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Newsletter

A publication of the Controlled Release Society

Volume 28 • Number 1 • 2011

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Cover photo: Zebra mussels feeding, courtesy of Geoffrey Moggridge.

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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From the Editor

Steven A. Giannos
Chrono Therapeutics, Inc.
Quincy, MA, U.S.A.

"Everything flows, nothing stands still."

Welcome to the New Year,

I don't know about the weather where you are, but for the last two months in Boston, MA, we have seen record weather; 20 inches of snow and bitter cold. Fortunately, I was able to get some time in San Diego, CA, with ample sunshine and warmer temperatures. While I was there, I was excited to attend UCSD's Center for Chronobiology 2nd annual symposium and learn more about the biology and physiology behind circadian rhythms. Now I'm back home with the cold and snow but the days are getting longer and I know that spring is on its way.

Change is a constant, and with the new year, there have been many changes in the world politically, economically, and within CRS. The last four months have seen an increase in merger and acquisition activity of drug delivery companies. Recently, Sanofi-Aventis announced the purchase of Genzyme (reported to be the second largest in biotechnology history). Drug delivery and controlled release technologies, new and old, are now forecast to fill the economic gap left from block-buster medications going off patent and financial pressures coming from health care reform.

The Controlled Release Society has been making changes too, such as updating by-laws and governance structure, staff reorganization, an upgraded website, etc. Please read Mark Tracy's "From the President" message on page 3, as well as view all CRS Headquarters & Staff contact information on page 12.

With the many changes within the CRS, there are also increased opportunities for learning. The CRS website features three informative webcasts, with more to come. Last November, the joint CRS-AAPS Workshop offered an outstanding program, "Using Novel Methods (including Population Pharmacokinetics) to Support the Development of Clinically Relevant Product Specification," in New Orleans, LA, giving an overview of QbD.

This year's CRS annual meeting theme, "Innovative and Low-cost Technologies for Healthcare and Consumer Products," could not be more perfectly timed. What better place to meet the people and learn about the creation, the science, and the development of cost effective controlled release technologies for pharmaceutical, consumer, agricultural, and animal needs than at the annual meeting. And also, please read Ijeoma Uchegbu's description of how the annual meeting is planned and assembled.

The CRS organization continues to flourish and there are a number of ways to get involved, such as helping with the website, submitting an article for the Newsletter, joining a committee, or participating in a CRS chapter workshop or meeting. The CRS Young Scientist Committee is an additional opportunity to mentor a young scientist, or for young scientists to find the right person in CRS that can help guide them as they start their career.

Please enjoy this issue of the Newsletter, and have a wonderful 2011.

Steven A. Giannos ■

Mark A. Tracy
Alnylam Inc.
Cambridge, MA, U.S.A.

Happy New Year! On behalf of the CRS, I would like to wish you and your family, friends, and colleagues the best for 2011. The beginning of the year is a good time to look forward and contemplate the year ahead. This upcoming year is an exciting one for the CRS as we prepare our Society for the new decade, launch new member benefits, and enhance our capabilities to provide you with more benefits year-round. It also coincides with the mid-point of my term as CRS President. So I would like to take this opportunity to present to you an update on the progress we are making in several of my top priority areas for my term as your President as well as highlight some of the special events coming up this year.

1. **Update By-laws and Governance Structure.** It has been about 10 years since the CRS by-laws and governance structure were last extensively reviewed. With our goal to prepare the CRS for the new decade and provide a strengthened foundation to support growth in member benefits, I named a Governance Task Force led by former Treasurer, Arthur J. Tipton, to review and recommend updates to our by-laws and governance structure. The task force submitted recommendations to the Board for updates to the by-laws in January 2011. After Board review and approval, we plan to seek membership approval to the revised by-laws later this year.

2. **New Website.** As I noted in my last newsletter article, the CRS has begun work to upgrade our website. This effort is coordinated by the CRS Website Committee led by Andy Lewis, and Steve Kronmiller from CRS staff. Our goal is to build a new website that reflects the sophistication of our members and our science that will serve as the primary home for our members worldwide and as a valuable resource for the field in general. We anticipate launching the new site later this year.

3. **Staff Reorganization.** As we enhance our benefits and activities for members, the CRS management needs are evolving. In order to adapt to our current and future needs, CRS staff was recently reorganized. As a part of this reorganization, Susan Kohn has joined the CRS staff as Executive Director. Over the course of the next several months, Susan will be immersing herself in her new role and getting to know the CRS leadership and membership. Susan, welcome to the CRS!

4. **Enhanced Financial Planning.** As we prepare the CRS for the new decade, we are committed to enhancing our Society's financial strength. The Finance Committee, led by Treasurer Debra Bingham, is updating our financial planning processes to strengthen budgetary review and oversight procedures and to promote multi-year financial planning and greater awareness amongst volunteers of the financial planning aspects for meetings.

As you see, this year we are focused on building a stronger foundation to support the development of the CRS now and into the future. A special thanks to all the CRS volunteers and staff who have committed their time and effort to advance these efforts. Finally, I would like also to highlight some special events in 2011.

- ***Drug Delivery and Translational Research* (*DDTR*) Inaugural Issue.** We are proud to have launched the first issue of our new journal *DDTR*. It is available to members online so log-on and be amongst the first to read it today!
- **2011 Annual Meeting and the new Innovation Weekend.** Make sure you have marked your calendar to attend the 2011 CRS Annual Meeting. We have a rich program planned! This year I also invite you to come a couple days early to participate in our new Innovation Weekend programs on July 30–31, 2011. Innovation Weekend is a new series of workshops/sessions focused on the translation of novel delivery systems to the clinic including preclinical, CMC, and regulatory aspects. The two themes to be covered in this year's Innovation Weekend are Turning Nanoparticle Delivery Systems into Innovative Medicines and Advances in Science and Technology for Delivery of Medicines to the Central Nervous System. More information on the program will be available soon but mark your calendars now to be in National Harbor, Maryland, from July 30–August 3, 2011.
- **College of Fellows Nominations Underway.** The call for nominations for the next class of CRS Fellows is underway. Please nominate a Fellow today! See www.controlledrelease.org for the nomination package requirements.

We are making great progress in bringing you new benefits and preparing the CRS to be THE leader in delivery science and technology in this new decade. So take a moment to make sure your membership is current and enjoy all the benefits available to our members. Again, all the best for 2011!

Mark A. Tracy ■

Ever Wondered How...

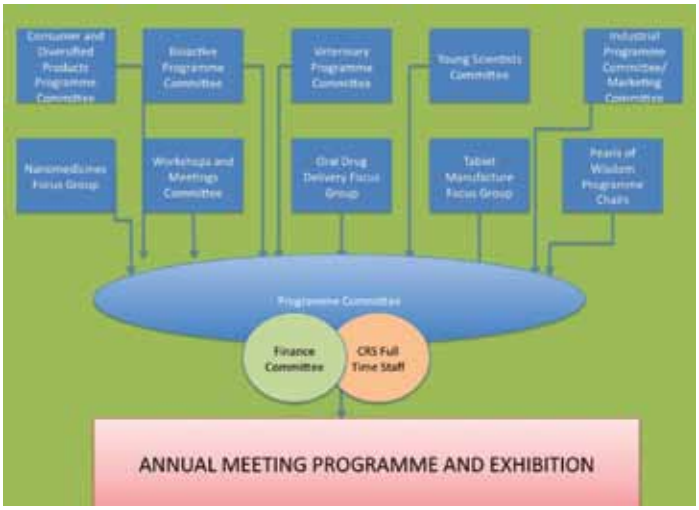
Ijeoma F. Uchegbu
Professor of Pharmaceutical Nanoscience
CRS Scientific Secretary

Ijeoma F. Uchegbu

Have you ever wondered how the Annual Meeting is brought to you by the CRS? Once again we bring you what promises to be an excellent line up of top notch scientists in a stunning location, just a bus ride away from the bright lights of the world's most important capital city. We will hear from no less than 1,000 scientific contributors and there promises to be some notable star performers such as Gordon Amidon of the University of Michigan, Walt Orenstein of the Bill and Melinda Gates Foundation, and senior pharmaceutical industry executive Gordon Muirhead of GSK. How is the meeting planned though? Well there are actually 10 CRS volunteer stakeholder groups who contribute to the programme—yes, 10—have a look at the organisational diagram above. The outputs of all of these groups are coordinated by the Programme Committee who in turn work within a budget framework set by the CRS Board of Directors. The CRS Finance Committee recommends and oversees the budget, forecasts, and balance sheets. Finally the nuts and bolts of the meeting are delivered by CRS full time staff—a core group of about five individuals. Which brings me to the point of this piece. If you have topic and speaker ideas that you would like to feed into these groups, simply email the contacts on the Annual Meeting Programming section of our website (www.controlledrelease.org). They would love to hear from you as we set about planning for 2012.

Planning the programme begins a whopping 15 months before the due date with a brainstorming session of the Programme Committee. There is a lot of coffee, doughnuts, and questions. What is likely to be topical in 15 months' time? What areas are scientists really concerned about when it comes to the desire to make a breakthrough? Who has actually broken through? Who has an interesting story to tell about their life's work? The list goes on. A whole day of tossing ideas in, throwing ideas out, re-adopting the discarded and finally writing the precious few down on a flip chart ensues. The end result is a much redrafted bullet point description of the forthcoming year's theme, a list of hot topics and finally a marketing tag line reflecting the vision for the Annual Meeting. This year the marketing tag line is "Innovative and Low Cost Health and Consumer Products". The pharmaceutical sciences are moving away from the blockbuster (at any cost imaginable) model and towards niche, and sometimes custom, products for diseases with impact. Innovation with an eye on the bottom line is the new paradigm. The same is broadly true for consumer products.

Next comes the hard part; who are the hottest scientists around? Who just invented something new? Who turned conventional thinking on its head? What is that new science that everyone is talking about? There is a list of names, fresh new names every year, engaging speakers with a good story. Oh, this bit takes a long time! Once the topics are agreed, the Programme Committee spends the next few months securing the speakers' agreement to participate and many telephone calls, emails and deliberate encounters later, a skeletal Annual Meeting Programme is born. A final Programme Committee meeting is held to organise the valuable contributed science into coherent sub-themes that deliver on the original vision for the year's meeting. At the end of the process, the Programme Committee is rewarded, not in dollars, but with the warm gratitude of its members and of course a wooden commemorative plaque! In essence what begins with a few hard working scientists and a few thoughts and tentative ideas matures over a 15 month gestation period into a programme that consistently receives an over 90% approval rating from you.



Changes for this year come in the form of daily panel discussions, an interactive two day within-meeting workshop on the regulatory requirements of paediatric dosage forms and a discussion on how to get drugs into the skin—shall we get physical or chemical?

Well don't just sit there—get involved by coming along to Washington next summer, and if you see the Programme Chairs Mark Prausnitz, Dody Reimer, Arzu Selen, Jamileh Lakkis, Marilyn Martinez or Ron Versic in the Exhibit Hall, do stop by and shake their hands. They have done a wonderful job. ■

See These Exhibitors at the 38th CRS Annual Meeting & Exposition

July 30 – August 3, 2011 • National Harbor, Maryland, U.S.A.

Exhibiting companies that have reserved space at the 38th Annual Meeting & Exposition of the Controlled Release Society, as of press time, are listed below. For ongoing updates, visit www.controlledreleasesociety.org/meeting/exhibitors/currentExhibitors.cfm.

3M Drug Delivery Systems
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Agere Pharmaceuticals
Analytical Solutions, Inc.
Asahi Kasei Chemicals Corp.
Ashland Aqualon Functional Ingredients
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Thank you.

Your donation will build the endowment, supporting the creation of a portfolio of fellowships and programs. The next award will be the **Tsuneji Nagai Postdoctoral Fellowship**.

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On behalf of the CRS Foundation, thank you for your support.

CRS Foundation Announces Tsuneji Nagai Postdoctoral Fellowship for 2011

On behalf of the CRS Foundation, it is our pleasure and honor to announce the Tsuneji Nagai Postdoctoral Fellowship. We invite you to be part of its development.

Tsuneji Nagai

To Honor Professor Nagai

The prestigious fellowship will be awarded to an outstanding postdoctoral scientist, and will honor Professor Nagai whose work in bioavailability studies and controlled drug delivery formulations has contributed greatly to the pharmaceutical science of Japan, Asia, and the world. Professor Nagai's distinguished career includes leadership positions at Hoshi University, service on multiple boards including the CRS presidency, and a body of work that includes three ethical drug products, more than 60 patents, and more than 500 refereed published research papers, resulting in multiple prestigious awards. Beyond measure, he has also influenced students and colleagues whose work continues to significantly impact our science. We look forward to Professor Nagai personally awarding the fellowship in July.

To Cultivate Future Leaders

Founded in 2007, the CRS Foundation's mission is to identify and acknowledge the future leaders of the Controlled Release Society (CRS) while honoring individuals who have made notable contributions to the Society and delivery technologies. Through recognition and financial support, the CRS Foundation's goal is to accelerate these postdoctoral fellows in their careers in delivery science and to find a welcome place for them within the CRS community.

About the Fellowship

The Tsuneji Nagai Postdoctoral Fellowship is open to candidates from academia, government, and industry who have completed their postdoctoral research by July of 2011. Full fellowship application and selection criteria as well as important dates are on the CRS Foundation's webpage. The chosen fellowship recipient will:

- Receive a one-year, $30,000 fellowship
- Receive a complimentary registration to the 38th CRS Annual Meeting & Exposition in National Harbor, Maryland, July 30–August 3, 2011
- Participate with an abstract and poster in the 2011 CRS Annual Meeting Poster Session
- Serve as a speaker at the 2012 CRS Annual Meeting to present outcomes of the research

Join in the Fellowship's Development

- Encourage the best and brightest postdoctoral candidates to apply
- Spread the news among your colleagues
- Contribute to the CRS Foundation Endowment
- Invite your organization to match your contribution and/or make a significant contribution from its foundation.

Thank you for helping the CRS Foundation create the Professor Nagai Postdoctoral Fellowship to support the future leaders in delivery science.

CRS Foundation Board of Directors

Susan Cady, Chair • Richard Guy • Robert Langer • Randall Mrsny • Kinam Park • Arthur Tipton ■

CRS Foundation Fellowships

Joseph R. Robinson Postdoctoral Fellowship 2009

David Nhu Nguyen

2009–2010 fellowship in Dr. David Lewis's laboratory at Stanford University School of Medicine.

Jorge Heller Postdoctoral Fellowship 2010

Qun Wang

2010–2011 fellowship in the laboratories of Prof. Robert Langer at MIT and Prof. Jeffrey Karp at Harvard Medical School.

Tsuneji Nagai Postdoctoral Fellowship 2011

Selection in June 2011, award in July

Macrophages Recognize the Size and Shape of Their Prey

*Nishit Doshi, Samir Mitragotri**
Department of Chemical Engineering, University of California, Santa Barbara, CA 93106

Introduction

The mononuclear phagocytic system (MPS) that mainly comprises macrophages plays a central role in defense against pathogens, cellular debris and other foreign entities. Recognition of the target by macrophages is a key process in generating the immune response. Identifying the different recognition mechanisms has therefore been a subject of great interest for several decades. Previous studies have mainly focused on target recognition through surface receptors present on the macrophage surface (1). Here, using polymeric particles of different geometries, the importance of target geometry in recognition was investigated.

The shape of therapeutic carriers has received significant attention in recent years in various biological processes (2). Hence, it is important to delineate the interactions of these novel carriers with the MPS. Moreover, bacteria exhibit extensive diversity in geometry, which may play a role in their interactions with the immune system. Although various biological mechanisms by which macrophage recognize bacteria have been reported in the literature (3), the importance of bacteria shape in MPS recognition has not received any significant attention.

In order to investigate the importance of target shape in interactions with the MPS, we fabricated polymeric particles of different geometries that are representative of the size and shape range of typical therapeutic carriers and bacteria. The attachment of these polymeric particles to the macrophage surface was studied since it is the first step in target recognition.

Results and Discussion

Spheres, rods and oblate ellipsoids (m&m shaped) of different geometries were used for this study (Figure 1). Rod and oblate ellipsoidal shaped particles were fabricated using the film stretching method (4). These particles together form a panel of representative shapes and sizes to study the effect of geometry on attachment to macrophages. The surface of the particles was coated with mouse IgG to mimic opsonization. Opsonization is the process in which foreign entities get coated with antibodies within the body to facilitate attachment to the macrophages and subsequent clearance. Particles were incubated with macrophages at 4°C to allow attachment and avoid internalization of particles. Particles of different geometries exhibited significantly different attachment propensity to the macrophage surface (Figure 2).

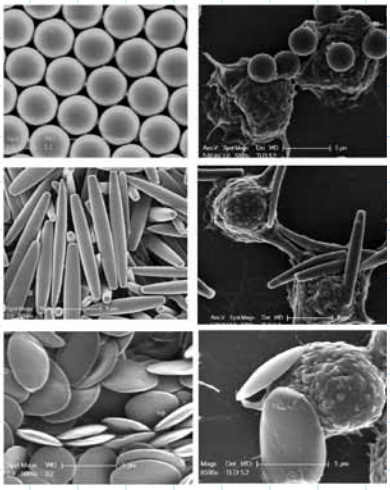

Figure 1. *SEM micrographs of spheres, rods, oblate ellipsoids (left panel) and attachment of these particles to the macrophage surface (right panel).*

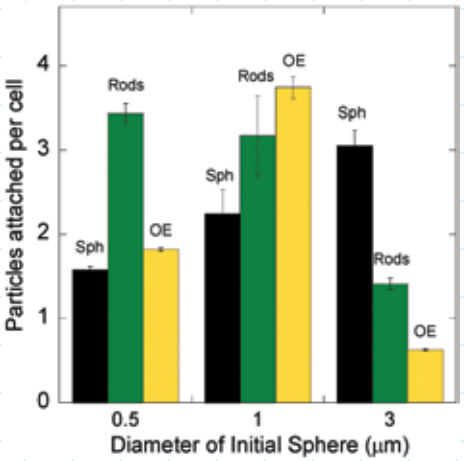

Figure 2. *Attachment propensity of particles of different geometry (Number of particles attached per cell).*

When the attachment propensity was plotted against the longest particle dimension, it showed a peak at 2–3 μm. The distance between the ruffles present on the macrophages surface is also of the same order (5). In order to test whether membrane ruffles have a role to play in particle attachment, the characteristic features on the mouse macrophage surface were eliminated by osmotic swelling of the cells. The attachment propensity indeed decreased drastically after osmotic swelling, especially for particles with longest dimension of 2–4 μm, which supports the hypothesis of ruffle-mediated shape recognition (Figure 3a). Particle and particle orientations that can fit well between the two membrane ruffles will exhibit stronger binding due to higher number of contact points with the macrophage (Figure 3b).

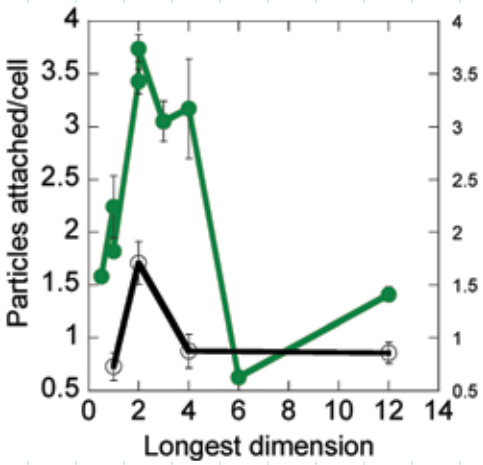

Figure 3. *(a) Attachment propensity of particles of different geometry as a function of largest particle dimension (green line). Effect of osmotic swelling on attachment (black line). (b) Particles of different geometry (green) fitting into the macrophage ruffles (black).*

There was a striking correlation between the geometry of

polymeric particles that exhibit the highest attachment tendency to the percentage of bacteria that possess similar geometric dimensions, which suggests the biological significance of the shape recognition properties of macrophages (Figure 4).

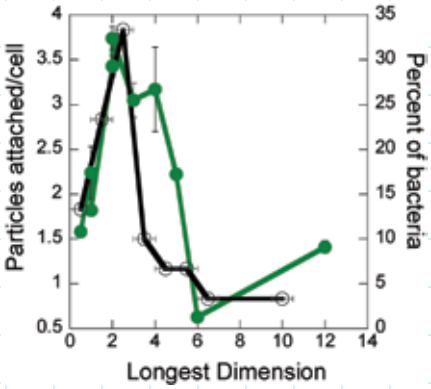

Figure 4. *Comparison of the attachment propensities of particles to macrophages with the size distribution of bacteria. Green line represents number of particles attached per cell plotted as a function of the longest particle dimension whereas the black line represents the percentage of bacterial population plotted as a function of the longest bacterial dimension.*

Given the strong patterns in size and shape of pathogens, development of capabilities to recognize pathogens based on physical features, in addition to surface biomolecules, perhaps represents an evolutionary step that the macrophages utilize in fighting bacterial infections.

This study not only provides an insight into the ability of macrophages to recognize target shapes, but also outlines the rules of thumb that will assist in the design of drug delivery carriers.

Conclusions

Using polymeric particles of different geometries, it was demonstrated that target geometry plays an important role in attachment to the macrophage surface. This can have wide implications on design of drug delivery carriers and on fundamental understanding of target elimination mechanisms used by macrophages.

Acknowledgements

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Nishit Doshi is a research scientist working at University of California Santa Barbara (UCSB) with Prof. Mitragotri. He received his Ph.D. from UCSB in 2010. His research interests include fabrication and characterization of novel carriers for drug delivery and diagnostic applications. He also actively works on developing synthetic mimics of natural blood cells for artificial blood and other biomedical applications (For more details visit http://drugdelivery.engr.ucsb.edu/Nishit%20Doshi.html).

Samir Mitragotri is a professor of chemical engineering and Director of the Center for Bioengineering at the University of California, Santa Barbara. He received his Ph.D. in chemical engineering from the Massachusetts Institute of Technology. His research interests include the development of novel methods of drug delivery including transdermal, oral, and particle-based methods. His honors include Ebert Prize, Technology Review Young Innovator award, Allan P. Colburn award and elected fellow of AIMBE. He is a member of the editorial boards of several journals and has authored over 125 publications and is an inventor of over 60 issued or pending patents.

Welcome New CRS Members

Natalie A. Akagi
Dennis Behreandt
Paul Buscemi
William B. Caldwell
Markus Hartmann
Mingguang Li
Ana Lucia Gomes Santos
Philip L. Smith
Shahid Uddin
Xiao Yu

CRS Delivering Bioactives

Putting the "i" in Veterinary

Arlene McDowell, Co-Chair, CRS Veterinary Committee

It seems that 2010 was the year of the letter "i." We had the launch by Apple of the iPad and iPhone 4 and also the story of ITAPs (Intraosseous Transcutaneous Amputation Prosthetics) made famous by Oscar, the world's first bionic cat and Noel Fitzpatrick, the veterinary surgeon who fitted the implants (http://www.bbc.co.uk/news/10404251). Oscar's story is a nice example of collaboration between a vet and a professor of biomedical engineering at Salford University to find an innovative way to solve a problem for an animal. With these "i" stories in mind, I was inspired to share with you some of what I did in 2010.

In November I was fortunate enough to be able to travel to America to attend the Globalization of Pharmaceutics Education Network (GPEN) conference in Chapel Hill, North Carolina. This was a great event organised by postgraduate students and postdocs and included some very high quality science and presentations. A highlight of my trip was a visit to the North Carolina University College of Veterinary Medicine. Here I met with Professor Mark Papich. Mark was kind enough to spend the time with me to show me around the college and discuss his research on the pharmacokinetics of a range of drugs in a even greater range of animal species. What a great resource to have a veterinary hospital, with as many blood samples as you need, right across the hall from your lab!

I also had the pleasure of spending an afternoon with Dr Gigi Davidson who is the Director of Clinical Pharmacy Services at North Carolina University Veterinary Teaching Hospital. The Veterinary Teaching Hospital has both a large (specializing in horses) and small (primarily cats and dogs) animal hospital as well as a pharmacy and clinical diagnostic laboratories. Gigi was infectiously enthusiastic about her work and I found it fascinating to see first hand the specialist compounding that is done for the range of species treated at the hospital.

A monument in bronze to cat and dog companions outside the Veterinary Teaching Hospital at North Carolina University.

I was also able to attend the 2010 FIP PSWC/AAPS conference in New Orleans. Of particular interest to me was attending the AAPS pre-conference workshop entitled "Veterinary Pharmaceuticals: Contemporary Challenges and Advances Impacting the Development of Veterinary Pharmaceuticals." The workshop was over two days and was a series of very high quality presentations with a strong regulatory focus. A main theme of the workshop was the globalization and harmonization of animal health and so this topic was developed by many of the speakers during their presentations. Colleagues very familiar to us within the CRS also presented at the workshop including Dr. Marilyn Martinez, who spoke on bioequivalence testing for animal health products, and Dr. Susan Cady, who discussed the challenges of bringing new animal health products to the market. Other interesting talks were given by Dr. Hans Coetzee (Kansas State University) on his work on studies to investigate analytical methods for Substance P and pain perception in cattle, Dr. Butch KuKanich (Kansas State University) in pharmacogenetics on animal drug development, and a talk on interspecies differences in P450 metabolism by Dr. Leposava Antonovic.

AAPS also has a veterinary group, the Animal Pharmaceutics and Technology Focus Group, that has similar interests to our group within CRS. I attended their focus group meeting and the desire to expand their group interested in animal health was also a theme for our colleagues within AAPS.

Planning is well underway for the vet program for the 2011 CRS Conference in Maryland, USA. Our Programme Chairs are Drs. Ramesh Panchagnula (Pfizer Pharmaceutical, India) and Marilyn Martinez (FDA Centre for Vet Medicine, USA) and they will be lining up some great speakers as part of the programme as well as some social activities. The conference dates are July 30 to August 3, 2011. Abstract deadline is January 27, 2011. Mark these dates in your calendar and I encourage you to make the effort to visit a colleague at another institution at the same time as your trip to the conference. Nothing beats face-to-face meetings and you can learn so much by seeing things firsthand.

Best wishes for a Happy New Year! ■

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CRS Staff Reorganization

The field of delivery science is rapidly advancing, offering many opportunities for our society and its members. In order to best support CRS and its goals during this growing period, a new staff structure has been put in place at CRS Headquarters.

Research was conducted to assess the structure that would best help CRS grow and offer strong value to its members. This new staffing structure will offer members more opportunities to advance professionally and gain new knowledge through a more robust portfolio of products and services.

As a result, a new CRS Executive Director, Susan Kohn, has started with the society. As a Certified Association Executive with a more than 15 years in association management, Susan brings considerable experience to the position. She has spent the past few months working closely with the Board and learning about CRS. In her new role, Susan is responsible for CRS program oversight and management, strategic plan execution, and committee relations. Her position is meant to be a "hub" for managing the various CRS activities undertaken by members and staff. Additional support will be provided by a strong customer and member services department, an experienced publishing and editorial department, and a larger marketing department.

If you have any questions or comments, please feel free to contact any of the key staff listed on this page. We are here to serve you and your feedback is always appreciated. ■

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Liquid-Fill Hard Capsule Technology to Enhance Colonic Drug Delivery

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Introduction
Liquid-fill hard capsule technology was established in the early 1980s as an alternative to soft gelatin capsules offering some specific advantages, e.g., lower moisture and gas transmission, use of high melting point excipients, plasticiser and preservative free, lower moisture content, and ease of coating.

Today liquid fill encapsulation can provide a valuable tool to enable drug developers to more rapidly progress clinical candidates. Simple liquid or thermo-setting formulations of actives can be developed, which are capable of accommodating batch to batch variations in API (particle size, shape, density and flow characteristics) and can scale easily from bench, with no minimum batch size, to high speed machines and batches of millions of unit doses.

Liquid-fill hard capsule technology also provides a vast range of oral drug delivery opportunities for:

i) Absorption enhancement, e.g., stabilised liquid suspensions and solid dispersion (for nano-sized and amorphous materials) SMEDDS & SEDDS (Self (Micro) Emulsifying Drug Delivery Systems)
ii) High-potency, removing product uniformity concerns by using solutions; with the added advantage of no dust generation, removing the need for expensive engineering controls.
iii) Controlled release; utilising formulation and coating technologies to produce controlled, targeted (e.g., ENCODE™) or multi-phase (e.g., DuoCap™) release.

They are also aesthetically suitable for OTC use.

Colonic delivery can be achieved from hard capsules by the use of coating technologies; such as Evoniks' EUDRAGIT® S grades, which rely on pH, or Encaps' licensed Phloral™, which utilises pH and colonic microbiota. One of the drawbacks to colonic delivery is the relatively low amount of water that is available for dissolution of dosage forms in this part of the gastrointestinal tract and the lack of mobility to assist in the breakup of solid dosage forms within this region. As part of Encaps' colonic delivery programme, ENCODE™, the challenge was to produce a stable formulation that met these requirements to enhance colonic release. This work was presented as a poster at CRS 2010 under the title "The Utilisation of Self Emulsifying Formulations to Enhance Colonic Drug Delivery."

Liquid lipids are an excellent base for stable formulations and easily resolve the mobility problems; however, formulations of

lipids commonly rely on digestion or partition to release the active material and these mechanism may not function within the colon.

By utilisation of self emulsifying technology and carefully selecting a lipid within which the active material is insoluble, it is possible to disperse the active ingredient rapidly.

A large number of pseudoternary phase diagrams were generated for SEDDS and SMEDDS work. These were examined to select appropriate formulation combinations, which would form an emulsion in a low aqueous environment. A dissolution model was then used to determine if the quantity of surfactants, suggested by the phase diagrams, was sufficient to disperse an active material, without requiring digestion or partition for release. Each formulation was also assessed to ensure it remained fluid.

Results and Discussion
Many formulation combinations tested as part of the SEDDS and SMEDDS trials did not disperse a model active when tested in the dissolution method, figure 1.

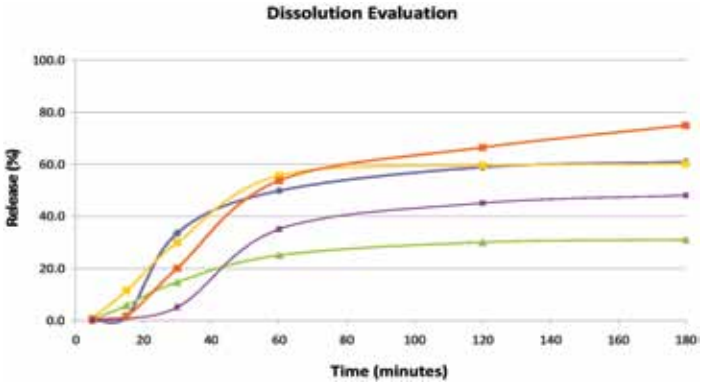

Figure 1. *Dissolution comparison of varying formulations of lipid and surfactants.*

Spotlight continued on page 14

Spotlight continued from page 13

Of those that proved successful, Miglyol 812 was selected as the oily lipid used for formulation. It is a caprylic/capric triglyceride and is a stable oily liquid with a low viscosity and has low potential to oxidation. As a surfactant; Gelucire 44/14 is a self emulsifying semi-solid commonly used as a bioavailability enhancer. It is a lauroyl macrogolglycerides (polyoxylglycerides), which is a waxy solid and would, on its own, consequently prove difficult to disperse in the low aqueous colonic environment.

A phase diagram of the Miglyol 812 and Gelucire 44/14, figure 2, was generated by titration of prepared mixtures at fixed ratios with water.

This phase diagram demonstrates that the mixture produces an emulsion at a relatively low water ratio. The combined mixture converts from a thin liquid to a paste over the range of 100% Miglyol to 50% Miglyol in Gelucire. The diagram suggests that in this concentration range a suitable Gelucire concentration could be found to emulsify Miglyol and still maintain the mixture as a mobile liquid.

Using a water soluble model drug substance at 25% w/w loading, capsules were prepared at formulation ratios corresponding to the coloured lines on the phase diagram: 100% Miglyol (red), 90% Miglyol / 10% Gelucire (blue), 25% Miglyol / 75% Gelucire (pink) and 50% Miglyol / 50% Gelucire (green).

The results of the dissolutions, figure 3, demonstrate that Miglyol 812 without Gelucire does retard the release of the model drug substance. With inclusion of 10%, 25% and 50% Gelucire, the release is no longer retarded and even though the emulsion for 10% Gelucire is transient, this is sufficient to allow

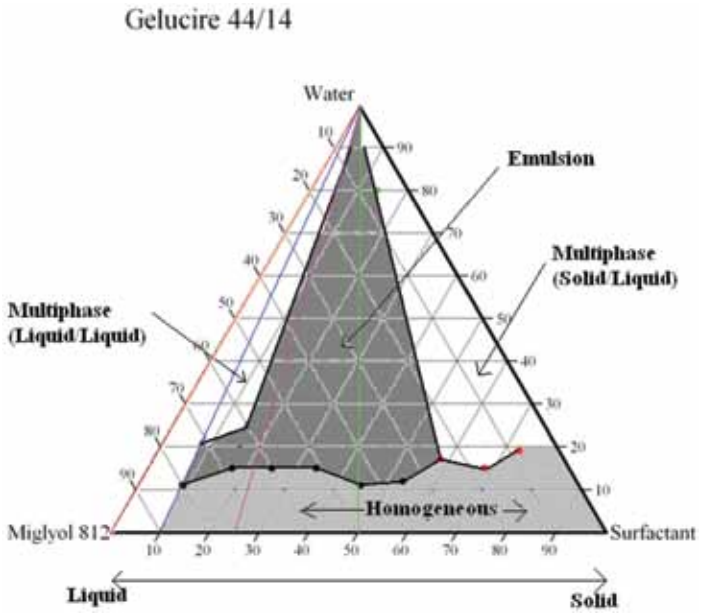

Figure 2. *Tertiary phase diagram for Gelucire 44/14, Miglyol 812 and water. 100% Miglyol (red), 90% Miglyol / 10% Gelucire (blue), 25% Miglyol / 75%Gelucire (pink), 50% Miglyol / 50% Gelucire (green).*

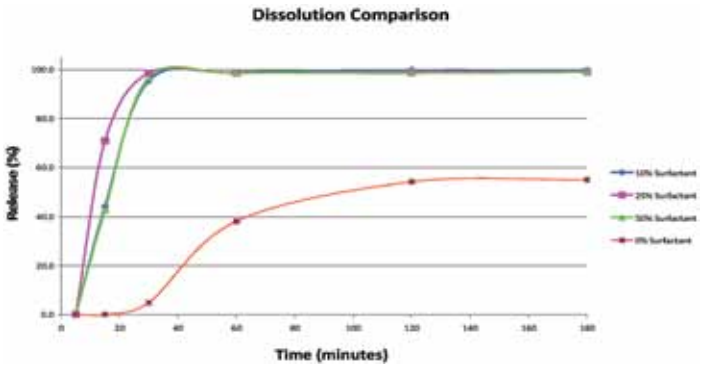

Figure 3. *Dissolution comparison of formulations at selected Gelucire and Miglyol ratios. 100% Miglyol (red), 90% Miglyol / 10% Gelucire (blue), 25% Miglyol / 75%Gelucire (pink), 50% Miglyol / 50% Gelucire (green).*

rapid dispersal of the drug substance.

Conclusion

These results clearly illustrate the potential of the Miglyol and Gelucire formulation to enhance the release behaviour of the active for colonic delivery.

The dissolution demonstrates that the 10% Gelucire formulation is sufficient to disperse the active material. The phase diagram supports that this formulation will form an emulsion in a low aqueous environment. This formulation also has a high degree of fluidity and therefore includes all the properties that are required to maximise potential for colonic delivery.

This data represents a single formulation approach, of many available, which demonstrates the potential of liquid fill hard capsules in the enhancement of colonic delivery.

Clearly the use of formulations that can stabilise sensitive molecules, deliver flowing liquids and yet still provide release and dispersion by the utilisation of self emulsification offers great potential in the growing use of colonic delivery.

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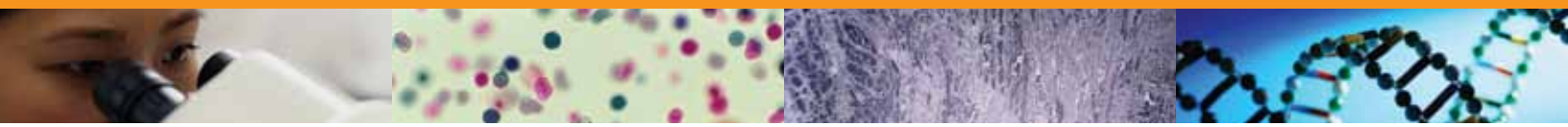

Encapsulated Toxins—A Trojan Horse Approach to the Control of Zebra Mussels

G.D. Moggridge
Department of Chemical Engineering and Biotechnology, University of Cambridge

Zebra mussels are freshwater molluscs (up to 4 cm long) native to the Caspian and Black Sea region, which have invaded North America and Europe. Uniquely for fresh water species, zebra mussels attach with byssus threads, or 'beards,' to hard substrates and are renowned as one of the world's most destructive invasive species.

The water supply and power generation industries are vulnerable to zebra mussels blocking intake pipes for water works or cooling water systems. The US military estimated in 1994 that lost revenue due to zebra mussels was two to three billion dollars per year in the United States alone. Zebra mussels also displace and kill many native species.

The Current Control Strategy

By far the most popular control strategy is chlorination. Mussels will close when water is chlorinated and can survive for three weeks in this state, so chlorination must be continuous for this period. Chlorine reacts with organic matter in water to produce carcinogens. For this reason chlorination is being phased out upstream of British water works, and is undesirable and expensive in any raw water system, especially where the treated water passes into the open environment.

The BioBullet

Zebra mussels are filter feeders, circulating water through their shells via two siphons. The larger, inhalant siphon sucks water into the mussel. Food particles of five to 200 microns are filtered over the gills and waste water and any rejected particles expelled via the smaller, exhalant siphon.

The BioBullet exploits the efficiency of zebra mussels as filter feeders. The mussels will filter out and concentrate poisons if they are disguised as food particles, by encapsulation in a waterproof and nutritious coating.

The BioBullet combines rapid killing of zebra mussels with minimum environmental damage. By using encapsulated particles instead of bulk molluscicides, the total quantity of toxin entering the water stream is greatly reduced.

The BioBullet (see Figure 1) is like a miniature, lethal Malteser!

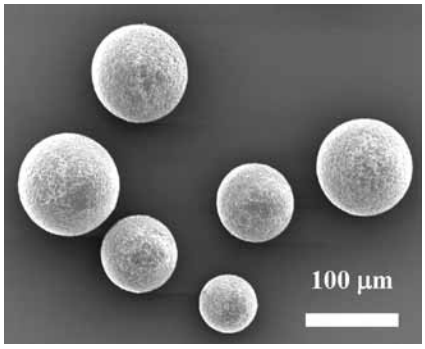

Figure 1. *SEM of BioBullets, consisting of a toxic core encapsulated in an edible and waterproof coating.*

In order to demonstrate the effectiveness of BioBullets, we have done two types of study on a prototype, using KCl as the toxic ingredient (1). First, we used endoscopy to observe individual zebra mussels feeding on the BioBullets (see Figure 2). Second, we have done trials at an infested waterworks. Here, we have specially constructed an array of pipes in which we have grown zebra mussels. We then treat the pipes with either our BioBullets or the same amount of toxin dissolved in the water. We test over 5,000 mussels at once. Figure 3 shows that the BioBullet is massively more effective than the same amount of chemical used directly.

Consumer and Diversified Products continued on page 16

Consumer and Diversified Products continued from page 15

Our new technology offers the possibility of clearing invasive zebra mussels from the pipework of water works and power stations, economically and with greatly reduced environmental damage. In recent years, we have developed the BioBullet concept, encapsulating two new toxins, and conducted a full scale, and highly successful, trial at a UK waterworks.

Since the proof of principle of the effectiveness of the BioBullet (1), the main research goal has been to develop more efficient and environmentally friendly products and means to apply them. Innovative application strategies and delivery methods for existing biocides rather than new toxins have been sought. Three concepts have been explored: (i) optimisation of encapsulation; (ii) combination of toxins; (iii) investigation of the seasonal variation of the species' tolerance to toxins. The unifying idea behind these three distinct approaches is "to define what to apply, how to apply it and when to apply it."

Optimisation of Encapsulation: Particle Size and Release Time

Particle size and toxic release time are both important variables in the effectiveness of BioBullets (2): if the particles are too large, they are rejected by the mussels; if they release their contents too quickly, they do so before being filtered from the water by the mussels. Ideally we would like particles of perhaps 20 µm (the typical size of an algae) and having a burst of release after perhaps an hour. Unfortunately the current manufacturing route, spray freezing, makes these two goals mutually exclusive: small particles release their contents too fast. Moreover, the manufacturing is not yet able to produce a well controlled burst of release, instead giving a gradual build up over a characteristic half-life. The present optimal compromise is particles of around 100 µm, with a half-life of toxic release around an hour. These particles are effective, much more effective than the toxin used alone, but there is certainly much room for improvement.

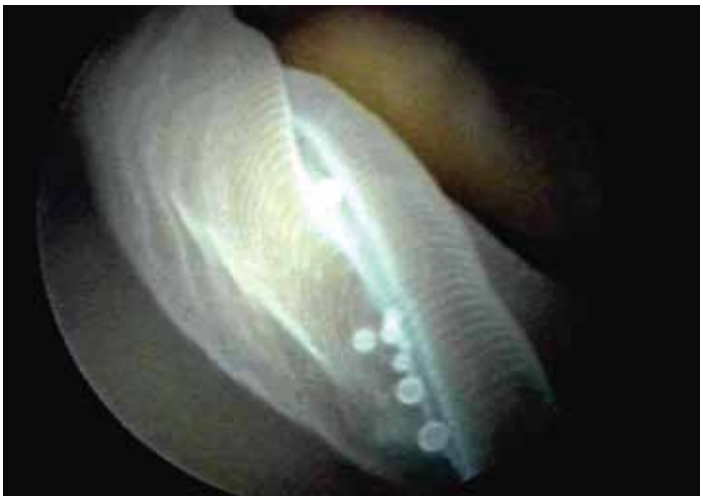

Figure 2. *Endoscopic photograph of BioBullets on the ctenidial gill of a live zebra mussel.*

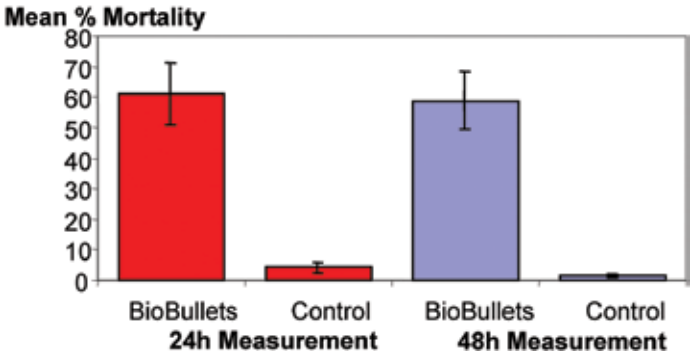

Figure 3. *Mortality of mussels caused by BioBullets versus a control of the same amount of toxin dissolved directly in the water. Experiments carried out on approximately 5,000 mussels at an infested waterworks.*

Combination of Toxins

The combination of toxins, with potentially cumulative and synergetic effects, is a promising approach to zebra mussel control. The toxicity of several combinations of potassium chloride and poly(diallyldimethyl ammonium chloride) (polyDADMAC) has been evaluated through laboratory bioassays (3). These toxins have been selected as model chemicals because they are each effective against zebra mussels and are licensed for application in UK drinking water treatment. In addition, potassium chloride has a paralytic effect on zebra mussels, and so seems promising for use in combined treatments since it could increase the exposure of mussels' soft tissues to other toxins. Adult zebra mussels were pretreated with potassium chloride for 12 hours and then exposed to mixtures for 30 days. The mortality in the test containers was monitored every 24 hours for the first 10 days and every 48 hours for the next 20 days. The contents of each container was renewed every 48 hours. The results (see Figure 4) showed that potassium chloride increases polyDADMAC toxicity for adult zebra mus-

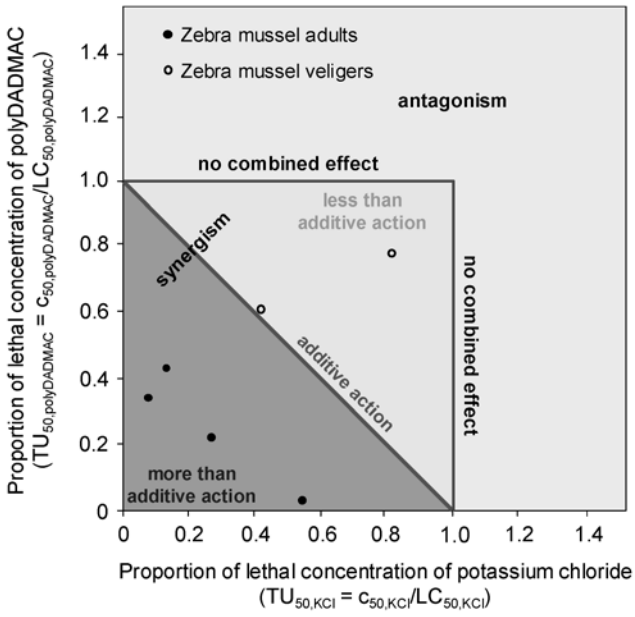

Figure 4. *Isobologram showing the sensitivity of zebra mussels to the joint effect of polyDADMAC and potassium chloride at a lethal response level of 5%. The circles show experimental data and the lines reference joint actions.*

sels but, interestingly, not for mussel veligers. This difference in joint action must the consequence of differences in feeding or other behaviour between adult mussels and larvae. Other results show, unsurprisingly, that the synergistic effects of the two toxins are maximised when both are used at moderate concentration. We have also found that some other combinations of toxins do not have synergistic effects on either veligers or adult mussels. There is clear potential in the use of combinations of toxins for the control of zebra mussels, but each combination and the appropriate concentrations must be assessed on a case by case basis for the desired application. It is unlikely that any general rules for the synergistic application of toxins can be found.

These results have potentially important practical consequences because when used synergistically, the combination of toxins found to be effective are both individually below the regulatory limits for UK drinking water.

Seasonal Variation of Tolerances to Toxins

The identification of a seasonal peak of increased susceptibility of zebra mussels to toxins is an appealing route to improved application strategies, generally applicable for existing toxins. Little previous work has been done on this and literature suggestions for peaks of sensitivity to toxins include June, the summer and autumn.

The annual profile of mussels' tolerance was recorded using static bioassays, conducted using three reference toxins with different biological mechanisms. The seasonal profiles of mussels' physical condition (expressed as the dry tissue weight of a standard mussel of 25 mm shell length) and filtration rate were also recorded. The annual cycle of water temperature was mimicked in the study, and so this effect on the mussels' response was taken into account. Freshly collected mussels were used in all experiments, thus including the effect of the seasonal profile of metabolic demands in the experiment.

The results (Figure 5) showed significant variation of the sensitivity of mussels to toxins over the year: it was highest in June/July. This peak of susceptibility coincides with low physical condition (monitored as dry weight) and high filtration rates and water temperature. High water temperature is expected to enhance chemicals' toxicity by raising their reactivity and promoting uptake. Higher filtration rates will enhance the exposure of the mussels' soft tissues to toxins.

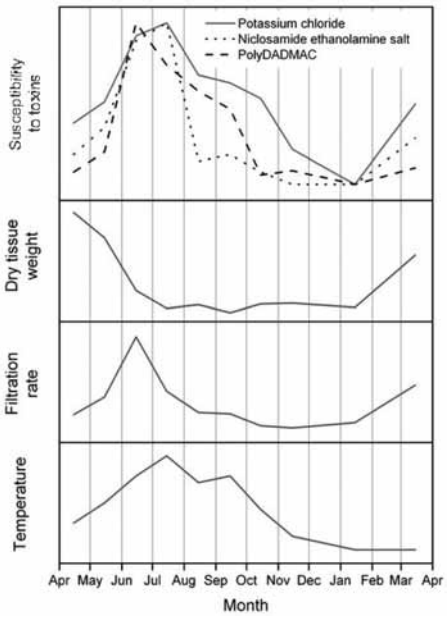

Figure 5. *The seasonal variation of the susceptibility of zebra mussels to three toxins. Water temperature, average mussel dry weight, and filtration rate are also shown for the same annual cycle.*

The outcome of this study has practical implications for designing protocols for toxicological studies on zebra mussels, the design and timing of control treatments, and water quality management.

Conclusion

This paper summarises the proof of principle of using encapsulated toxins for the control of zebra mussels and significant subsequent discoveries aimed at improved solutions for zebra mussel control. Three different approaches have been examined in order to design innovative application strategies for existing toxins. The development of encapsulated toxins requires a careful choice of materials and processing techniques in order to develop effective particles. The goals of slow release and small particle size are contradictory given current manufacturing techniques and the current optimum represents a compromise with much room for improvement. The combination of toxins to achieve a synergistic effect has been shown to be feasible in one combination of potentially significant compounds. The method should have more general applicability, but each pair of toxins needs to be individually tested and optimal doses determined. It is interesting that different stages of the mussel's lifecycle show differing responses to combinations of toxins. The identification of the seasonal peak of susceptibility to toxins is a consequence of the mussels' condition, filtration rate and the water temperature; thus, it can be expected to be generally applicable to any control strategy based on toxins.

Each of the approaches summarised has its own benefits and problems. However, one significant advantage is that the three approaches are not mutually exclusive and can be integrated in a single control strategy. For example, it should be possible to produce particles of improved size and release time, which release multiple, synergistic toxins, and which could be dosed at a time of the year when the mussels are at their most vulnerable.

In conclusion, the three strategies outlined may each have an important impact on the future of zebra mussel control, particularly if used together.

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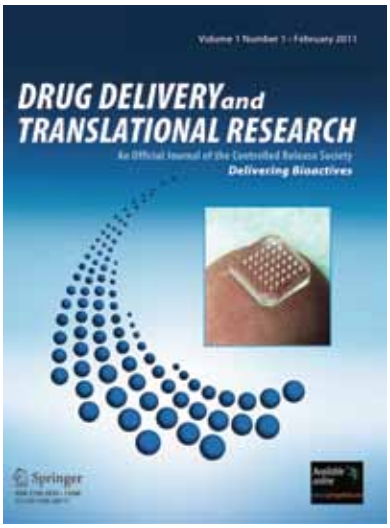
Inaugural Issue
Drug Delivery and Translational Research

An official journal of the Controlled Release Society

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



The Controlled Release Society (CRS) and the editorial team of the journal are proud to announce publication of the inaugural issue of *Drug Delivery and Translational Research* (*DDTR*). The new journal's aim is to provide a unique forum for scientific publication of high-quality research that is exclusively focused on translational aspects of drug delivery.

As rightly stated in the preface by Diane Burgess and Mark Tracy, past and current presidents of the CRS, *DDTR* represents an important milestone in the growth of the CRS as we continue to create new vehicles to bring controlled release and, more generally, delivery science and technology to our members and the world. We anticipate that *DDTR* will foster multidisciplinary collaborative efforts and thinking that could move research and discoveries from bench to bedside through technological innovation. Daniel Kohane and Robert Langer also echo this sentiment. As they point out in their preface, new drug delivery systems are constantly being designed and developed for numerous applications, encompassing a very broad cross-section of the sciences and medicine. One example of such an innovation in drug delivery technology is a microneedle patch for vaccination, as shown on the cover and described by Yeu-Chun Kim and Mark Prausnitz in this first issue of *DDTR*. The successful development of such a system could have a global impact on health care and on the lives of people worldwide.

Modern therapeutic agents, particularly protein- and nucleic acid-based drugs, require the development of specialized delivery systems to maximize their therapeutic efficacy. For example, the potential of small interfering RNA (siRNA) for therapeutic applications cannot be fully explored without an effective delivery system. In their research article in this issue of *DDTR*, Tamara Minko's group shows the efficacy of siRNA and antisense oligonucleotides against hypoxic damage, a critical issue in many pathological conditions. The field of siRNA delivery is relatively new, and hence there is a continuing effort to improve efficacy through drug delivery technology. Vladimir Torchilin's group describes a system based on phospholipid-polyethylenimine conjugate-based micelle-like nanoparticles for siRNA delivery.

Nanomedicine, which explores medical applications of nanotechnology, is poised to make a significant impact on drug therapy. This is evident from the steady stream of nanotechnology-based pharmaceutical products entering the market and from several ongoing clinical studies. In this issue of *DDTR*, Mark Saltzman's team describes a convection-enhanced delivery of camptothecin-loaded polymer nanoparticles for treatment of intracranial tumors. Malignant glioma is a devastating disease with a median survival of approximately 15 months from time of diagnosis. There are several challenges for effective drug delivery to the tumor, and this new method could potentially resolve the issue. The Labhasetwar laboratory reports sustained p53 gene expression using biodegradable nanoparticles in a prostate cancer model. The p53 tumor suppressor gene, the most commonly altered gene in human cancer, plays a central role in regulating cell-cycle progression, senescence, differentiation, DNA repair, and apoptosis. Elka Touitou's laboratory has developed a new formulation that facilitates delivery of an anticancer drug into the deep layers of the skin for the treatment of skin cancers. This is an important issue as the incidence of skin cancers has been on rise in recent past. Liposomes have been extensively investigated for drug delivery applications. Massimo Fresta's group has developed an innovative multicompartmental formulation of liposomes that can deliver two anticancer drugs simultaneously. They have demonstrated that such a formulation has better anticancer efficacy than the one carrying only a single drug.

Treating diseases affecting the posterior segment of the eye, such as choroidal neovascularization-associated age-related macular degeneration, diabetic macular edema, and proliferative diabetic retinopathy—all leading causes of blindness—is a challenging task because of drug delivery issues. In this issue of *DDTR*, Uday Kompella's group reports work on investigating microparticles to effectively deliver drugs to the posterior of the eye. Cell transplantation has potential application in regenerative medicine. Numerous strategies to induce tissue regeneration employ scaffolds to create space and present biological cues that promote development. Lonnie Shea's group describes results with microporous scaffolds filled with hydrogels to deliver lentivirus to support cell adhesion.

Many disease conditions could potentially be treated with effective drug delivery systems. *DDTR* thus can serve as a focal point for publication of drug delivery research that could have a direct impact on clinical outcomes in the relatively near term. To

that effect, the articles published in this inaugural issue reflect the main theme of the journal.
We welcome the interest of our colleagues in this growing and promising multidisciplinary field and encourage all investigators to consider submitting their clinically relevant data to *DDTR* (http://www.editorialmanager.com/ddtr/).

Because of the significance of drug delivery research to many CRS members, *DDTR* will be available online to CRS members as a benefit of membership. To view articles, CRS members need only log in to the CRS website (http://www.controlledrelease.org/), select the tab "Journal Access," then click the link to the *DDTR* home page.

Announcing the *DDTR* Outstanding Paper Award

We are pleased to announce that the CRS and Springer Science + Business Media have also established the *DDTR* Outstanding Paper Award to recognize outstanding research published in *DDTR*. A selection committee will be established to evaluate all research papers published in *DDTR* within a calendar year and to recommend the award recipient. The first award will be presented at the 2012 CRS Annual Meeting, and the recipient will also give an award-based presentation highlighting the winning research paper.

Important Dates

CRS Annual Meeting & Exposition
July 30 – August 3, 2011
Gaylord National Hotel & Convention Center
National Harbor, Maryland, U.S.A.

February 25
Housing Opens*

March 15
Advance Registration Opens*

May 2
Advance Registration Deadline
Registration fees increase after this date!

May 9
Exhibits reserved for listing in
CRS Annual Meeting program book

Many prime sponsorship opportunities are still available.
Contact Debby Woodard for best selection.
E-mail: dwoodard@scisoc.org,
Tel: +1.651.994.3917

**dates subject to change*

CRS-AAPS Workshop Offers an Outstanding Program

The Controlled Release Society and the American Association of Pharmaceutical Sciences cosponsored a workshop, Using Novel Methods (including Population Pharmacokinetics) to Support the Development of Clinically Relevant Product Specification on November 13, 2010 in New Orleans, LA, just prior to the FIP Pharmaceutical Sciences World Congress 2010 that was held in association with the AAPS Annual Meeting.

Marilyn Martinez, FDA Center for Vet Medicine, organized an outstanding program that focused on developing a QTPP through PK/PD modeling and simulation approaches that will enable linking CQAs to clinical outcome. Through the integration of population PK/PD models established on the basis of clinical trial data, this integrative approach could ensure the establishment of *in vitro* drug dissolution/release methods that link to the desired *in vivo* product performance, thereby providing dissolution/release criteria that are consistently informative and clinically relevant.

Topics included: "Quality by design: impact on drug development and its global applications," by Terrance Ocheltree, Food and Drug Administration; "Design space and product specifications: a risk assessment approach," by Raafat Fahmy, Food and Drug Administration; "Quality product target profile: integrating product *in vivo* performance in a patient population with product design," by Arzu Selen, Food and Drug Administration; "Development of oral drug delivery platforms based upon patient GI characteristics," by Kevin Johnson, Intellipharm LLC and John Crison, Bristol-Myers Squibb; "A nonlinear mixed effects IVIVC model for multi-release drug delivery systems," by Adrian Dunne, Johnson & Johnson and University of College Dublin; "The use of therapeutic drug monitoring to identify the relationships between optimized dosing strategies (input function) versus patient characteristics (covariates): using this information to develop a target for *in vivo* product release characteristics," by Roger Jelliffe, University of Southern California; "The development of mechanistic population pharmacokinetic models to support the development of targeted release characteristics from modified release dosage forms," by William Jusko, University at Buffalo; "The use of modeling and simulation to target dosing strategies and predict optimal *in vivo* product release characteristics in a pediatric population," by Jeffrey Barrett, Children's Hospital of Philadelphia; and finally, "Integrating patient *in vivo* performance characteristics into product design and specifications: a manufacturing perspective," by Maria Cruañes, Merck & Co.

CRS thanks the workshop's generous sponsors, AstraZeneca and Simulations Plus, Inc. ■

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The Australian and New Zealand Chapters of the Controlled Release Society (CRS) Joint Workshop on "*In Vitro* Drug Release and Dissolution Testing"

29–30 November 2010, Monash University, Australia
2–3 December, 2010, University of Auckland, New Zealand

Ali Seyfoddin (Ph.D. candidate)
NZCRS Postgraduate Representative, University of Auckland, Auckland, New Zealand

For the third year in a row, the Australian and New Zealand Chapters of CRS have held joint workshops, this year focussing on the theme "*In Vitro* Drug Release and Dissolution Testing." The workshops are held over two days at an Australian venue (this year in Melbourne at Monash Institute of Pharmaceutical Sciences) and two days in New Zealand (University of Auckland) between 29th November and 3rd December, 2010. The workshops are free for students to attend. Prof. Diane Burgess, past president of CRS, was our plenary speaker, kindly giving up her time to share her wisdom with both audiences in Australia and New Zealand.

The 2010 joint workshops were again a highly successful event with more than 50 delegates from both industry and academia attending at both venues. The workshop brought together scientists with expertise in pharmaceutical formulation and drug delivery. Both NZCRS and AUS-CRS have been trying hard to bridge the gap between industry and academia and the industry attendance at both meetings was strong.

The program in Australia and New Zealand were essentially the same, with most speakers providing lectures at both venues. Dr. Raid Alany opened the workshop in both venues and welcomed the audience, speakers, and thanked the sponsors for their generous contributions (Sotax in Melbourne; A.J. Park, Bomac, Douglas, iZON and Sotax in Auckland). Jean-Louis Raton from Sotax attended both workshops and was keen to discuss *in vitro* dissolution testing at every opportunity! Dr. Ben Boyd (President of AUS-CRS) was the first speaker for the day. He entertained the audience with a talk on the fundamentals of drug dissolution and *in vitro* release. The audience were from diverse fields and greatly appreciated this introductory talk.

Keynote speaker Prof. Diane Burgess, University of Connecticut, USA.

Dr. Ben Boyd chaired the second session and introduced Prof. Diane Burgess from the University of Connecticut, USA. Prof. Burgess discussed the problems associated with dissolution method development and future possibilities. She also discussed IVIVC, which helps formulation scientists to establish a meaningful relationship between *in vitro* and *in vivo* release profiles.

The next presenter was Dr. Clare Strachan from the University of Otago discussing spectroscopic aspects of dissolution. Spectroscopy is ideal for monitoring solid dosage forms during dissolution and Raman spectroscopy could be especially used to interpret drug release behaviour.

The lunch breaks at both venues were valuable networking sessions. In Auckland the audience reconvened for the first industry speaker Dr. Fadil Alawi, Bomac, Auckland, New Zealand. Bomac is an Auckland-based pharmaceutical company dedicated to animal health. Dr. Alawi's talk was about innovative drug delivery systems for parasite control in cattle. Dr. Andrew Barker from the law firm A.J. Park, Auckland, New Zealand was the next speaker. He highlighted some of the regulatory aspects of drug dissolution.

Delegates from the industry and academia attended the workshops.

Dr. Clare Strachan addressing the Q&A after her talk.

He stressed the importance of drug dissolution in defining the inventive aspect of patentee's claim and helping to establish if infringement had occurred. This was followed by an interesting talk on mathematical modelling of drug release data by Dr. Simon Young of the University of Auckland. Dr. Zimei Wu of the University of Auckland was the next speaker. She spoke about drug dissolution enhancement using cyclodextrins. The last talk for the day was given by Dr. Clare Strachan on Process Analytical Technology. The workshop audience in Auckland were then invited to a local brewery where they had the opportunity to enjoy dinner and sample some local beer. In Melbourne, the workshop dinner was held in an informal hotel restaurant.

Prof. Diane Burgess was first to address the delegates on the second day of the workshop with an interesting talk on release methods for micro- and nanoparticles.

The second session was chaired by Mr. Darren Svirskis (Ph.D. candidate and Secretary of NZCRS). Prof. Clive Prestidge of the University of South Australia was the next speaker. He presented exciting findings on drug release from silicone microparticles, nanoporous particles, nanoparticle coated emulsions and liposomes.

The secretary of NZCRS, Mr. Darren Svirskis.

Prof. Clive Prestidge talking about his fascinating colloidal systems.

The next speaker was Associate Professor Paul Young of the University of Sydney, Australia. He reviewed the concept of drug release from dry powders for inhalation and challenges that formulation scientists face.

In Auckland, the next session began after lunch and was chaired by Mr. Ali Seyfoddin (Ph.D. candidate at the University of Auckland and Post Graduate representative / NZCRS). Prof. Thomas Rades of the University of Otago, New Zealand, spoke about physical aspects of dissolution. This was followed by Dr. Raid Alany's talk on drug release from microemulsions, liquid crystalline systems, and SMEDDS. Dr. Ben Boyd then spoke about drug release from responsive systems.

The last session of the two-day workshop was chaired by Mr. Travis Badenhorst (Ph.D. candidate at the University of Auckland). The first speaker was Dr. Ilva Rupenthal, the past

Ph.D. students from the University of Auckland amongst the delegates (L to R. Meghna Talekar and Sara Zargar).

NZCRS secretary from the University of Auckland. Ilva spoke about drug release from in situ gelling systems and PLGA nanoparticles. The last speaker for the day was Dr. Sam Yu of IZON science, Christchurch, New Zealand. Sam introduced a newly developed instrument for measurement of particle size and concentration of nano- or microparticular systems.

Both events were again successful from both an educational and networking perspective, and future joint events will be communicated through the CRS Newsletter, and via our Chapter websites at crsaustralia.org and nzcrs.org.nz. ■

Do you have a great image of your science?

Submit it now!

The *CRS Newsletter* Editorial Board is inviting submission of images to be used on the cover for each issue of the *CRS Newsletter* in 2011.

Requirements
The image (photo, micrograph, etc.) must be an original, unpublished work that does not violate a third party's intellectual property rights. Images submitted for possible cover use must be no less than 7.375 inches (187 mm) wide × 10 inches (254 mm) deep at 300 dpi at the original image size. Acceptable file formats include tif, eps, and jpg.

Please send electronic copies of your images to the *CRS Newsletter* through our online dropbox at http://dropbox.yousendit.com/scisoc. Please include your e-mail address, the subject line "CRS Newsletter Cover," and a message that includes a short phrase that describes the image.

In the News

Compiled by Steven Giannos
Industrial Editor

January 2011

New Treatment for Breakthrough Cancer Pain Accepted for Use in Scotland

PRNewswire: January 17, 2011 - READING, ENGLAND - Archimedes Pharma Ltd., a leading international specialty pharma company, today announced the decision by the Scottish Medicines Consortium (SMC) to accept PecFent® (fentanyl pectin nasal spray) for use within NHS Scotland. PecFent is indicated for the treatment of breakthrough pain in adults who are already receiving maintenance opioid therapy for chronic cancer pain. Following the SMC clinical effectiveness and health economic review of the product, PecFent has been accepted for use in Scotland for breakthrough cancer pain (BTCP) patients unsuitable for short-acting oral opioids or as an alternative to other fentanyl preparations.

Jeffrey H. Buchalter, President and Chief Executive Officer of Archimedes Pharma, commented: "This is a key outcome from one of Europe's foremost Health Technology Assessment agencies. The SMC's balanced review of PecFent's clinical effectiveness and health economic value supports Archimedes' belief that PecFent provides a real opportunity for patients, for healthcare professionals, and for payors to improve the management of breakthrough cancer pain and the cost effectiveness of that management. We welcome the decision by the SMC to accept PecFent for use within the NHS in Scotland."

Professor Marie Fallon, Edinburgh Cancer Research Centre, commented: "BTCP is a challenge for current treatment options as it can be so rapid in onset, of short duration and severe to excruciating in intensity. The launch of PecFent was long awaited and I am very pleased PecFent will be available in Scotland to provide another important treatment option for patients with this challenging condition. This option is definitely an advance in the delivery of breakthrough cancer pain relief."

PecFent contains fentanyl, a highly potent opioid analgesic, and uses the Archimedes Pharma nasal drug delivery system PecSys® to deliver fentanyl in a rapid but controlled manner, designed to help match the time course of the typical breakthrough pain episode. In two randomised, controlled, double blind, phase 3 clinical trials, PecFent demonstrated evidence of onset of pain relief as early as 5 minutes, as well as clinically meaningful pain relief from 10 minutes.

Archimedes Pharma is an international specialty pharmaceutical company focused on the oncology, pain, and critical care sectors. Archimedes Pharma is marketing an expanding portfolio of specialist products to hospital-based prescribers in Europe and has established commercial organizations in the UK, U.S., France, Germany, Ireland, and Spain. For more information, please visit: http://www.archimedespharma.com.

TransPharma Changes the Name of Its Transdermal Drug Delivery System from ViaDerm to ViaDor™

Business Wire: January 17, 2011 - LOD, ISRAEL - TransPharma Medical Ltd., a specialty pharmaceutical company focused on the development and commercialization of drug products utilizing a proprietary active transdermal drug delivery technology, announced today that it is replacing the name of its drug delivery system from ViaDerm to ViaDor™. The new name better reflects TransPharma's enhanced commercialization efforts and global collaborations.

"The new name that we have chosen for our transdermal drug delivery system is a natural consequence of TransPharma's increasing success and expansion." ViaDor or the "golden path" expresses the capabilities of TransPharma's system to introduce drugs to the systemic circulation without pain or discomfort and also alludes to the transdermal "doors"—the microscopic channels the system creates in the upper layer of the skin that enable an efficient delivery of a wide array of drug molecules.

The new name also serves to disassociate TransPharma's drug delivery system from other products carrying the name ViaDerm, thus preventing confusion. "The new name that we have chosen for our transdermal drug delivery system is a natural consequence of TransPharma's increasing success and expansion," said Dr. Daphna Heffetz, CEO of TransPharma Medical. "It not only helps to showcase the various beneficial characteristics of our system, but also serves to better differentiate our technology. The ViaDor system is currently being studied in advanced-stage clinical trials for three distinct drug products: ViaDor-hPTH (1-34) for the treatment of osteoporosis, in collaboration with Eli Lilly; ViaDor-GLP1 agonist for the treatment of type II diabetes; and ViaDor-Calcitonin for the treatment of musculoskeletal diseases."

Diamyd Medical: Diamyd Starts Phase II Study in Cancer Pain

Business Wire: January 17, 2011 - STOCKHOLM, SWEDEN - Diamyd has dosed the first subject in a Phase II clinical trial in the United States evaluating the ability of the candidate drug NP2 Enkephalin to reduce cancer pain. Diamyd's Phase II clinical trial with the candidate drug NP2 Enkephalin will recruit approximately 32 subjects with severe cancer pain and follow their pain scores and concomitant opioid pain medication usage. It is a multi-center, randomized, double-blind, placebo controlled study designed to provide a statistical evaluation of pain relief. The trial has a four week, double-blind main study period and following this period, all patients will be offered up to two additional doses of active NP2 Enkephalin in an open label study extension.

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The open label study extension will measure pain scores following repeat dosing as well as provide additional safety evaluations. "Based on the encouraging results of the Phase I trial investigating NP2 Enkephalin as a potential therapy for chronic pain, Diamyd has been able to rapidly initiate this new study in cancer patients with chronic severe pain," states Darren Wolfe, CEO of Diamyd Inc., the U.S. subsidiary of Diamyd Medical. Diamyd has previously announced that substantial and sustained reduction in pain scores were reported in its Phase I clinical trial intended to test the safety of NP2 Enkephalin and the Company's Nerve Targeting Drug Delivery System (NTDDS) in patients with intractable pain due to cancer. No treatment related Serious Adverse Events have been observed in the Phase I study to date. "The serious unmet medical need of efficient pain relief is a strong driver for our team to continue development of NP2 Enkephalin and the NTDDS platform," says Elisabeth Lindner, CEO and President of Diamyd Medical. "With the Phase II study Diamyd intends to show proof-of-concept for the NP2 Enkephalin treatment, which is the furthest advanced project in our portfolio of pain-relieving drug candidates based on the proprietary NTDDS platform."

NTDDS represents a new class of pharmaceutical products that delivers gene-based drugs directly to nerve cells, providing a direct effect in the cells targeted by the treatment. The drug candidate NP2 Enkephalin has been engineered to deliver the human Enkephalin gene, which naturally produces opioid peptides involved in pain control, directly to the site of pain in the peripheral nervous system. "In preclinical studies, vector-mediated gene delivery has been shown to be effective in models of inflammatory pain, including arthritis pain, and pain from nerve damage due to injury or diabetes in addition to cancer pain. This Phase II clinical trial is an incredibly important step not only for cancer pain, but for establishing proof-of-principle in patients for this approach to treating pain," says David Fink, MD, Robert Brear Professor and chair of the department of neurology at the University of Michigan, and lead investigator of the trial.

Dance Pharma, Aerogen Ltd. to Develop Proprietary Inhaled Insulin Device

Business Wire: January 12, 2011 - SAN FRANCISCO, CA and GALWAY, IRELAND - Dance Pharma and Aerogen Ltd. will develop Dance's inhaled insulin product in a novel aerosol device based on Aerogen's proprietary OnQ™ Aerosol Generator technology, it was announced today by both companies. Aerogen has granted Dance an exclusive worldwide license to their aerosol technology for insulin delivery. Other terms of the agreement were not disclosed.

"Dance's team of inhaled insulin experts considered all potential aerosol technologies worldwide and chose Aerogen's technology because we're convinced it's the best, most patient-friendly technology for our first inhaled insulin product. Aerogen has done an outstanding job optimizing technology performance and achieving low cost production," said John S. Patton, Ph.D., Chief Executive Officer of Dance Pharma. "Most diabetics avoid taking insulin for years because the treatment requires multiple daily injections. The consequences for the patient and the healthcare system due to that kind of delay are dramatic. Our mission at Dance is to provide inhaled insulin in small, discreet, pain-less, and low cost form to patients throughout the world."

Aerogen's Chief Executive Officer John Power said, "We feel privileged to be involved in this potentially life changing venture. Building upon the wealth of knowledge and experience of prior ventures in the field, I firmly believe the time is now right when the advancements made in Aerogen's technological capability can combine with Dance's unrivaled clinical and specialist product expertise and finally enable the delivery of an aerosol solution that diabetes sufferers globally have so long waited for.

TransPharma Announces Successful Results of a Phase I Clinical Trial of ViaDerm-Calcitonin for the Treatment of Musculoskeletal Disorders

Business Wire: January 11, 2011 - LOD, ISRAEL - TransPharma Medical Ltd., a specialty pharmaceutical company focused on the development and commercialization of drug products utilizing a proprietary active transdermal drug delivery technology, announced today successful results of a Phase I clinical trial of its self-applied ViaDerm-Calcitonin product for the treatment of musculoskeletal disorders such as osteoarthritis and musculoskeletal pain.

"It leads us to believe that enhancing these capabilities with the ease of use, virtual painlessness, small size and portability of our ViaDerm system may open up a myriad of possibilities to expand the therapeutic applications of Calcitonin beyond the current approved indications."

The Phase I study was an open label single dose cross-over trial to assess the safety, pharmacokinetics (PK) and pharmacodynamics (PD) of ViaDerm-Calcitonin in 12 postmenopausal women treated with 4 different transdermal Calcitonin doses (60–300 mcg) compared to 100 IU of Miacalcin, the subcutaneous injected form of the Calcitonin.

Study results demonstrated a clear PK dose response corresponding to the escalating doses of the ViaDerm-Calcitonin patches. Furthermore, a single administration of ViaDerm-Calcitonin resulted in a statistically significant reduction of bone resorption and cartilage degradation biomarkers, CTX-I and CTX-II, similar to the reduction obtained with daily injections of 100 IU Miacalcin. All doses of ViaDerm-Calcitonin were safe and well-tolerated and demonstrated a favorable profile with regard to skin safety.

"We are very pleased with the results of this study, which demonstrate that our transdermal Calcitonin is safe and as efficacious as a subcutaneous injection," said Dr. Daphna Heffetz, CEO of TransPharma Medical. "It leads us to believe that enhancing these capabilities with the ease of use, virtual painlessness, small size and portability of our ViaDerm system may open up a myriad of possibilities to expand the therapeutic applications of Calcitonin beyond the current approved indications."

New Oral Biologics Delivery Company, Entrega, Announces Strategic Partnership with Pharma

PRNewswire: January 10, 2011 - BOSTON, MA - Entrega, Inc., a new company developing oral drug delivery technologies, today announced its formation by Enlight Biosciences, a Boston-based company established in partnership with a group of leading global pharmaceutical companies. As part of its initial development program, Entrega will use its unique spatially-directed proprietary drug delivery platform to create orally bioavailable formulations of several of the biologic drugs of Enlight's pharmaceutical industry partners, for which Entrega will receive undisclosed payments including upfront and research milestone payments. Entrega will remain independent and retain all rights to the platform technology.

"Entrega's technology could have a major impact on medicine by enabling the oral delivery of drugs that would typically require injection," said Dr. Robert Langer, David H. Koch Institute Professor at MIT, Entrega SAB Chair. "The relationship with pharma will support Entrega's unique technology and strengthen the platform significantly."

Biologic drugs (biologics), such as insulin and antibodies, represent over $120 billion in annual revenues and address major medical needs in areas such as cancer and inflammatory disease. However, most biologics need to be delivered by injection, which leads to challenges in compliance and effectiveness. The ability to deliver biologics orally would address a significant unmet need for patients around the world. Entrega's proprietary drug delivery technology offers an innovative approach to deliver a wide variety of peptides and proteins via oral administration.

Entrega, Inc. was formed by Enlight Biosciences, a unique entrepreneurial collaboration to discover and develop platform technologies that will have a transformational impact on drug discovery and development. "Enlight's innovative model, bringing together pharma companies and academic innovators, is addressing what has fundamentally been one of the foremost challenges in drug delivery," said Dr. Bennett Shapiro, former EVP of Worldwide Research at Merck, and currently PureTech Ventures Senior Partner, and Enlight Board member. Enlight was founded by PureTech Ventures and a group of the world's leading pharmaceutical companies.

Celator® Pharmaceuticals and Cephalon, Inc. Agree to Extend Research Agreement into Next Phase of Development

Business Wire: January 10, 2011 - PRINCETON, NJ - Celator Pharmaceuticals today announced that it has agreed with Cephalon, Inc. to extend an existing research agreement into the next phase of development. The research agreement provides for the utilization of Celator's proprietary technology in an ongoing drug development and life-cycle management program at Cephalon.

"We are pleased that our progress to date allows Cephalon and Celator to advance this promising work," said Scott Jackson, chief executive officer, Celator Pharmaceuticals. "It is rewarding to have a company of Cephalon's stature demonstrate the potential of our technology in its portfolio and make the ongoing financial commitment to continue this research."

Celator is advancing a number of its own programs based on the Company's proprietary nano-scale delivery platforms. The Company has announced positive results from its Phase 2 study of CPX-351 (Cytarabine:Daunorubicin) Liposome Injection versus conventional cytarabine and daunorubicin therapy (known as the "7+3" regimen) in patients with newly diagnosed acute myeloid leukemia. The study showed that patients treated with CPX-351 demonstrated a higher aplasia rate, a higher remission rate (including complete remissions [CR] and complete remissions with incomplete neutrophil/platelet recovery [CRi]), lower induction mortality, improved median event-free survival (EFS), and improved median overall survival (OS). Even more noteworthy were the improvements seen in high-risk patients.

CPX-351 is one of a pipeline of investigational cancer therapies developed using Celator's CombiPlex® drug-ratio technology. Celator also has an agreement with the National Cancer Institute's Nanotechnology Characterization Laboratory (NCL) whereby the NCL selected the Company's hydrophobic docetaxel prodrug nanoparticle formulation for intensive physical characterization, *in vitro* studies, and *in vivo* pharmacology and toxicology protocols to support an eventual investigational new drug (IND) filing with the U.S. Food and Drug Administration.

EffRx Pharmaceuticals SA Announces Submission of New Drug Application to FDA for Osteoporosis Treatment Targeting Increased Convenience for Patients

Business Wire: January 10, 2011 - LAUSANNE, SWITZERLAND - EffRx Pharmaceuticals SA, a Lausanne, Switzerland based drug delivery company, announces the NDA submission of the company's lead project to the U.S. Food and Drug Administration.

"We are very pleased to have reached this stage of our lead product and are confident that EX101 will provide a convenient alternative to the patients with the aim of improving compliance rates, which is a common issue of today's available bisphosphonate tablet treatments."

EX101 is a proprietary buffered effervescent dosage form of alendronate sodium administered once weekly for prevention and treatment of osteoporosis in postmenopausal women and incensement of bone mass in men with osteoporosis. The EX101 formulation is the first and only effervescent bisphosphonate alternative to tablets. EX101 has a pleasant taste of strawberry and is quickly and completely dissolved in half the water dose required for the administration of common bisphosphonate tablet treatments.

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EffRx is in the process of securing partnership for distribution of EX101 in the U.S.A. and Japan. In the rest of the world EffRx has licensed commercialization of EX101 to Nycomed. "We are very pleased to have reached this stage of our lead product and are confident that EX101 will provide a convenient alternative to the patients with the aim of improving compliance rates, which is a common issue of today's available bisphosphonate tablet treatments," said Christer Rosén, CEO.

NextWave Pharmaceuticals Announces Launch of NEXICLON™ XR – First Extended-Release, Once-Daily Clonidine Oral Suspension and Tablet

Business Wire: January 6, 2011 - CUPERTINO, CA - NextWave Pharmaceuticals announced today the launch of NEXICLON™ XR (clonidine) for the treatment of hypertension. NEXICLON XR provides for once-daily dosing, in suspension and tablet form, to be taken alone or concomitantly with other antihypertensive agents.

Clonidine, a centrally acting alpha-adrenergic agonist, is a safe and effective treatment for hypertension that has been available for decades. However, until now there have been no once-daily formulations available. NEXICLON XR is manufactured using the proprietary OralXR+™ extended-release technology through which clonidine is formulated into orally-administered tablets or suspension. The availability of NEXICLON XR in both a liquid oral suspension and scored tablet allows for precise dose titration.

"The launch of NEXICLON XR is a milestone for our company," said Jay Shepard, president and CEO of NextWave Pharmaceuticals. "These novel formulations of clonidine will provide unique dosing options for patients. We are proud to showcase it as our first FDA-approved drug. Our mission at NextWave is to develop products, such as NEXICLON XR, that address the unmet needs of patients; we are excited about this launch as well as the further development of other extended-release products we have in our pipeline."

NextWave is collaborating with Tris Pharma, creator of the OralXR+ technology, and manufacturer of NEXICLON XR for NextWave. NEXICLON XR will be available in retail pharmacies starting January 2011. For additional information on NEXICLON XR, please visit www.nexiclonxr.com.

CPEX to Be Acquired by FCB I Holdings Inc.

Business Wire: January 4, 2011 - EXETER, NH - CPEX Pharmaceuticals, Inc. (NASDAQ: CPEX) announced today that it has entered into a definitive agreement with FCB I Holdings Inc. ("FCB"), a newly formed company which is controlled by Footstar Corporation, under which FCB, through a wholly-owned subsidiary, will acquire all of the outstanding common stock of CPEX. The transaction was unanimously approved by the CPEX Board of Directors.

"This transaction is the result of the CPEX Board's comprehensive review of our strategic alternatives to maximize shareholder value," said John A. Sedor, CPEX President and Chief Executive Officer. "After engaging with multiple parties during the review process, it was clear that this agreement was the most compelling outcome for our shareholders, delivering them significant and immediate value. We look forward to closing the transaction in the second quarter of 2011."

CPEX Pharmaceuticals, Inc. is an emerging specialty pharmaceutical company focused on the development, licensing and commercialization of pharmaceutical products utilizing CPEX's validated drug delivery platform technology. CPEX has U.S. and international patents and other proprietary rights to technology that facilitates the absorption of drugs. CPEX has licensed applications of its proprietary CPE-215® drug delivery technology to Auxilium Pharmaceuticals, Inc. which launched Testim, a topical testosterone gel, in 2003. CPEX maintains its headquarters in Exeter, NH. For more information about CPEX, please visit www.cpexpharm.com.

Nano Particle Polymer Micelles DDS Technology for Cancer Therapy

January 6, 2011 - CHIBA, JAPAN - NanoCarrier Co., Ltd., a research, development and production company of pharmaceuticals using micellar nanoparticles technology, announces the publication of their research in the journal, Science Translational Medicine. Professor Kazunori Kataoka, at the University of Tokyo, describes NanoCarrier's cutting-edge work in the paper "Improving Drug Potency and Efficacy by Nanocarrier-Mediated Subcellular Targeting." The nanocarriers (micellar nanoparticles) consist of polyethylene glycol copolymer.

Nanocarrier®, for mediated drug targeting, is an emerging strategy for cancer therapy and is being used, for example, with chemotherapeutic agents for ovarian cancer. Nanocarriers are selectively accumulated in tumors as a result of their enhanced permeability and retention of macromolecules, thereby enhancing the antitumor activity of the nanocarrier-associated drugs. The authors investigated the real-time subcellular fate of polymeric micelles incorporating (1,2-diaminocyclohexane) platinum(II) (DACHPt/m), the parent complex of oxaliplatin, in tumor tissues by fluorescence-based assessment of their kinetic stability. Observations revealed that DACHPt/m was extravasated from blood vessels to the tumor tissue and dissociated inside each cell.

Furthermore, DACHPt/m selectively dissociated within late endosomes, enhancing drug delivery to the nearby nucleus relative to free oxaliplatin, likely by circumvention of the cytoplasmic detoxification systems such as metallothionein and methionine synthase. Thus, these drug-loaded micelles exhibited higher antitumor activity than did oxaliplatin alone, even against oxaliplatin-resistant tumors. These findings suggest that nanocarriers targeting subcellular compartments may have considerable benefits in clinical applications.

NanoCarrier's core technology, micellar nanoparticles technology, was invented and has been studied by Professor Kazunori Kataoka of University of Tokyo, Professor Teruo

Okano of Tokyo Women's Medical University and Associate professor Masayuki Yokoyama of the Jikei University.

The aforementioned professors demonstrated that when drug-encapsulating micellar nanoparticles were intravenously administered, the particles could function as stable drug carriers in the bloodstream and they accumulated in cancerous tissues. It is hoped that, if efficacy and safety of drugs are further improved by utilizing our micellar nanoparticles technology, NanoCarrier will be able to contribute to the advance in medication of cancer and other intractable diseases. As a pioneer of micellar nanoparticle technology, it is a task to harness the potential of micellar nanoparticles technology to the product development.

December 2010

HepaLife Technologies Announces Name Change to "Alliqua, Inc."

Business Wire: December 22, 2010 - NEW YORK, NY - HepaLife Technologies, Inc. (OTCBB:HPLF) (FWB:HL1) ("HepaLife"), an advanced biomedical products company focused on the development and manufacturing of proprietary drug delivery and liver health technologies, today announces that the Company has changed its name to "Alliqua, Inc." effective December 20, 2010. The name change to Alliqua, Inc. will be reflected in SEC filings and all future corporate communications with the investor community. The Company will retain its current ticker symbol until assigned a new one by FINRA.

"In order to more accurately reflect our focus on emerging solutions in the fields of drug delivery and advanced wound care, we have adopted a corporate name change to Alliqua, Inc.," said Richard Rosenblum, President. "As demonstrated by our recent announcements, such as the 510(k) submission for our silver-based antimicrobial wound care dressing, we are committed to becoming a leading distributor of innovative product solutions in our respective healthcare verticals. With various new products in the pipeline, we look forward to keeping our loyal shareholders and prospective investors apprised of our developments into 2011 and beyond."

Alliqua's strategic initiatives have evolved around the concept of utilizing its proprietary and patented technologies to address drug delivery and advanced wound care needs through the use of its AquaMed subsidiary's proprietary hydrogel platform. Hydrogels are gel-like or colloidal substances made of water and solids that are highly absorbent, and are well suited for wound care and transdermal purposes. Alliqua's dressings create a moist environment that facilitates healing, naturally produces pain relief at the wound site, and inherently stays in place without bonding to the wound, skin or hair. For additional information, please visit www.alliqua.com, www.aquamedinc.com and www.hepalife.com

Gold Nanomedicine Clinical Trial Delivers Promising Results

PRNewswire: December 21, 2010 - LONDON, UK - The World Gold Council (WGC) is delighted with the successful phase 1 clinical trial of a unique nanomedicine that uses nanoparticles of gold as the core of a delivery system for tumour targeted drug delivery. The research, published in the current edition of Clinical Cancer Research, was carried out by U.S.-based life sciences company CytImmune Sciences Inc.

CytImmune's technology is at the forefront of a raft of gold-based innovations as described earlier this year by the WGC in a paper entitled 'Gold for Good: Gold and nanotechnology in the age of innovation.' The report demonstrates how gold nanoparticles exhibit a variety of unique properties which are showing great potential in a range of fields.

Dr. Richard Holliday, Director, Technology at the WGC said: "Gold has a long history in the biomedical field, being the material of choice in many diagnostic platforms and a key constituent for rheumatoid arthritis treatment. The dawn of the 'nano-age' has further broadened the potential of gold in biomedical applications and it is exciting to see the outcome of this clinical trial which suggests that gold can act as an effective and safe drug delivery system."

In medicine, gold nanoparticles can serve as a simple, elegant platform upon which potent therapies may be bound. In this clinical trial the nanoparticles, which were coated with both an immune-avoiding molecule and a potent anti-cancer agent, were shown to be very well tolerated and to target solid tumours. There is hope that such targeting technology will be effective against a range of cancers, including lung, pancreatic, breast and ovarian cancer.

Dr. Lawrence Tamarkin, CEO of CytImmune Sciences Inc., said: "This phase 1 clinical study potentially marks the beginning of a new strategy in cancer treatment where gold nanoparticle-based cancer therapeutics are used first, before surgery, to reduce tumour burden. Reducing tumour size may require less sophisticated surgeries to remove any residual tumour, leading to shorter hospital stays and to improved patient outcomes. Phase 2 clinical studies will prove the value of this novel drug delivery platform."

Dr. Holliday continued: "By continuously reviewing and monitoring the global research landscape in gold science and technology, we are able to identify and, where appropriate, help accelerate the time to market key, new technologies that have social, environmental or medical benefits." Further information may be found at http://www.cytimmune.com/ and http://clincancerres.aacrjournals.org/content/16/24/6139.abstract.

Quinnova Pharmaceuticals, Inc. Joins the Amneal Enterprises, LLC Alliance

Business Wire: December 20, 2010 - BRIDGEWATER, NJ - Amneal Enterprises, LLC, an alliance of life science companies, is pleased to announce the addition of Quinnova Pharmaceuticals, Inc., Newtown, PA, as an independent affiliate of Amneal Enter-

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prises, LLC via its acquisition by AmDerma Pharmaceuticals, LLC. This exciting move enables Amneal Enterprises to expand strategically into the fast-growing dermatology market.

"Dermatology has long been an area of strong interest to us. There are enormous unmet needs, a culture of innovative physicians and important opportunities for newer and better technologies. We are determined to create a much-needed next generation dermatology company and have identified Quinnova as an ideal organization with the potential to grow into a great enterprise," explained Chirag Patel, Co-Chairman of Amneal Enterprises, LLC. "We see exciting times ahead with Quinnova's outstanding team and unique topical delivery platforms, further empowered by leveraging the full range of Amneal Enterprises resources."

As a member of the Amneal Enterprises alliance of life science companies, Quinnova can take advantage of extensive resources in research & development, marketing strategy, intellectual property, business development and other areas across the member alliance companies. The dermatology firm is expected to accelerate its growth with this broad-based support. Quinnova and other companies aligned under the Amneal Enterprises umbrella stand to gain significant value from the affiliation by leveraging each company's strengths to move faster toward realizing aggressive and bold long-term goals. Under the new ownership, Quinnova Pharmaceuticals will remain an independently operating company.

"I'm very excited about becoming a member of the Amneal Enterprises family of aligned companies and what it represents for all of us at Quinnova Pharmaceuticals. It will allow us to revitalize initiatives we started four years ago, ramp up our commercial operations, complete high-potential R&D projects, build out a robust pipeline and fulfill the vision of what we've always believed our company can be," said Jeffrey S. Day, Quinnova's President and CEO.

Quinnova Pharmaceuticals is a specialty pharmaceutical company that develops and markets novel topical delivery platforms based on prescription dermatology drugs. The company's FDA-approved Proderm Technology™ Delivery System ("Proderm") addresses the need for improved, cost-effective treatment options for skin disorders such as dermatitis, fungal infection, psoriasis, and acne while simultaneously enhancing efficacy and patient compliance. Quinnova currently has several prescription medications on the market, including its FDA-approved NEOSALUS™ brand of foam and cream, which are available through dermatologists, podiatrists, and pediatricians. Because of its flexibility, Proderm presents an excellent platform for future product development in a variety of indications.

Novo Nordisk A/S and Emisphere Technologies, Inc. Announce License Agreement to Develop Oral Formulation of Insulin

PRNewswire: December 21, 2010 - PRINCETON, NJ - Emisphere Technologies, Inc. (OTC Bulletin Board: EMIS) and Novo Nordisk A/S (NYSE: NVO) today announced that they have entered into an exclusive Development and License Agreement to develop and commercialize oral formulations of Novo Nordisk's insulins, which have the potential of treating diabetes, using Emisphere's Eligen® Technology. This is the second license agreement between the two companies. The first agreement for the development of oral formulations of GLP-1 receptor agonists was signed in June 2008 with a potential drug currently in a phase 1 clinical trial.

"This is an encouraging agreement on a promising technology for oral administration of proteins. We are delighted to continue working with Emisphere and their Eligen® Technology. It fits very well with Novo Nordisk's strategy within diabetes research," said Peter Kurtzhals, senior vice president, Diabetes Research Unit at Novo Nordisk.

This extended partnership with Novo Nordisk is important for Emisphere for several reasons, said Michael V. Novinski, president and chief executive officer of Emisphere. "To date, our collaboration with Novo Nordisk has been very productive, and today's agreement has the potential to offer significant new solutions to millions of people with diabetes worldwide. Finally, it also serves to further validate our Eligen® Technology."

Emisphere's broad-based drug delivery technology platform, known as the Eligen® Technology, uses proprietary, synthetic chemical compounds, known as Emisphere delivery agents, sometimes called carriers. Emisphere's Eligen® Technology makes it possible to deliver a therapeutic molecule without altering its chemical form or biological integrity.

Generex Receives New Patent for Buccal Drug Delivery Platform Technologies

PRNewswire: December 15, 2010 - WORCESTER, MA - Generex Biotechnology Corporation (www.generex.com) (OTC Bulletin Board: GNBT) announced today that it has received a new patent for its buccal drug delivery platform technologies. The Canadian Intellectual Property Office has granted to Generex Canadian Patent No. 2,354,148, a patent titled Aerosol Formulations for Buccal and Pulmonary Application.

This new patent increases the number of issued patents related to the Company's buccal drug delivery platform technologies to 162. A total of 101 patent applications in the field remain pending.

"We continue to augment the breadth and depth of the intellectual property protection for our drug delivery platform," observed Rose C. Perri, the Company's Chief Operating Officer, "as we continue to pursue the platform's commercialization opportunities for insulin and other active pharmaceutical ingredients." For more information, visit the Generex website at www.generex.com or the Antigen Express website at www.antigenexpress.com.

Pacira Pharmaceuticals Announces FDA Acceptance of EXPAREL™ New Drug Application for Pain Management

PRNewswire: December 14, 2010 - PARSIPPANY, NJ - Pacira Pharmaceuticals, Inc., an emerging specialty pharmaceutical

company, announced today that the New Drug Application (NDA) for EXPAREL™, a long-acting bupivacaine for postsurgical pain management, has been accepted for filing by the U.S. Food and Drug Administration (FDA). Pacira submitted the EXPAREL NDA in September 2010 for the initial indication of postsurgical analgesia by local administration. The FDA also notified Pacira that its Prescription Drug User Fee Act (PDUFA) target date (the date the FDA expects to complete its review of the EXPAREL NDA) is July 28, 2011.

Pacira Pharmaceuticals, Inc. is an emerging specialty pharmaceutical company focused on the development, commercialization, and manufacture of novel pharmaceutical products, based on its proprietary DepoFoam drug delivery technology, for use in hospitals and ambulatory surgery centers. The company's most advanced product candidate, EXPAREL, a bupivacaine-based product, has completed Phase 3 clinical development for postoperative analgesia by infiltration. EXPAREL consists of bupivacaine encapsulated in DepoFoam, which is designed to address the limitations of widely used medications by enhancing their dosing and/or administration profile. Additional information about Pacira is available at www.pacira.com.

MonoSol Rx and Midatech to Develop Insulin in PharmFilm®; to Establish Joint Venture

PrNewswire: December 8, 2010 - WARREN, NJ and OXFORD, ENGLAND - MonoSol Rx, the developer of PharmFilm® drug delivery technology, and Midatech Group Ltd., a global leader and centre of excellence for the design, development, synthesis, and manufacture of nanomedicines, today announced their intent to form a joint venture that will focus on the development and commercialization of products combining the two companies' respective technologies in the diabetes field. Initially, the joint venture will focus on commercializing buccally delivered insulin with an appropriate partner.

Preclinical testing in multiple species has demonstrated the companies' ability to deliver active insulin across the buccal mucosa and to decrease circulating levels of glucose in all animal models. Additionally, the companies have successfully evaluated the safety of the nanoparticles in tolerability, acute and chronic toxicity studies in multiple species with no evidence of adverse effects. In support of an investigational new drug (IND) submission for human clinical studies, Midatech and MonoSol Rx are concluding additional pre-clinical studies of buccally delivered insulin in diet-induced diabetic primates and expect to announce data by year's end 2010. The companies plan to initiate Phase I clinical trials during the second quarter of 2011.

A. Mark Schobel, president and CEO of MonoSol Rx, stated, "Based on the results of our pre-clinical studies to date, Midatech and MonoSol Rx intend to accelerate the development of Nanoinsulin™ PharmFilm, which we believe has the potential to offer an unprecedented treatment option for diabetes sufferers around the world. The strength of the data generated so far, and the early indications from our primate study, give us confidence that our nanoparticle oral film platform is capable of delivering a therapeutic insulin dose into the systemic circulation and thus look forward to initiating human clinical trials in early 2011. For the future, it's important to acknowledge that the combination of our respective technologies is applicable to other biologics, and we look forward to exploring additional opportunities together."

The mission of the joint venture will be to address the longstanding unmet need of millions of diabetics who are dependent on insulin injections and who lack a convenient, non-invasive delivery option. Nanoinsulin PharmFilm has the potential to offer diabetic patients the first-ever truly-oral alternative to injectable insulin, and to revolutionize the growing multi-billion dollar global diabetes treatment market.

Professor Tom Rademacher, Chairman of the Midatech Group, remarked, "Following preclinical proof-of-mechanism studies for Nanoinsulin PharmFilm, our collaboration with MonoSol Rx has achieved groundbreaking results in delivering proteins across the buccal mucosa utilizing PharmFilm and our nanoparticle technology. Bioavailability studies in multiple species have demonstrated repeatedly that Nanoinsulin PharmFilm delivers significantly more bioactive insulin than all previous attempts to deliver insulin across the oral mucosa or the gastrointestinal tract.

"Based on the existing bioavailability data, the companies believe that the Nanoinsulin PharmFilm offers a significant commercial opportunity and are committed to moving the product into the clinic. Forming a joint venture represents an important step forward in our collaboration and in the pursuit of delivering a predictable dose of insulin in a convenient, transbuccal dosage form for millions of diabetics worldwide."

PharmFilm is a registered trademark of MonoSol Rx. Nanoinsulin is a trademark of Midatech Inc. For press releases and other company information visit www.monosolrx.com.

Taiwan Liposome Company Signs Distribution Agreement With Ildong Pharmaceutical

PRNewswire: December 6, 2010 – TAIPEI, TAIWAN - Taiwan Liposome Company (TLC) announced today the signing of a collaboration agreement with Ildong Pharmaceutical, one of the top ten pharmaceutical companies in Korea, for the marketing, distribution, and sale of ProFlow®, the super generic drug developed by TLC.

"The collaboration with a well-established company such as Ildong is certainly very exciting for us," said Dr. Hong, Chairman and CEO of TLC. "We are very much looking forward to having ProFlow® distributed by such an experienced partner in Korea." George Yeh, President of TLC, further commented, "Now we have extremely strong partners in Japan and Korea for the distribution of ProFlow®, we're most confident in the future outlook of the product and its positive reflection on TLC."

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ProFlow® is an improved Prostaglandin E1 emulsion with extended shelf stability of more than two years, developed by TLC with its proprietary formulation, patented worldwide. ProFlow® is used for treating Peripheral Arterial Disease (PAD), diabetic neuropathy, and ulcers, with a global market potential of US$500 million. "We realize the market potential and the product advantage due to its improved technology, thus expect that ProFlow will make a market share of at least 30% in the Korean market," said Yeongwook Kim, B&D Director, Ildong Pharmaceuticals.

"We are delighted on the progress that the Taiwan Liposome Company, one of our portfolio companies, is making," said Dr. Ann Hanham, Managing Director, Burrill & Company. "Ildong Pharmaceutical has a strong presence in Korea and they are an ideal partner to promote and sell ProFlow® to their expanding customer base." ProFlow® has also been licensed out in Japan territory to the largest hospital pharmacy chain, Nihon Chouzai, expecting to gain 30%–40% of the US$300 million market.

ProFlow® is an improved Prostaglandin E1 emulsion. Prostaglandin E1 (PGE1), also known as Alprostadil, is an arterial vasodilator and platelet-aggregation inhibitor. Emulsion form enables sustain release and target delivery. Our patented formulation and know-how in the process make a significant improvement in preventing PGE1 degradation in emulsions. Stability data shows at least 2 years of shelf stability in comparison to the one year displayed by the currently marketed products, making transportation and storage of the product much easier.

MiMedx Receives Grant for Its CollaFix™ Drug Delivery Device

PRNewswire: December 1, 2010 - MARIETTA, GA - MiMedx Group, Inc. (OTC Bulletin Board: MDXG), an integrated developer, manufacturer and marketer of patent protected biomaterial-based products, announced today that it has been awarded a Qualifying Therapeutic Discovery Project grant (QTDP) from the U.S. government. The grant, in the amount of $244,479, has been made to defer some of the company's research expenditures related to the development of its novel and patented technology, CollaFix™, as a drug delivery device.

The CollaFix™ collagen fiber technology was designed by MiMedx to mimic the natural composition, structure, and mechanical properties of musculoskeletal tissues in order to augment their repair. CollaFix™ is the only biological, biodegradable, biomimetic technology that matches human tendon in strength and stiffness. CollaFix™ also has unique characteristics as a potential drug delivery device which may enable it to deliver therapeutics while facilitating soft tissue repair.

Parker H. "Pete" Petit, MiMedx Chairman and Chief Executive Officer, stated, "CollaFix™ was developed with our patented cross-linking polymers and is designed to mimic native tissue biomechanics. We believe CollaFix™ has an array of potential applications for use. As a drug delivery device, CollaFix™ has the potential to be far superior to conventional drug delivery devices. We anticipate CollaFix™ may have greater stability *in vivo* and its unique characteristics may permit it to deliver drugs and other therapeutics to a very precise site over an extended time. This potentially could minimize tissue damage."

"One of the remarkable qualities of CollaFix™ is its potential to absorb and deliver antibiotics and other therapeutics," said Bill Taylor, President and Chief Operating Officer of MiMedx. "CollaFix™ as a drug delivery device potentially could treat both acute and chronic diseases. Some of its possible applications include the administration of anti-inflammatory drugs during ligament and tendon surgery, administration of antibiotics to prevent infections associated with implantable medical devices such as pacemakers and glucose monitors, and antibiotics administration for the treatment of chronic diabetic ulcers."

Pearl Therapeutics' PT003 Combination Therapy for COPD Demonstrates Superior Bronchodilation Compared to Spiriva® and Foradil® in Randomized Phase 2b Study

PRNewswire: December 1, 2010 - REDWOOD CITY, CA - Pearl Therapeutics Inc. today announced that their lead combination bronchodilator, PT003, met the primary efficacy endpoint in a recently completed Phase 2b clinical trial in patients with moderate to very severe chronic obstructive pulmonary disease (COPD). These top-line results show that PT003 provides superior bronchodilation compared to the current market leader, tiotropium bromide (Spiriva® Handihaler®), as well as to formoterol fumarate (Foradil® Aerolizer®), placebo, and the individual components of PT003 ($p \leq 0.0002$ for all comparisons). In addition PT003 was shown to be safe and well tolerated.

PT003 is an inhaled combination bronchodilator product comprised of glycopyrrolate, a long-acting muscarinic antagonist (LAMA), and formoterol, a long-acting beta-2-agonist (LABA), delivered via a hydrofluoroalkane metered dose inhaler (MDI). In this Phase 2b study, two doses of PT003 were compared to Spiriva, Foradil, placebo, glycopyrrolate MDI (PT001), and formoterol MDI (PT005). The primary assessment for this study was change in lung function following one week of dosing, as assessed by FEV1 AUC (0–12) (forced expiratory volume in one second), relative to baseline at the start of treatment. Both doses of PT003 were superior to Spiriva ($p<0.0001$), Foradil ($p \leq 0.0002$), placebo ($p<0.0001$), PT001 ($p<0.0001$), and PT005 ($p<0.0001$).

In addition to FEV1 AUC, which assesses overall improvement in lung function over the duration of treatment, Pearl measured peak FEV1 on days one and seven, which measures the maximum improvement in lung function observed during the assessment period. Both doses of PT003 were superior to Spiriva and Foradil on day one ($p<0.03$), with further benefit observed on day seven ($p<0.002$).

"In order to assess the incremental benefit of PT003 over current treatments, we included Spiriva and Foradil, two widely used

products for the management of patients with COPD as active comparators. The impressive results generated by PT003 validate our combination approach and the strength of our porous particle technology," said Dr. Colin Reisner, chief medical officer and EVP of clinical development of Pearl Therapeutics. "The improvement in lung function demonstrated by PT003 in this trial is encouraging and supports the potential of this product in the treatment of patients with COPD."

November 2010

Micell Technologies Enrolls First Patient in DESSOLVE I First-In-Human Study of MiStent DES

PRNewswire: November 29, 2010 - DURHAM, NC - Micell Technologies,™ Inc. today announced it has enrolled at Mercy Hospital in Auckland, New Zealand, the first patient in DESSOLVE I (DES with Sirolimus and a bioabsorbable polymer for the treatment of patients with de novo lesions in the native coronary arteries), a first-in-human clinical trial of the company's investigational MiStent™ Drug Eluting Coronary Stent System (MiStent DES).

DESSOLVE I is a prospective, open-label, non-randomized, single-arm study that is expected to enroll 30 patients at five clinical sites in Belgium, Australia, and New Zealand. Candidates for the trial are patients with documented stable or unstable angina pectoris or ischemia. The primary endpoint is in-stent late lumen loss, as measured with angiography in treated de novo lesions ranging in diameter from 2.5 to 3.5 mm and amenable to treatment with a maximum 23 mm long stent.

Along with secondary clinical endpoints such as major adverse cardiac events and revascularization rates, intravascular ultrasound (IVUS), and optical coherence tomography (OCT) will also be employed at multiple time points. The DESSOLVE I study uses multiple imaging modalities to better understand the time to complete tissue coverage of the stent struts relative to polymer absorption. More information on the DESSOLVE I trial can be found at http://www.clinicaltrials.gov/ct2/show/NCT01247428.

"Drug-eluting stents represent a significant advance in interventional cardiology," said John Ormiston, M.D., Mercy Hospital, Auckland, New Zealand, and co-principal investigator. "However, the rare but potentially catastrophic consequences of late in-stent thrombosis remain to be addressed. The MiStent DES is designed to maintain the polymer-drug matrix on the stent only as long as drug delivery is required. It slowly reverts to a bare-metal stent by the time that drug treatment is completed. These are exactly the properties that interventional cardiologists are looking for in a drug-eluting stent."

The MiStent DES employs Micell's proprietary supercritical fluid technology that applies a precisely controlled bioabsorbable polymer–active drug (sirolimus) matrix onto a cobalt-chromium stent. The polymer dissolves and releases the drug into the surrounding tissue in a controlled manner, designed to optimize dosing of the drug throughout the affected artery. In pre-clinical trials, the drug completely elutes and the polymer is eliminated within 90 days *in vivo,* resulting in a bare metal stent.

Arthur J. Benvenuto, Chairman and Chief Executive Officer of Micell, said, "We designed the MiStent DES to bring together the clinical advantages of a drug-eluting stent with the long-term safety and stability of a bare metal stent. Our supercritical fluid technology enables us to develop a drug-eluting stent with precise and consistent dissolution kinetics that can be adjusted for a specific requirement. In addition, we believe we can effectively manage the development risk since all components—the active drug, sirolimus; the polymer material, PLGA; and the CE Marked Genius MAGIC Cobalt-Chromium stent—are currently on the market. Our technology also does not expose the polymers, drugs, or stents to the conventional liquid solvents that are used in the manufacturing process."

Lilly and Acrux Receive FDA Approval for Axiron® (Testosterone) Topical Solution CIII

PRNewswire: November 23, 2010 - INDIANAPOLIS, IN and MELBOURNE, AUSTRALIA - Eli Lilly and Company (NYSE:LLY) and Acrux (ASX: ACR) announced that the U.S. Food and Drug Administration (FDA) has approved Axiron® (testosterone) topical solution CIII for replacement therapy in men for certain conditions associated with a deficiency or absence of testosterone. Safety and efficacy of Axiron in males younger than 18 years of age have not been established.

Axiron is the first testosterone topical solution approved for application via an armpit (underarm) applicator. Other forms of testosterone replacement therapy include: oral tablets, buccal tablets, subcutaneous pellets, transdermal patches, injections, and topical gels applied by the hands.

Although the total number of men with testosterone deficiency is unknown, it has been estimated that up to 13 million men over 45 years of age in the U.S. may have symptoms associated with low testosterone. Clinical trial data indicated that Axiron can restore blood concentration of testosterone within the normal range in most men.

"Lilly is proud to expand our focus in men's health," said David Ricks, president, Lilly U.S.A. "The addition of Axiron to our product portfolio reinforces Lilly's commitment to provide innovative treatment options for patients." "The FDA approval is a major milestone for Axiron and for Acrux," said Dr. Richard Treagus, chief executive officer, Acrux. "After years of research, we are excited to partner with Lilly to provide this novel application method for men with low testosterone."

Soligenix Announces Issuance of United States Patent for RiVax™, its Vaccine Against Ricin Toxin

PRNewswire: November 22, 2010 - PRINCETON, NJ - Soligenix, Inc. (OTC Bulletin Board: SNGX) (Soligenix or the Company), a late-stage biopharmaceutical company, announced today that the United States Patent and Trademark Office

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(USPTO) has granted patent #7,829,668, entitled "Compositions and methods for modifying toxic effects of proteinaceous compounds." This patent includes composition claims for the modified ricin toxin A chain which is the immunogen contained in RiVax™. Conceived by Soligenix's collaborative partner Ellen Vitetta, Ph.D., Director of the Cancer Immunobiology Center and colleagues at the University of Texas Southwestern Medical Center in Dallas (UT Southwestern), RiVax™ is a vaccine that contains a recombinant subunit of the A chain of ricin toxin which induces ricin neutralizing antibodies in humans and animals.

The issued patent contains claims that describe alteration of sequences within the ricin A chain that affect vascular leak, one of the deadly toxicities caused by ricin toxin. Ricin is a potent plant toxin that is composed of two molecular chains: the A chain, which contains several sites that inactivate cellular machinery and induce its characteristic toxicity, and the B chain, which causes it to bind to cells with high affinity. The issued patent contains claims for specific mutations in this site that induce vascular leak syndrome (VLS). The combination of mutations in each of the key sites for ricin toxicity ensures that the recombinant subunit will not produce this devastating effect. Studies conducted by Dr. Vitetta and her colleagues have indicated that the specific mutations introduced into the ricin A chain eliminate the toxic activity of the molecule, but do not alter the structure, permitting a highly immunogenic and safe vaccine.

"This patent issuance is another milestone towards obtaining broad patent coverage for RiVax™," said Robert N. Brey, Ph.D., Chief Scientific Officer of Soligenix. "We continue to be enthusiastic about the prospects of developing a ricin vaccine to anticipate civilian and military biodefense requirements. We believe the technology that Dr. Vitetta and her colleagues at UT Southwestern have developed for RiVax™ is the most advanced in this area."

Titan Pharmaceuticals Presents Phase 3 Probuphine™ Data at Society for Neuroscience Annual Meeting

PRNewswire: November 17, 2010 - SOUTH SAN FRANCISCO, CA - Titan Pharmaceuticals, Inc. (OTC Bulletin Board: TTNP) today announced that data from its Phase 3 clinical development program for Probuphine were presented at the Society for Neuroscience Annual Meeting, being held Nov. 13–17 in San Diego. The presentation, "Development of an Implantable Formulation of Buprenorphine for Opioid Addiction," was delivered by Katherine Beebe, Ph.D., senior vice president, clinical development and medical affairs at Titan and outlined the positive data demonstrated by Probuphine in Phase 3 clinical trials conducted to date in patients with opioid addiction. These trials include a six-month randomized, placebo-controlled study and a six-month, open-label retreatment study.

Probuphine is an innovative, subcutaneous implant formulation designed using Titan's proprietary ProNeura™ technology to deliver a steady, round-the-clock low dose of the marketed drug buprenorphine over six months following a single treatment.

"We continue to be extremely encouraged and excited by these compelling Probuphine data," stated Dr. Beebe. "Our findings show that Probuphine—which with only one treatment can provide a round-the-clock, effective low dose of buprenorphine over six months—has been effective in significantly decreasing illicit opioid use. We look forward to completing our currently ongoing Phase 3 confirmatory study early next year and potentially providing patients suffering from opioid addiction with a novel, safe, and effective treatment."

Data from Titan's completed Phase 3 randomized, placebo-controlled clinical trial of Probuphine in patients with opioid addiction were also recently published in the Journal of the American Medical Association (JAMA) October 13, 2010 issue. That article highlighted data from the 163-patient trial, which showed that patients receiving Titan's Probuphine implant had significantly less illicit opioid use, experienced fewer symptoms of withdrawal and craving, stayed in treatment longer, and had greater overall improvement when compared to placebo patients over the course of the six-month study.

Titan's ongoing Phase 3 confirmatory clinical trial of Probuphine for the treatment of opioid addiction is 50% funded by a grant from the National Institutes of Health (NIH) and the National Institute on Drug Abuse (NIDA). Patient enrollment in that trial is now complete and results are expected in the second quarter of 2011, approximately three months ahead of the original schedule. This study is part of Titan's registration-directed program intended to obtain marketing approval of Probuphine for the treatment of opioid addiction in the U.S. and Europe. For information concerning Titan Pharmaceuticals, Inc., please visit the company's website at www.titanpharm.com.

Blue Medical Receives European CE Mark Approvals for Drug Eluting Balloon and Stent on Drug Eluting Balloon Combination Device

PRNewswire: November 16, 2010 - HELMOND, NETHERLANDS - Blue Medical today announced that the company received CE Mark approval for Blue Medical science based Drug Eluting Balloon (DEB) and simultaneously for Blue Medical's coronary CoCr stent mounted on a Drug Eluting Balloon (CoCr Stent on DEB) in Europe for treatment of coronary diseases.

DEB therapy delivers a controlled dose of Paclitaxel to the coronary artery during balloon angioplasty. A unique combination of a one-time short and precise drug delivery with DEB during placement of a coronary stent is now for the first time approved and available in Europe.

"Increased late stent thrombosis risk and the long term dual anti-platelet medication which are associated with the majority of current drug eluting stents is a concern in treating our patients today," said Primary Investigator of the PIONEER Study Peter

Smits, M.D., head of Intervention Cardiology at the Maasstad Hospital, Rotterdam, The Netherlands. "DEB therapy in combination with bare metal coronary stents offers a potential solution for reducing late lumen loss without the need for long term dual-anti-platelet medication, improving patent comfort and reducing risks for bleeding and stent thrombosis."

The CE Mark approval is based on extensive *in vivo* research performed worldwide and preliminary data collected in Blue Medical's clinical trial, PIONEER. Based on the CE mark, Blue Medical will introduce the CoCr stent on DEB, called Pioneer, and its DEB, called Protege, across Europe by the end of the year.

"This CE Mark is the first approval by a regulatory agency for the use of DEB therapy in combination with a bare metal stent and provides a new attractive treatment for patients in Europe who are in need of other options," said Ronald Horvers, CEO of Blue Medical. "We worked closely with the respected Dutch competent authority CBG and with KEMA as notified body to ensure a solid science base for this CE approval."

Echo Therapeutics Announces Filing of 510(k) Submission Seeking Market Clearance from FDA for its Prelude SkinPrep System and 4% Lidocaine Cream

PRNewswire: November 11, 2010 - FRANKLIN, MA - Echo Therapeutics, Inc. (OTC Bulletin Board: ECTE), a company developing its needle-free Symphony™ tCGM System as a non-invasive, wireless, transdermal continuous glucose monitoring system and its Prelude™ SkinPrep System for transdermal drug delivery, today announced that a 510(k) premarket notification has been submitted to the U.S. Food and Drug Administration (FDA) for its Prelude SkinPrep System and 4% lidocaine cream. Market clearance is expected to take ninety (90) days.

"This is an important milestone in our initiative to create novel applications for our proprietary technology and follows the successful completion, in August 2010, of a clinical study that was designed to evaluate the effectiveness of Prelude to ablate the skin prior to the application of OTC 4% lidocaine cream for faster-acting local dermal anesthesia," stated Patrick T. Mooney, M.D., CEO, President and Chairman of the Board of Echo Therapeutics. "The use of Prelude to enhance the onset of topical lidocaine represents a near-term revenue opportunity for Echo Therapeutics. Together with our partner, Ferndale Pharma Group, Inc., we look forward to receiving FDA clearance and the subsequent generation of royalty revenue from product sales."

The Company believes that its needle-free Symphony™ tCGM System, which includes the Prelude™ SkinPrep System, can allow effective, needle-free glucose monitoring resulting in better patient outcomes in a critical care setting and for diabetic patients in an ambulatory environment. Prelude incorporates a patented skin permeation control feedback technology with a wireless, hand-held device that facilitates efficient and effective permeation of the tough outer layer of the skin. Prelude prepares a small area of the skin for Symphony's non-invasive biosensor and transceiver or for transdermal drug delivery applications.

Nuvo Research Announces Positive Top-Line WF10 Phase 2 Trial Results

PRNewswire: November 8, 2010 - MISSISSAUGA, ON - Nuvo Research Inc. (TSX: NRI), a specialty pharmaceutical company focused on the research and development of drug products that are delivered into and through the skin using its topical and transdermal drug delivery technologies and on the development of its immune modulating drug candidate WF10, today announced that its European Phase 2 clinical trial evaluating WF10 as a treatment for severe allergic rhinitis met its primary endpoint.

"These top-line results support our view that WF10 has the potential to become an effective treatment for patients with certain autoimmune conditions, such as severe allergic rhinitis," said Henrich Guntermann, President, Europe & Immunology Group for Nuvo Research. "We will evaluate the entire data set when it is available and consult with our advisors to determine the optimal path forward to maximize the value of WF10 for Nuvo and its shareholders."

The randomized, double-blind, placebo-controlled, single-centre trial assessed the efficacy and safety of WF10 infusions for the treatment of patients with severe persistent allergic rhinitis. The trial enrolled 60 patients who have at least a two-year history of persistent allergic rhinitis and who had a positive allergen skin test.

The trial met its primary endpoint as measured by the change in Total Nasal Symptom Score (TNSS) from baseline to assessment after three weeks comparing the WF10 group with the placebo group. The TNSS is a validated scale to measure the aggregation of nasal symptoms associated with allergic rhinitis. The p-value for the primary endpoint was less than 0.001 for the intent-to-treat and per protocol groups. No significant adverse events were observed during the trial, which was conducted at a clinic site that specializes in airway diseases in Leipzig, Germany.

The immune system provides an essential defense to microorganisms, cancer, and substances it sees as foreign and potentially harmful. WF10 focuses on supporting the immune system by targeting the macrophage, a type of white blood cell that coordinates much of the immune system, to regulate normal immune function. In conditions such as allergic rhinitis, the body's immune system inappropriately responds to the presence of foreign allergens. Research suggests that in some cases, WF10 may rebalance improperly functioning immune systems.

Nuvo is primarily focused on the research and development of drug products delivered into and through the skin using its topical and transdermal drug delivery technologies, and on the development of its immune modulating drug candidate WF10. Nuvo's lead product is Pennsaid, a topical non-steroidal anti-inflammatory drug (NSAID), which is sold in Canada, the United States, and several European countries. Pennsaid was approved for marketing in the U.S. by the United States Food

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and Drug Administration on November 4, 2009, and is being sold throughout the United States by Nuvo's licensing partner, Mallinckrodt Inc., a Covidien (NYSE: COV) company. Nuvo intends to create a portfolio of products through internal research and development and by in-licensing and acquisition. Nuvo is a publicly traded, Canadian pharmaceutical company headquartered in Mississauga, Ontario. Nuvo's Pain Group is located in West Chester, Pennsylvania. Its manufacturing facilities are located in Varennes, Québec and Wanzleben, Germany, and its research and development centers are located in San Diego, California and Leipzig, Germany. For more information, please visit http://www.nuvoresearch.com.

NovaSperse^{SM} Nanoparticle Innovator, PharmaNova, Inc., Awarded Four Government Grants Toward Development of New Therapeutic Products Under Congressional Qualifying Therapeutic Discovery Project Initiative

PRNewswire: November 8, 2010 - VICTOR, NY - PharmaNova, Inc., of Victor, NY, announced today that the company has been awarded multiple grants worth in excess of $500,000 under the Qualifying Therapeutic Discovery Project (QTDP), which was created by Congress as part of the Patient Protection and Affordable Care Act of 2010. In July, PharmaNova applied for project grants to support development of multiple NovaSperse^{SM} based nanoparticulate products. NovaSperse^{SM} is a unique process developed by PharmaNova for the de novo creation of nanoparticles of tightly controlled particle size. The process facilitates particle surface modifications and treatments that further influence solubility, absorption, distribution, and e.g., drug-tissue targeting. Grants were awarded to PharmaNova to support further research in the areas of anti-viral treatments, new treatments for ophthalmic disease, targeted delivery of oncology medicines, and the design and development of an implantable drug delivery device. The QTDP is overseen by the Internal Revenue Service and Health & Human Services Department, and is specifically designed to assist small biotech companies engaged in competitive and innovative discoveries in healthcare.

PharmaNova Inc. is a privately held pharmaceutical company. Our product candidates are derived from the re-positioning and enhancement of known drugs using our proprietary NovaSperse^{SM} nanoparticle technology platform. We address low risk, fast to market products in areas of clear medical need and generate revenue from partnering and licensing strategies with commercialization partners and clients worldwide. PharmaNova also conducts contractual formulation development work applying NovaSperse^{SM} technology to client-owned products and compounds to support new product development or the extended life cycle management of existing products. PharmaNova has new product candidates in various stages in its development pipeline. Our focus is on the development of novel, improved nanoparticle formulations of ophthalmic, anti-infective, and injectable oncology products. ■

38th Annual Meeting & Exposition of the Controlled Release Society

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

Innovative and Low-Cost Technologies for Healthcare and Consumer Products is the overall theme for this year's annual meeting. Here is a sample of the programming excellence that awaits you at the 38th Annual Meeting & Exposition of the Controlled Release Society.

PRE-MEETING EDUCATIONAL AND YOUNG SCIENTIST WORKSHOPS

Saturday

Young Scientist Workshop I: Understanding siRNA

Saturday–Sunday

CNS Drug Delivery: From Proof of Concept to Clinical Readiness
Introduction to Encapsulation and Controlled-Release Technologies

Sunday Morning

Pharmacologic and Regulatory Issues for the Translational Development of Nanoparticle Agents
Young Scientist Workshop II: Professional and Self Development for Young Scientists and Protégés

Separate registration is required for CRS Educational Workshops. Register by the advance registration deadline for the best rates and to ensure your place in one of these popular workshops! Young Scientist workshops are free of charge.

CRS INNOVATION SUNDAY

- Releasing Technology Workshops
- Soapbox Sessions
- Nanomedicine Product Development Summit
- CRS Innovation Sunday Special Programs
- Welcome Reception / Opening of the Exposition and Poster Hall

FEATURED PLENARY SPEAKERS

Gordon Amidon, Professor of Pharmacy, University of Michigan, U.S.A.
Gordon Muirhead, Global VP Manufacturing, GSK, United Kingdom
Walt Orenstein, Deputy Director for Vaccine-Preventable Diseases, Gates Foundation, U.S.A.

MINI-SYMPOSIA

The following mini-symposia and scientific sessions will be offered throughout the week providing attendees with a broad range of topics in controlled release and delivery.

Biological Research Tools
Bioresponsive Systems
Cancer Therapeutics
Exploiting the Nanoscale to Deliver Poorly Soluble Drugs
Microdevices
Quality by Design and Pediatric Drug Development

SCIENTIFIC SESSION TOPICS

Bioactive Materials

Biomaterials
Clinical Evaluations of Novel Drug Delivery Systems
Delivery to the Brain
Diagnostics
DNA and RNA Delivery
Functionalized Nanoparticles
Intracellular Delivery
Low Cost Drug Delivery Solutions
Medical Devices
Microspheres
Mucosal Delivery (nasal, vaginal, buccal and rectal)
New Polymer Chemistries
Oncology and Tumor Targeting
Ophthalmic
Oral Controlled Release
Pharmaceutical Manufacturing
Protein Delivery
Pulmonary Delivery
Regenerative Medicine Technologies
Transdermal Delivery - Debate Angstrom vs. Micron
Vaccines

Consumer & Diversified Products

Advances in Cyclodextrins for CR Applications
Characterization of Encapsulated Systems
Microencapsulation in Cosmetics, Personal and Homecare
Microencapsulation in Foods, Flavors and Nutraceuticals
Nanoparticles, Nanospheres and Nanopolymers
Regulations of Microencapsulated Products

Veterinary

New Frontiers in Drug Development: Translational Research and Models for Veterinary and Human Health

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The most up-to-date CRS Annual Meeting registration, housing, and program information can be found at www.controlledreleasesociety.org and click on "meetings." CRS Annual Meeting registration is scheduled to open mid-March, 2011.

CRS Delivering Bioactives

Speakers, topics, and dates subject to change.

Photo courtesy of National Harbor.

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

Calendar of Events

2011

2011 Society for Biomaterials Annual Meeting

April 13-16
Orlando, FL, U.S.A.
www.biomaterials.org

2011 AAPS National Biotechnology Conference

May 16-19
Hilton San Francisco Union Square
San Francisco, CA, U.S.A.
www.aapspharmaceutica.com/NationalBiotech

Second International Congress Immunopharmacology 2011

June 26–30
Meliá Varadero Hotel
Varadero Beach, Cuba
www.immunopharmacologycuba.com/

38th Annual Meeting & Exposition of the Controlled Release Society

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

71st FIP World Congress of Pharmacy and Pharmaceutical Sciences

September 2-8
Hyderabad, India
www.fip.org/congresses

2012

9th World Biomaterials Congress

June 1-5
New International Exhibition & Convention Center
Chengdu, China
www.wbc2012.com

39th Annual Meeting & Exposition of the Controlled Release Society

July 14-18
Centre des Congrès de Québec
Québec City, Canada
www.controlledreleasesociety.org/main/meetings