisz, CEO of Femina Pharma, stated: "We are pleased with the Order denying the Merck Respondents' Motion for Summary Determination on the basis of lack of Domestic Industry. Femina continues to exploit the claimed technology and has every right to seek redress at the ITC to protect US industry from infringing foreign imports. Femina Pharma initiated Investigation No. 337-TA-768 to stop the unlawful importation of infringing product sold as NuvaRing®. We look forward to the ITC hearing scheduled for January 2012. Separately, we have initiated the District Action to seek monetary damages for current and past infringement."

US Patent Office Rejects All 191 Claims in Key MonoSol Patent Asserted Against BioDelivery Sciences

PRNewswire: November 28, 2011 – RALEIGH, NC, U.S.A. – BioDelivery Sciences International, Inc. (Nasdaq: BDSI) has been informed by the United States Patent & Trademark Office (USPTO) that it has rejected all claims of U.S. Patent No. 7,824,588 (the '588 Patent), which is currently being asserted against BDSI by MonoSol RX, LLC (MonoSol). The USPTO's action follows BDSI's September 2011 request for reexamination of the '588 Patent by the USPTO.

The USPTO's action is a significant and positive development for BDSI as the '588 Patent is a key element of claims first asserted in a litigation filed by MonoSol in November 2010 against BDSI and its commercial partners for BDSI's ONSOLIS. In its action, MonoSol claimed that BDSI's confidential, proprietary manufacturing process for ONSOLIS infringes on the thin film manufacturing process claimed in the '588 Patent.

BDSI has defended the case on the grounds of non-infringement and invalidity of the '588 Patent. In September 2011, BDSI filed an Inter Partes Request for Reexamation of the '588 Patent with the USPTO based on a number of prior art references that anticipate and/or render obvious (and thus unpatentable and invalid) all of the claims of the '588 Patent. The recent action by the USPTO supports BDSI's position on this matter. The USPTO granted BDSI's request for the reexamination, because it found substantial new questions of patentability affecting all 191 claims of the '588 Patent, and it issued an official action rejecting all 191 claims as unpatentable over a number of prior art references. MonoSol has two months to respond to this action, after which BDSI may comment to the USPTO on MonoSol's response.

In light of this development, BDSI will continue its aggressive defense of this matter towards what the Company believes will be a positive resolution for BDSI. It is BDSI's position that two additional patents MonoSol added to its case against BDSI only recently are similarly invalid and unenforceable.

Dr. Mark A. Sirgo, President and Chief Executive Officer of BDSI, commented, "This is a very significant and positive development for BDSI and its commercial partners involved in this case. We have consistently maintained that we do not infringe the '588 Patent or any other patent of MonoSol, and importantly, that the '588 Patent is clearly invalid based on prior art. The USPTO's official action convincingly validates this latter position. The fact that our reexamination request was granted so quickly by the USPTO was welcome but not surprising given the information we provided to them. However, the fact that they took the extra step to reject every single claim of the '588 Patent as invalid over the prior art was extraordinary and raises serious questions as to the enforceability of the '588 Patent. The USPTO's rejection of all 191 claims of the '588 patent enhances our confidence in defending against MonoSol's claims. We intend to continue to aggressively pursue whatever actions are

necessary to defend our position and expect that all of MonoSol's claims will ultimately be defeated."

Radius Closes $27.65 Million Second Tranche of Previously Announced Financing

PRNewswire: November 23, 2011 – CAMBRIDGE, MA, U.S.A. – Radius Health, Inc. ("Radius") announced today the closing of the second of the company's three-tranche $91 million financing round announced in May 2011. The $27.65 million second tranche included $21.4 million in equity financing from Radius' current investors and $6.25 million in debt financing from GE Capital, Healthcare Financial Services, and Oxford Finance LLC, bringing gross proceeds received to date from the $91 million financing to $57.3 million. As previously disclosed, Radius receives the second and third tranches of the equity financing round upon written request to the company's investors.

Radius will use the proceeds from the second tranche primarily to continue advancing the ongoing Phase 3 clinical study of BA058 Injection, the company's novel anabolic (bone-building) drug for the treatment of osteoporosis. Data from the study are intended to form the primary basis for an efficacy claim to support applications for marketing authorization of BA058 Injection in the United States and Europe.

"With the additional funding, we will continue our company strategy of moving quickly to execute on the pivotal Phase 3 study of BA058 Injection and prepare for initiation of Phase 2 for the transdermal BA058 Microneedle Patch," said Nick Harvey, Chief Financial Officer of Radius. "Our goal is to provide a new treatment option for patients with osteoporosis that builds new bone, reduces risk of future fractures, improves convenience, and optimizes patient outcomes."

Engineered, Drug-Secreting Blood Vessels Reverse Anemia in Mice

PRNewswire: November 15, 2011 – BOSTON, MA, U.S.A. – Patients who rely on recombinant, protein-based drugs must often endure frequent injections, often several times a week, or intravenous therapy. Researchers at Children's Hospital Boston demonstrate the possibility that blood vessels, made from genetically engineered cells, could secrete the drug on demand directly into the bloodstream. In the November 17 issue of the journal *Blood*, they provide proof-of-concept, reversing anemia in mice with engineered vessels secreting erythropoietin (EPO).

The technology could potentially be used to deliver other proteins such as Factor VIII and Factor IX for patients with hemophilia, alpha interferon for hepatitis C, and interferon beta for multiple sclerosis, says the study's principal investigator, Juan Melero-Martin, PhD, of the Department of Cardiac Surgery at Children's.

Such drugs are currently made in bioreactors by engineered cells, and are very expensive to make in large amounts. "The paradigm shift here is, 'why don't we instruct your own cells to be the factory?'" says Melero-Martin, also an assistant professor at Harvard Medical School.

The researchers created the drug-secreting vessels by isolating endothelial colony-forming cells from human blood and inserting a gene instructing the cells to produce EPO. They then added mesenchymal stem cells, suspended the cells in a gel, and injected this mixture into the mice, just under the skin. The cells spontaneously formed networks of blood vessels, lined with the engineered endothelial cells. Within a week, the vessels hooked up with the animals' own vessels, releasing EPO into the bloodstream.

Tests showed that the drug circulated throughout the body and reversed anemia in the mice, both induced by radiation (as often occurs in cancer patients) and by loss of kidney tissue (modeling chronic kidney failure). Mice with the vessel implants had significantly higher hematocrits (a measure of red blood cell concentration) and recovered from anemia more quickly than controls.

The system also had a built-in on/off control: the inserted EPO-encoding gene was linked to a repressor protein that prevented it from being turned on unless the mice were given the oral drug doxycycline (added to their drinking water). Doxycycline disabled the repressor protein, allowing EPO to be made. When doxycycline was added to the water on a weekly on/off schedule, the animals' hematocrit fluctuated accordingly. When hematocrit reached a normal level, the system could be switched off by simply giving them plain water.

Melero-Martin and colleagues are looking at ways to deliver doxycycline through the skin to avoid exposing the whole body to an antibiotic. There are also other ways to design the genetic on/off control, using synthetic systems or even regulatory elements used naturally by the body—sensing blood oxygen levels and stimulating EPO production when oxygen levels dip.

A traditional barrier to gene therapy has been getting the genetically altered cells to engraft and stay in place. Blood-vessel implants are an ideal platform technology for gene therapy applications whose goal is systemic drug delivery, says Melero-Martin.

"Blood vessels are one of the few tissues where we have good control over engraftment," he says. "Endothelial cells are easily isolated from blood, are good at assembling themselves into blood vessels, and are ideal for releasing compounds into the bloodstream, since they line the blood vessels."

The lab is interested in trying this system with other therapeutic proteins, and is also exploring ways to get cells to release therapeutics at a moment's notice by accumulating stores in advance that could be released upon the proper signal, as beta cells in the pancreas do with insulin, for example.

In addition, Melero-Martin wants to explore regenerative medicine applications, creating blood vessels with genetic instructions to produce factors that attract stem cells or induce cells to differentiate. For more information about research and clinical innovation at Children's, visit: http://vectorblog.org or

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contact Colleen Connolly, Children's Hospital Boston, Colleen.Connolly@childrens.harvard.edu.

Bend Research Signs Technology Licensing Agreement with Merck

PRNewswire: November 14, 2011 – BEND, OR, U.S.A. – Bend Research Inc. (www.bendresearch.com), a leading independent drug-formulation development and manufacturing company, announced today that it has entered into a licensing agreement with Merck, through a subsidiary.

Under the terms of the agreement, Bend Research will provide Merck access to its proprietary spray-dried dispersion (SDD) technology. Depending on Merck's additional needs, Bend may also provide Merck with access under the license agreement to additional drug-delivery platforms and intellectual property, including modified-release technologies and drug-discovery formulation tools.

Under the collaboration, the two companies hope to use their complementary fundamental scientific and engineering capabilities to solve complex formulation and process-development problems with an eye toward transferring these solutions to a cGMP [current good manufacturing practices] environment.

"We are excited to extend our working relationship with Merck," said Rod Ray, Chief Executive Officer of Bend Research. "Building stronger collaborative relationships with leading companies like Merck is important to Bend Research's future. This relationship expands our opportunities to deliver best-in-class medicines and fits well with Merck's mission to help provide innovative products that save and improve people's lives."

Advisory Committee for Reproductive Health Drugs Meeting Scheduled for January 20, 2012

PRNewswire: November 10, 2011 – LIVINGSTON, NJ & PARSIPPANY, NJ, U.S.A. – Columbia Laboratories, Inc. (Nasdaq: CBRX), and Watson Pharmaceuticals, Inc. (NYSE: WPI), today confirmed that the Advisory Committee for Reproductive Health Drugs of the U.S. Food and Drug Administration (FDA) is scheduled to review Columbia's New Drug Application (NDA) for progesterone vaginal gel for the reduction of risk of preterm birth in women with short uterine cervical length regardless of other risk factors in the mid-trimester of pregnancy on January 20, 2012.

The Advisory Committee for Reproductive Health Drugs is an independent panel of experts that evaluates data concerning the efficacy and safety of marketed and investigational products for use in the treatment of reproductive conditions and makes non-binding recommendations to the FDA. While the FDA will consider recommendations of the committee, the final decision regarding the approval of the product rests solely with the FDA.

The companies announced on June 27, 2011, that the FDA accepted the NDA for filing. The FDA's goal is to review and act on the NDA by February 26, 2012, under the Prescription Drug User Fee Act IV (PDUFA). The NDA includes data from two Phase III clinical trials evaluating the use of progesterone vaginal gel in reducing the risk of preterm birth in women, as well as supportive pharmacokinetic studies.

The FDA will publish materials pertaining to the meeting at http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/ReproductiveHealthDrugsAdvisoryCommittee/ucm262537.htm. Changes to the Advisory Committee meetings calendars may also be found on the FDA website at http://www.fda.gov/AdvisoryCommittees/Calendar/ucm153468.htm.

Micell Technologies Announces Positive Preliminary Data from DESSOLVE I Study of MiStent® Sirolimus Drug Eluting Coronary Stent System

PRNewswire: November 8, 2011 – DURHAM, NC, U.S.A. – Micell Technologies, Inc. today announced the release of preliminary data from the first-in-human clinical study of the MiStent® Sirolimus Drug Eluting Coronary Stent System (MiStent DES), a thin-strut drug-eluting stent distinguished by a rapid-absorbing drug/polymer coating designed for controlled drug release. Four, six, and eight month data from the DESSOLVE I trial were presented at the Transcatheter Cardiovascular Therapeutics Conference (TCT 2011) by John Ormiston, M.D., Mercy Angiography Unit, Auckland, New Zealand, a principal investigator in the study. TCT will make the presentation available on its website at www.tctmd.com following the conference.

"These preliminary study results demonstrated excellent performance by the MiStent DES at up to eight months post-procedure—when patients typically experience the greatest increase in neointimal hyperplasia," said Dr. Ormiston. "MiStent DES is intended to provide enhanced patient safety and outcome by eliminating long-term exposure to DES non-erodible polymers. In addition to delivering clinical performance, MiStent DES may also enable physicians to pursue shorter duration dual anti-platelet therapy, and offer a safer choice to their non-compliant patients or patients who may be undergoing additional surgical procedures."

Thirty patients were treated with the MiStent DES with independent subgroups of 10 patients assigned to a four month, six month, or eight month follow-up. The primary efficacy endpoint was in-stent late lumen loss (LLL). Safety was assessed by incidence of major adverse cardiac events (MACE) and presence of tissue coverage within the treated artery at each time point. Angiography, intravascular ultrasound (IVUS), and optical coherence tomography (OCT) imaging results were measured by independent core laboratories. Preliminary analysis of the data demonstrated a very low median in-stent late lumen loss of 0.03 mm at four months, 0.10 mm at six months, and 0.08 mm at eight months follow-up with no binary restenosis or revascularizations. The mean in-stent late lumen loss values at four, six, and eight months were 0.01, 0.21, and 0.09 mm, respectively. The mean and median values were comparable

except at the six month time point, in which one patient experienced a high late loss value due to treatment of a highly calcified lesion and under-expansion of the stent. When data from this patient is excluded, the six month mean LLL is 0.10 mm. The median percent of stent struts covered by tissue was 96% at eight months, 97% at six months, and 90% at four months per OCT analysis. IVUS confirmed good inhibition of neointimal hyperplasia. A MACE rate of 6.7%, including two non-Q wave myocardial infarctions (MI), one peri-procedural, and one non-target vessel MI, was reported through eight months follow-up.

"The MiStent DES was designed to address a need for improved patient safety while providing equivalent or better efficacy as compared to currently available drug eluting stents," observed Dennis Donohoe, M.D., Chief Medical Advisor to Micell. "The excellent clinical outcomes of the DESSOLVE I trial demonstrate the value of the MiStent design in enabling elimination of drug and polymer from the stent in 45 to 60 days and providing patients the best of DES and BMS in one solution."

The MiStent DES innovative stent system includes a proprietary stent coating that contains crystalline drug (sirolimus) and an absorbable polymer. As the polymer softens and disperses from the stent into the adjacent tissue, the coating provides controlled and sustained release of therapeutic levels of drug within the surrounding tissue. Results of animal studies have determined that the drug/polymer coating is cleared from the stent in 45 to 60 days, leaving a bare metal stent, and the polymer is completely absorbed into the surrounding tissue in 90 days to promote long-term patency and compatibility with the artery. The MiStent Sirolimus-Eluting Coronary Stent System is an investigational device currently being evaluated in international clinical studies and is not yet approved or available for sale in any market. More information at www.micell.com.

Access Pharmaceuticals Signs Agreement for CobaCyte® and CobOral® in RNAi Therapeutic Delivery

PRNewswire: November 8, 2011 – DALLAS, TX & NEW YORK, NY, U.S.A. – ACCESS PHARMACEUTICALS, INC. (OTCBB: ACCP), a biopharmaceutical company leveraging its proprietary drug-delivery platforms to develop treatments in areas of oncology, cancer supportive care, and diabetes, announced it has entered into an agreement with a major player in RNAi industry to exploit its CobaCyte and CobOral technology for the targeted delivery of RNAi therapeutics. Access will provide the pharmaceutical company with CobOral and CobaCyte siRNA formulations for evaluation of gene knockdown following oral and intravenous administration. Access indicated that any successful formulation developed will be jointly owned by the Parties and subject to a subsequent full licensing agreement.

"We are pleased to have signed an agreement with another major player in RNAi therapeutics as it continues to validate the advances in both our CobOral and CobaCyte technology platforms," said Phillip Wise, VP Business Development and Strategy, Access Pharmaceuticals, Inc. He continued, "We believe the distinct advantages our CobOral and CobaCyte technologies offers is well-suited for the company's RNAi products, and we look forward to the collaborative work ahead."

RNAi is typically initiated by the introduction of small fragments of RNA, typically siRNA or miRNA, into cells at disease sites. Due to their large size and high negative charge, these RNA fragments are not able to cross cell membranes. Therefore, to develop effective RNAi therapeutics, a delivery system must be developed that can transport the siRNA into cells, and release undamaged siRNA into target cell cytoplasm. Access' CobOral and CobaCyte delivery technologies, which are based on vitamin B12, are particularly well-suited for this purpose. Most human cells have a requirement for vitamin B12 which is served by cell surface receptors which facilitate absorption of this vitamin. In many diseases, the demand for vitamin B12 is increased, with a corresponding upregulation of the receptor. Using the "Trojan Horse" principle, the CobaCyte nanoparticle technology can utilize the vitamin B12 uptake mechanism to transport siRNA into cells, whereupon native siRNA can be released for incorporation in messenger RNA (mRNA) to initiate the beneficial therapeutic effect. In this way, CobaCyte offers the potential for targeted delivery of siRNA following intravenous administration. The fact that Access' vitamin B12 technology also facilitates oral drug delivery (the CobOral technology) indicates that it may also be possible for this technology to provide effective siRNA treatments by oral drug delivery.

BEMA Fentanyl Submitted for Marketing Authorization in Taiwan

PRNewswire: November 7, 2011 – RALEIGH, NC, U.S.A. – BioDelivery Sciences International, Inc. (Nasdaq: BDSI) announced that TTY Biopharm Co., Ltd. (TTY), BDSI's commercial partner for BEMA Fentanyl in Taiwan, has submitted a New Drug Application (NDA) for marketing authorization of BEMA Fentanyl to the Taiwan Food and Drug Administration.

TTY is responsible for the regulatory filing of BEMA Fentanyl in Taiwan as well as future commercialization in that territory. In October 2010, BDSI granted TTY the exclusive rights to develop and commercialize BEMA Fentanyl. Under terms of the agreement, BDSI is eligible for milestone payments of up to $1.3 million, which included an upfront payment of $300,000. This NDA submission results in an additional milestone payment of $300,000 to BDSI. In addition, upon regulatory approval, BDSI will receive an ongoing royalty based on net sales.

BEMA Fentanyl is currently marketed in the U.S. and Canada under the tradename ONSOLIS (fentanyl buccal soluble film). BEMA Fentanyl is licensed to Meda for all territories with the exception of Taiwan and South Korea. In South Korea, BEMA Fentanyl is licensed to Kunwha Pharmaceutical Co.

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NanoSmart™ Pharmaceuticals Joins Forces with Children's Hospital Los Angeles to Fight Pediatric Cancer

PRNewswire: November 1, 2011 – ORANGE COUNTY, CA, U.S.A. – NanoSmart Pharmaceuticals, Inc., a corporation developing novel cancer pharmaceuticals, has entered into a research collaboration with Children's Hospital Los Angeles, one of the nation's top pediatric hospitals, to develop and assess NanoSmart's novel drug-delivery platform.

NanoSmart is developing a tumor-targeting platform utilizing human autoimmune antibodies that target areas of necrosis found in many different types of cancer. By combining these antibodies with different cancer drugs, NanoSmart plans to develop numerous novel biopharmaceutical products. NanoSmart's drug-delivery system promises to increase the safety and efficacy of existing cancer drugs by increasing localization at the tumor site.

Collaborative research with Children's Hospital Los Angeles will be conducted under the guidance of Timothy Triche, M.D., Ph.D., Professor of Pathology and Pediatrics and Director of the Children's Hospital Los Angeles Department of Pathology's Center for Personalized Medicine.

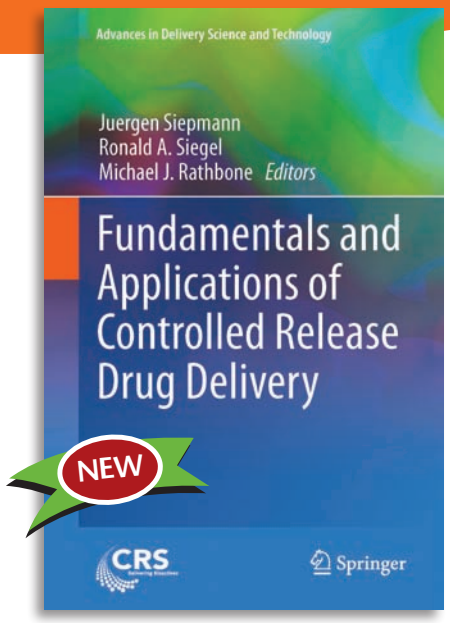
"We are pleased to work with NanoSmart as part of our ongoing research program in nanoparticle-mediated therapy of Ewing's sarcoma. This research will complement other research currently in progress in our lab. It is unique in that NanoSmart has leveraged a naturally occurring human antibody to target the nanoparticles to the tumor, which if successful should facilitate rapid approval from the FDA for use on Ewing's sarcoma patients," said Dr. Triche.

"This strategic alliance will give NanoSmart access to critical preclinical and clinical resources," said Dr. James Smith, President of NanoSmart Pharmaceuticals. "In addition to Dr. Triche's expertise and guidance, we look forward to initial characterization and testing of NanoSmart's formulations in the unique model of metastatic Ewing's Sarcoma at Children's Hospital."

Note to readers: While compiling the news items for this issue of the *CRS Newsletter*, I noticed many changes occurring for businesses in controlled release and drug delivery. News items for the last three months show many changes and several companies closing or at risk of closing, new financing for small companies, and decisions from the FDA. Let's hope the next few months bring success and better circumstances for the people and businesses involved in controlled release. ■

TWO NEW TITLES
from the Controlled Release Society!

Watch for more titles in 2012



Edited by
Juergen Siepmann, Ronald A. Siegel, and Michael J. Rathbone

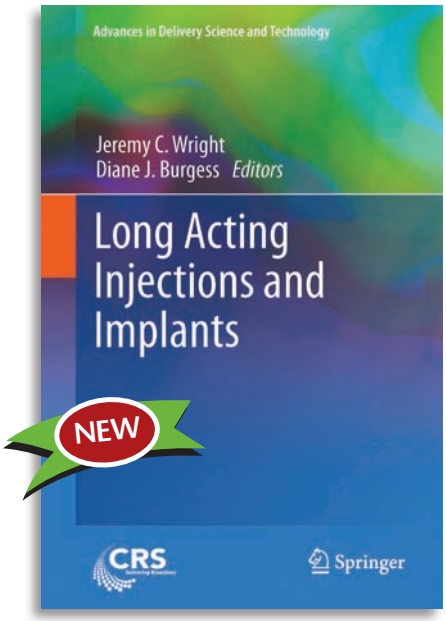
Fundamentals and Applications of Controlled Release Drug Delivery covers the fundamentals relating to the science and technology of drug delivery. The book is written at a level that is understandable to those entering the field and who are not familiar with its common phrases or complex terms. It is a book that provides a simple encapsulation of concepts and expands on them using a building block approach to each subject, starting at a basic level and building to extend the reader's knowledge and application of the subject. In each chapter the basic concept is explained as simply and clearly as possible without a great deal of detail, and then in subsequent sections additional material is introduced in order to build up the reader's understanding and comprehension of the subject matter.

This book will be indispensable to scientists interested in the science and technology of drug delivery and essential for those developing delivery systems designed to improve the clinical performance of a drug.

2012 1st Edition; hardcover; 592 pages; ISBN 978-1-4614-0880-2

These new titles join the growing CRS library, which includes

- *Controlled Release in Oral Drug Delivery*
- *Controlled Pulmonary Drug Delivery*



Edited by
Jeremy C. Wright and Diane J. Burgess

Long Acting Injections and Implants includes the historical development of the field, drugs, diseases and clinical applications for long acting injections and implants, anatomy and physiology for these systems, specific injectable technologies (including lipophilic solutions, aqueous suspensions, microspheres, liposomes, *in situ* forming depots and self-assembling lipid formulations), specific implantable technologies (including osmotic implants, drug eluting stents and microfabricated systems), peptide, protein and vaccine delivery, sterilization, drug release testing and regulatory aspects of long acting injections and implants.

This volume provides essential information for experienced development professionals but was also written to be useful for scientists just beginning work in the field and for others who need an understanding of long acting injections and implants. This book will also be ideal as a graduate textbook.

2012 1st Edition; hardcover; 557 pages; ISBN 978-1-4614-0553-5

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

Calendar of Events

2012

AAPS Workshop on Lipid-based Delivery for Improving Drug Absorption: Mechanistic Understanding and Practical Approaches
Sponsored by CRS
April 23–24
Baltimore, MD, U.S.A.
www.aaps.org/Lipids

Microneedles 2012 – 2nd International Conference on Microneedles
Sponsored by CRS
May 13–15
Cork, Ireland
www.microneedles.ie

9th World Biomaterials Congress
June 1–5
New International Exhibition & Convention Center
Chengdu, China
www.wbc2012.com

IWPCPS-14 (International Workshop on Physical Characterization of Pharmaceutical Solids)
June 25–28
Barcelona, Spain
www.assainternational.com/workshops/iwpcps_14/iwpcps_14.cfm

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

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