CRS Delivering Bioactives

Newsletter

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Delivering Bioactives

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

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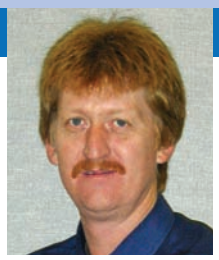


Roderick B. Walker
Rhodes University
Republic of South Africa

Transformation, Transparency, Governance, and Change

As the dust settles on the successful annual meeting held in National Harbor, I have had some time to reflect on a number of issues relating to the Society; in particular, to digest the changes that have been made to the governance of the society and the annual meeting. I do not intend to be comprehensive but I will share some thoughts relating to issues I feel are important for the Board to consider, and these relate specifically to those terms in the title of this editorial.

Change is inevitable, but it must take place in an open and transparent way (much as the bylaws were changed for the better) and the addition of new members to the Board is welcomed. Mark Tracy is to be commended for his efforts in changing the governance of the society so as to ensure that members have additional opportunities to participate in making the society a success. The society is in good hands as Martyn Davies takes over the reins as I am sure the Controlled Release Society (CRS) will thrive under his leadership. However, the role of scientific secretary seems to have been changed to be operated by a committee. Ijeoma Uchegbu did a great job, so perhaps there is truth in the idea that when you replace a woman you need a team to replace her. We need to see what transpires in this respect. Another particular area that requires attention is defining the role of the Board of Scientific Advisors in the society. They are advisors to the Board but in my opinion are hopelessly underused and their role should be transformed to ensure that they become an integral part of the planning committees of future meetings and workshops. Their position is vital, in my opinion, in ensuring that future meetings are of the highest quality and meet the needs of the members. Transformation of their role is imperative if the society wants to rise to even greater heights.

Another concern for me in particular relates specifically to the society considering itself global when it is still very much centered on the Northern Hemisphere (although the Australian Chapter won an award) and even then very much in North America and Europe. In order for it to be truly global, CRS must embrace the diversity of its members and must do so in such a way that acknowledges that attendance of the annual meeting (which is costly) is not possible for everyone.

The key to successful participation buy-in and to keeping people on board, in all structures in any organization, is good (no, excellent!) communication. The CRS Board has realized this and set up an ad hoc committee to look at this vital, yet neglected issue. Their work has commenced and we will look forward to their suggestions. However, a thank-you to those volunteers already working hard will go a long way to encouraging some to stay on and others to get the news that their participation is appreciated, and the society will move forward. Thank you to all volunteers that make the society what it is. Your input is vital and welcomed.

With these few thoughts, I am challenging CRS, the Board, and the membership to give thought to their role and how we can become a transformed CRS, with excellent governance structures that operate in a transparent way so that all of us are on the same page. If we get that right, the change to make the society better for the members will not be resisted but rather embraced.

Enjoy the information relating to the society and the annual meeting in this edition of the newsletter as it really is a great read. Well done to the Newsletter editorial team led by Yvonne Perrie, you have helped us do it again. ■

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

What a full year it has been for CRS! We have accomplished a lot for the Society as we prepare it for the new decade. As your President over the last year, I have really enjoyed the opportunity to work with so many of you. I feel very fortunate to be a part of the CRS family and deeply appreciate your support.

I have dedicated my term toward enhancing the strength of CRS in multiple dimensions and enabling increased benefits for members worldwide, year-round. As my term as President has now come to an end, I wanted to present to you a brief progress report on the top ten priorities for CRS in 2010–11:

1. Update governance structure and bylaws
   - ✓ Updated bylaws approved by CRS membership in June.
2. Build new, information rich website
   - ✓ New, updated website launched in July along with new LATTE database, a new CRS jobs center, annual meeting abstracts, and growing webinar program.
3. Complete management review
   - ✓ CRS management reorganized in January with staff leadership and marketing resources strengthened.
4. Establish multi-year financial planning process
   - ✓ Multi-year financial planning process initiated with enhanced committee oversight of budget.
5. Organize and hold effective Leadership Team meeting
   - ✓ Leadership Team conference calls and face-to-face meeting held July 29, 2011 at the annual meeting.
6. Review annual meeting and future meeting sites
   - ✓ Annual meeting model updated and sites picked for 2013 (Honolulu) and 2014 (Chicago) Annual Meetings. Selection of European site for 2015 in progress.
7. Enhance our industry-oriented science and technology activities
   - ✓ Held new delivery translational R&D and regulatory programs including January Product Development Meeting in Miami and Annual Meeting Innovation Sunday Program, workshops, and sessions.
8. Disseminate world-class science through an innovative annual meeting and successful launch of new publications
   - ✓ Held successful 2011 Annual Meeting, achieved highest impact factor to date (7.164) for *Journal of Controlled Release,* launched new journal *Drug Delivery and Translational Research* and first volume in new CRS book series entitled Controlled Pulmonary Drug Delivery.
9. Initiate strategic research and planning process toward defining a 20/20 roadmap for CRS
   - ✓ Initiated strategic planning process in January toward updating CRS Strategic Plan.
10. Enhance communication of CRS: mission, priorities, activities, and plans
    - ✓ *CRS Newsletter,* News Capsules and emails, Leadership Team meetings, and website included regular updates on priorities, activities, and plans.

In addition, over the last year, we importantly established the CRS College of Fellows and have now inducted two classes into the new College. We also established a new chapter in China, continued our strong young scientist and mentorship programs, continued our new CRS Partnering program and important networking activities, awarded a scholarship in honor of Prof. Nagai through the CRS Foundation, and advanced our webinar program and library in preparation for a formal launch after the new website is in place.

All this is to say, we had a productive year and met our primary goals and more. The CRS leadership, volunteers, and staff are truly dedicated to delivering delivery science and technology to you, the CRS family of members, across the globe every day of the year. There is more work to be done of course as we complete and implement the new strategic plan. I have been working closely with new President Martyn Davies to ensure a smooth transition as his presidency begins. He will write to you beginning with the next edition of the *CRS Newsletter*. As immediate Past-President, I look forward to working with Martyn to build on the recent progress and continue to advance CRS for the new decade. Thank you again for your support over the last year! ■

CRS 2011 Awards

College of Fellows

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

Diane Burgess
University of Connecticut
U.S.A.

Jonathan Hadgraft
University of London
U.K.

Harlan Hall
Coating Place
U.S.A.

W. E. Hennink
Utrecht University
The Netherlands

Ram I. Mahatok
University of Tennessee
U.S.A.

Antonios Mikos
Rice University
U.S.A.

Ron Versic
Ronald T. Dodge Co.
U.S.A.

Founders Award

Mauro Ferrari
The Methodist Hospital Research Institute
U.S.A.

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

Young Investigator Award

Co-sponsored by Aptalis Pharmaceutical Technologies

Molly Stevens
Imperial College
U.K.

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

CRS T. Nagai Postdoctoral Research Achievement Award

Co-sponsored by The Nagai Foundation Tokyo

Christopher Jewell
Massachusetts Institute of Technology
U.S.A.

Darrell Irvine
Massachusetts Institute of Technology
U.S.A.

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

Jorge Heller *Journal of Controlled Release* Outstanding Paper Award

Co-sponsored by Elsevier

This award recognizes an outstanding regular paper related to the science of controlled release (not an invited, review, or special meeting paper) that was published during 2010 in the Journal of Controlled Release.

Fabio Pastorino
Gaslini Children's Hospital
Italy

Co-Authors
Theresa Allen, *University of Texas, U.S.A.*
Wadih Arap, *University of Texas, U.S.A.*
Pamela Becherini, *Gaslini Children's Hospital, Italy*
Chiara Brignole, *Gaslini Children's Hospital, Italy*
Federico Bussolino, *University of Torino, Italy*
Irene Caffa, *Gaslini Children's Hospital, Italy*
Michele Cilli, *National Cancer Institute, Italy*
Angelo Corti, *San Raffaele Institute, Italy*
Flavio Curnis, *San Raffaele Institute, Italy*
Daniela De Paolo, *Gaslini Children's Hospital, Italy*
Claudio Gambini, *Gaslini Children's Hospital, Italy*
Monica Loi, *Gaslini Children's Hospital, Italy*
Renato Longhi, *CNR, Italy*
Serena Marchio, *University of Torino, Italy*
Beatrice Nico, *University of Bari, Italy*
Gabriella Pagnan, *Gaslini Children's Hospital, Italy*
Renata Pasqualini, *University of Texas, U.S.A.*
Patrizia Perri, *Gaslini Children's Hospital, Italy*
Mirco Ponzoni, *Gaslini Children's Hospital, Italy*
Domenico Ribatti, *University of Bari, Italy*
Marco Soster, *University of Torino, Italy*

Outstanding Consumer & Diversified Products Best Paper Award

Co-sponsored by Colgate-Palmolive Company

This award recognizes a CRS member whose winning abstract relates specifically to delivery of active ingredients in consumer or industrial products.

Tridib Bhowmick
University of Maryland
U.S.A.

Outstanding Pharmaceutical Best Paper Award

Co-sponsored by Elan Drug Technologies

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

Oleh Taratula
Rutgers University
U.S.A.

Outstanding Oral Drug Delivery Best Paper Award

Co-sponsored by Banner

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

Daniel Cho
Brown University
U.S.A.

Novel Cationic Lipids for Safe and Efficient siRNA Delivery

Mamta Kapoor [1], Muthusamy Jayaraman [1], David Butler [1], Kallanthottathil G. Rajeev [1], Diane J. Burgess[2], and Muthiah Manoharan[1]

Introduction

RNAi (RNA interference), a gene silencing mechanism used by cells, was discovered in the late 1990s. This new approach utilizes small RNAs (silencing RNA – siRNA) to silence expression of certain genes that are responsible for specific disease conditions. Since the discovery of siRNA, several research groups are focusing on using this technology for therapeutic purposes (1–3). Unfortunately, siRNA, like DNA, also has issues with delivery, specifically with cellular uptake and endosomal escape. To solve these issues, several viral and non-viral vectors have been employed (4,5). Nevertheless, non-viral vectors are the preferred choice due to their safety and non-immunogenicity compared to viral vectors (6,7). Of the non-viral vectors, cationic liposomes profoundly help in both cellular entry and endosomal escape of the siRNA (5). Being cationic, these liposomes are toxic (8) due to interaction with negatively charged serum proteins. Optimization of cationic content and the use of structurally modified cationic lipids can be used to prepare liposomal formulations with minimal toxicity. This is possible since it has been shown that the silencing efficiency and toxicity of cationic liposomes can be altered by structural modification of three key domains of cationic lipid namely, the head group, the hydrophobic tail, and/or the linker (between the head and the tail). Several novel cationic lipids have been designed and synthesized in the past to achieve efficient *in vivo* siRNA delivery (9,10). Some examples of modifications that resulted in improved efficacy are: unsaturation in the hydrophobic lipid chain (11), guanidinium (12), hydroxyalkyl (13), or cyclic amino groups (14) in the head group and ether linkage between the head group and the tail (15). To minimize the toxicity of cationic lipids, ester linkages are ideal compared to other linkages such as ether and carbamate due to biodegradability of the former (16).

To further improve the silencing efficiency and reduce the toxicity of cationic liposomes, cationic lipid concentration and N/P (amines to phosphates) ratios have been shown to be crucial (17–19).

From the above cited literature, it is understood that lipid structure modification can help prepare liposomes that are safe and efficient for siRNA delivery. Therefore, in this work, we have designed and synthesized permanently charged novel cationic lipids and developed these into transfection agents for safe and efficient *in vitro* siRNA delivery in adherent mammalian cell lines such as HeLa, Hep3b, and B16F10 cells.

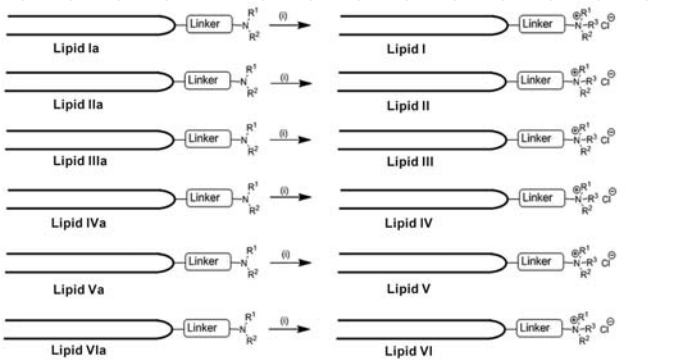
Experimental Methods

We synthesized six cationic lipids (coded as Lipids **I, II, III, IV, V** and **VI**) by quaternization of six structurally different tertiary amines with unsaturated hydrophobic tails, using microwave synthesis for 2 h at 100°C. Lipids **I–VI** were structurally different. Lipid **Ia** (Figure 1) was synthesized and reasonable head group, linker and or tail modifications were performed to potentially alter the silencing efficiency. For example, all lipids except Lipid **IIIa** had an unsaturated hydrophobic tail with one saturated lipid chain. Lipid **Ia** and its modified versions (Lipid **IIa–VIa**) were then quaternized to obtain their respective cationic lipids (Lipid **II–VI**).

Six individual liposome formulations were prepared, using each lipid in combination with DOPE and cholesterol and the component ratios were optimized for safety and efficacy. The liposomes were prepared using film hydration, followed by extrusion to obtain a mean particle size of approximately 200 nm. Anti-*firefly* luciferase was used as the siRNA. Transfection studies were performed in the presence of 10% serum. *Firefly* and *renilla* luciferase expression was determined at 24h post transfection using a luminometer. In the case of HeLa cells, the *firefly* luciferase expression was normalized to *renilla* luciferase expression to obtain accurate results. For the same reason, in the case of Hep-3b and B16F10 cells, the firefly luciferase expression was normalized to siRNA that doesn't knockdown *firefly/renilla* luciferase (scrambled control). Cell viability studies were performed using Promega Cell-Titer Blue reagent with (2.5 h, 37°C). A spinning disc confocal microscope was used (488/647 laser) to image the uptake of Alexa488 labeled siRNA and this was quantified via flow cytometry.

Results and Discussion

Transfection studies using a novel cationic lipid based liposomal formulations in HeLa cells with 10 nM siRNA, showed efficient silencing by all six formulations (Lipids **I, II, III, IV, V** and **VI**).



***Scheme 1**: Representative scheme for synthesis of cationic lipids. (i) Chloroalkane (R^3-Cl)/ $CHCl_3$-ACN (1:1 v/v), 100°C, microwave, 2 h. Lipids **I-VI** were purified by flash silica gel column chromatography; yield 75-90%.*

Figure 1. *Representative scheme for synthesis of cationic lipids. (i) Chloroalkane (R^3-Cl) / $CHCl_3$-ACN (1:1 v/v), 100°C, microwave, 2 h. Lipids **I–VI** were purified by flash silica gel column chromatography; yield 75–90%.*

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2 Department of Pharmaceutical Sciences, University of Connecticut, Storrs, CT, 06269, U.S.A.

Due to structural differences in the lipids, the liposomes were not equally efficient at the same mol%. Liposomes prepared with lipids **V** and **VI** (85% knockdown) were the most efficient in HeLa cells while those prepared with lipid **III** were the least efficient (66% knockdown). The efficiency of lipid **V** and **VI** was comparable to LF2000 (83%) and RNAiMax (90%) and much better than DOTAP:DOPE (20%) (Figure 2A). Lipid **III** was less efficient than Lipid VI, even in Hep3b cells (hepatocellular carcinoma) (Figure 2B) and B16F10 cells (murine melanoma). (Figure 2C) Silencing efficiency (knockdown) of lipid **III** was 35% and 21%, respectively in the two cell lines, when compared lipid **VI** (51% and 46%, respectively).

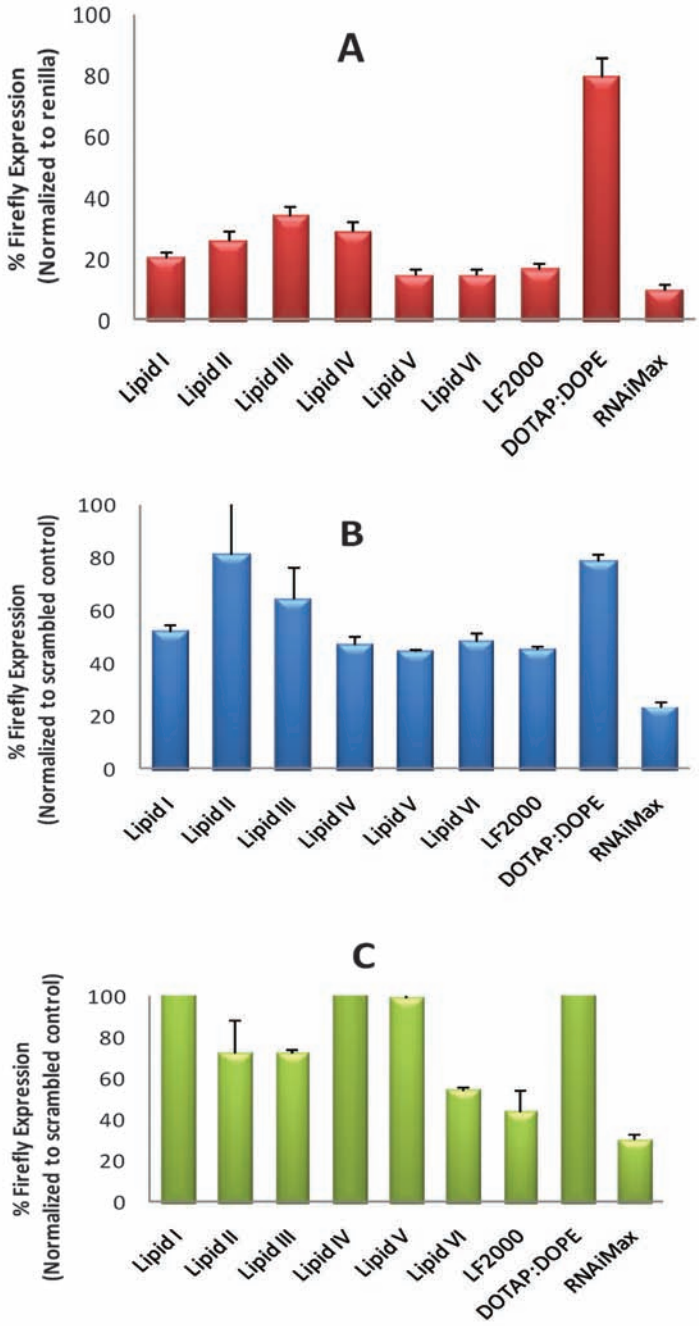

Figure 2. *Percentage firefly expression from novel cationic lipid formulations, (A) HeLa cells, (B) Hep3b cells, and (C) B16F10 cells, at 10 nM siRNA concentration. RNAiMax was used as per manufacturer's protocol.*

The high transfection efficiency of lipid **VI** was supported by its superior uptake into HeLa cells as indicated by intense accumulation of the nucleic acid after 4 h (Figure 3). Although the uptake of Lipid **VI** was comparable to LF2000 and RNAiMax, there was relatively less punctate and more diffused staining with Lipid **VI,** thus demonstrating its ability to efficiently assist in endosomal escape. On the contrary, Lipid **III** showed poor uptake which is in agreement with the flow cytometry data, where the median fluorescence intensity (MFI) of lipid **III** was 478 compared to 1,774 for Lipid **VI.** Lipid **III** also showed poor endosomal escape, as indicated by more punctuate than diffused staining. This may be the key reason for the poor silencing efficiency of lipid **III** which may be related to its structural interaction with the fusogenic lipids. Poor uptake and poor endosomal release are probably the key reasons for the inferior silencing efficiency of Lipid **III** compared to Lipid **VI.**

These observations can further be explained by differences in structural interactions of biological membranes with the structurally different lipids. Lipid **VI** contains two unsaturated lipophilic tail whereas in Lipid **III** one of the two lipophilic tails is replaced with a saturated alkyl with the same number of carbon atoms. The structural change in the Lipid **III** chain may

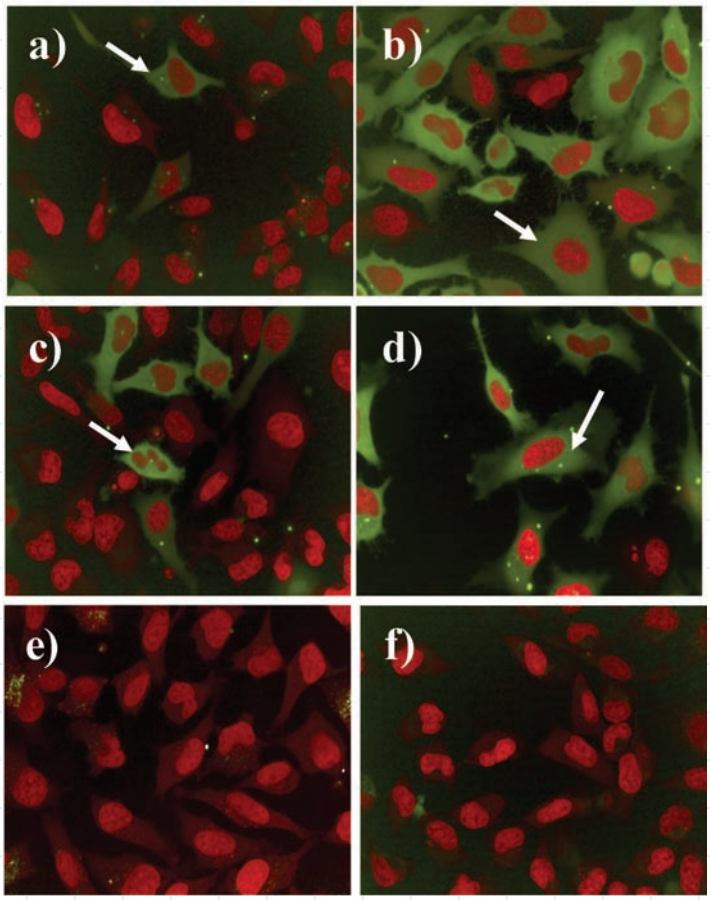

Figure 3. *Confocal images of novel lipid formulations (2µg/mL) with 100 nM siRNA after 4 h uptake (n=3) in HeLa cells. Draq5 (red) was used to stain nucleus and weakly stain cytoplasm. Alexa488 (green) indicates siRNA (arrows). a) Lipid III, b) Lipid VI, c) LF2000, d) RNAiMax, e) DOTAP:DOPE, f) siRNA alone.*

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Scientifically Speaking Kapoor continued from page 7

attribute to the less observed uptake due to an unfavorable change in fusogenicity of the lipid chain to biological membranes (20).

As far as the toxicity profile of the lipids is concerned, Lipid **VI** was far safer than LF2000 and Lipid **III,** even at 30 µg/mL lipid concentration, where the observed cell viability was 80% compared to 50% with LF2000 and Lipid **III.** The cytotoxicity profile as determined by IC50 values shown in Table 1, further confirms the tolerability of the transfection agents with the cell lines evaluated.

Table 1. IC50 values (µg/mL) obtained from novel lipid formulations determining their cytotoxicity, in HeLa cells. IC50 value refers to the lipid concentration that keeps 50% of cells as viable.

	IC50 (µg/mL)
Lipid **III**	48.15
Lipid **VI**	> 100
LF2000	27.35
DOTAP:DOPE	> 100

Conclusion

Six novel cationic lipids were synthesized in high yield and assessed for their ability to transfect siRNA and elicit gene silencing in various mammalian cell lines *in vitro*. Of these, the formulation using the novel cationic Lipid VI had comparable transfection efficacy and an improved safety profile compared to the commercially available formulations. In contrast, Lipid III showed inferior transfection efficiency, an observation which is probably related to key differences in the lipid structure that affects both cellular uptake and endosomal release.

The Lipid **VI** formulation qualifies as a potential candidate as an *in vitro* transfection reagent for siRNA delivery.

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Mamta Kapoor received her M.S. in Pharmaceutics from the National Institute of Pharmaceutical Sciences and Research (NIPER), Punjab, India. After gaining industrial experience as a research associate in Nicholas Piramal (now called Piramal Life Sciences) in Mumbai, India, she is currently pursuing her Ph.D. degree under the supervision of Dr. Diane J. Burgess at the School of Pharmacy in the University of Connecticut, CT, U.S.A. Her research work is related to formulation development using cationic/anionic lipid-based delivery vectors for safe and highly efficient siRNA delivery.

Dr. Muthusamy Jayaraman (MJ) is a Principal Scientist in the Drug Discovery group at Alnylam Pharmaceuticals, Cambridge, MA, since January 2006. His current work focuses on drug delivery in general and lipid nanoparticle mediated delivery of oligonucleotides in particular. Prior to joining Alnylam, MJ worked at Organix Inc. in Woburn, MA for six years. MJ did his postdoctoral research at Purdue University with Professor Mark Cushman in Medicinal Chemistry focusing on oncology research. MJ's doctoral research at the National Chemical Laboratories, Pune, India was on asymmeric synthesis of beta-lactams from readily available homochiral precursors.

Dr. David Butler, Principal Scientist in the Drug Discovery group, has been with Alnylam for four years. Prior to joining Alnylam, David worked with Dr. Jayaraman at Organix for six years. He obtained his Ph.D. in 1997 under the supervision of Prof. David Cole-Hamilton at the University of St. Andrews in Scotland studying the catalysis of organic reactions. Postdoctoral stints at the University of Ottawa with Dr. Howard Alper, then at Queen Mary, University of London with Dr. Christopher J. Richards were followed by his relocation to the Boston area.

Dr. Kallanthottathil G. Rajeev, Director of Drug Discovery at Alnylam Pharmaceuticals, Cambridge, MA joined the organization in June 2003. Prior to joining Alnylam, Rajeev worked at Isis Pharmaceuticals, Carlsbad, CA. He obtained his Ph.D. in 1997 with Dr. Krishna N. Ganesh at the National Chemical Laboratory, Pune, India. He carried out postdoctoral research at the University of Utah with Prof. Arthur D. Broom before joining Isis Pharmaceuticals in October 2000.

Dr. Diane Burgess is Distinguished Professor of Pharmaceutics at the University of Connecticut. She has over 140 refereed publications, over 360 research presentations at major scientific meetings, over 180 invited lectures, and 14 keynote addresses. Research efforts focus on gene and drug delivery: microspheres, emulsions, liposomes, hydrogels, as well as interfacial chemistry and implantable biosensors. Dr. Burgess was the 2002 President of the American Association of Pharmaceutical Scientists (AAPS) and is an AAPS fellow. She was President of CRS in 2009–2010. She is editor of the International Journal of Pharmaceutics and serves on the editorial boards of nine international journals.

Dr. Muthiah Manoharan is the Senior Vice President of Drug Discovery at Alnylam Pharmaceuticals where he has led the chemistry group since 2003. He was the former Executive Director of Medicinal Chemistry at Isis Pharmaceuticals, Inc., where he had 12-year tenure. He was born in Madurai, Tamil Nadu, India and received his college education at American College, Madurai. He earned his Ph.D. in Chemistry at the University of North Carolina-Chapel Hill (with Prof. Ernest Eliel) and conducted post-doctoral work in Bioorganic Chemistry at Yale University and the University of Maryland (with Prof. John Gerlt). With a distinguished career as a nucleic acid chemist, Dr. Manoharan is an author on over 150 publications and over 250 abstracts, as well as the inventor on over 125 issued U.S. patents. ■

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Microencapsulation and Controlled Release of Probiotic Bacteria for Functional Foods

Claude P. Champagne
Agriculture and Agri-food Canada, Food R & D Centre, 3600 Casavant, St. Hyacinthe, QC, J2S 8E3, Canada

Functional Foods and Probiotics

The link between food and health is of increasing interest to consumers and attention has focused beyond the basic contribution of foods in protein, vitamin, mineral, or sugar nutrients. Many consumers now look for specific bioactive ingredients that reportedly reduce the risk of developing cancer or various cardiovascular, immune, and intestinal diseases. Foods that contain these ingredients are often called "functional foods." Popular "health-promoting" ingredients that are used to "enrich" foods include fibers, phytosterols, antioxidants, omega-3 oils, and probiotic bacteria. Probiotics are defined as "live microorganisms which, when administered in sufficient quantity, confer a health benefit to the host." As this definition implies, there are two critical components in the functionality of probiotics: they must be viable and there must be a certain quantity.

There is no "magical number" of probiotics required for activity. In the past, a million cells per mL was considered enough, but the trend today is about ten times that. As an example, the Canadian Food Inspection Agency requites a billion (10^9) cells per portion at the "best before" date in order to apply for a non-strain related allegation (1).

Probiotics: What Makes them Different from Other Bioactives for Functional Foods?

The main difference between probiotics and the other bioactives mentioned previously is that they are alive! This brings a specific set of problems in foods: probiotics may die during processing (freezing, heating, high-shear operations) as well as during storage (exposure to oxygen or high acidity). Therefore, means of keeping them alive must be developed. Microencapsulation (ME) of the cells is one of the tools food processors have to achieve this goal. As a function of the food matrix, we may therefore ask of ME to enhance survival of the cells to a heating step or reduce their exposure to a potentially toxic compound such as organic acids.

Figure 1. *Addition of a freeze-dried* Lactobacillus rhamnosus *culture to a cold cranberry juice concentrate resulted in a loss of cell viability of more than 99% within 15 minutes (7).*

To illustrate the challenge, let's look at the simple task of adding them to a beverage. Unfortunately, the mere act of mixing a powder of probiotic bacteria to a cold fruit drink, for example, might result in the death of more than 99% of the cells within 15 minutes (Figure 1). First of all, rehydration of probiotics in a cold (4°C) environment results in much lower viability than if done in a warm medium (30°C to 37°C). Secondly, a medium pH around neutrality is much better for cell viability. Thirdly, the oxygenation of the juice that inevitably occurs during mixing might in itself threaten viability of these often anaerobiosis-preferring organisms. And if the subsequent life-threatening conditions in food processing and storage were not enough, there is the additional challenge of surviving exposure to the high acidity of stomach and to the bile salts. Life can be tough for probiotics in foods!

Microencapsulation to the Rescue

The losses in viability are very much dependent on the strain used. Therefore, when a non strain-dependant allegation is targeted, selection of the strain is the paramount concern for the development of the functional food. However, if a given strain is chosen because of demonstrated clinical benefits, then stability might become an issue. Numerous studies have shown that ME works in improving the stability of probiotics during heating (4,7), freezing (8), and storage (6). Therefore, scientific benefits of this technology are well established.

There are many encapsulation methods for ingredients in foods. One of the most popular is spray-drying of emulsions, which encapsulates oils or lipophilic compounds. Unfortunately, spray drying is ill-adapted to probiotics because of the high temperatures used. Nanotechnologies are also inadequate because of the size of the bacteria. Therefore, after having to discard some popular ME technologies, the two most widely used techniques for the ME of probiotics are alginate gel beads (Figure 2) and spray-coated powders (Figure 3). The alginate particle will delay mass transfer of heat and solutes and temporarily provide a microenvironment which is different from that of the food matrix. The spray-coated products are more efficient than alginate in delaying entrance of solutes inside the particle because the coating is typically constituted of lipids.

Scientifically Speaking Champagne continued on page 12

Scientifically Speaking Champagne continued from page 11

Microencapsulation for Survival in Foods: It Works Indeed but…

Let's imagine a case where a manufacturer hopes to market a product with 1 billion cells per portion. This is the number that has to be found at the end of the storage period. Adding 1 billion cells costs less than 1 cent ($0.005) which, at first glance, is not much. But if 1 log of viability loss occurs during processing and storage, then 10^{10} cells need to be initially added. That means the cost of supplementation rises to $0.05 per portion. In yogurt, this represents about 5% of the cost of the product. Arguably, for most food and beverage manufacturers where profit margins are thin, this is a considerable per-portion cost for a single ingredient. Therefore, for many food applications, manufacturers must keep viability losses under 1 log. Unfortunately, in many cases (and this is very much dependant on the strain used), viability losses are much greater than 1 log. An example for biscuits is shown in Table 1.

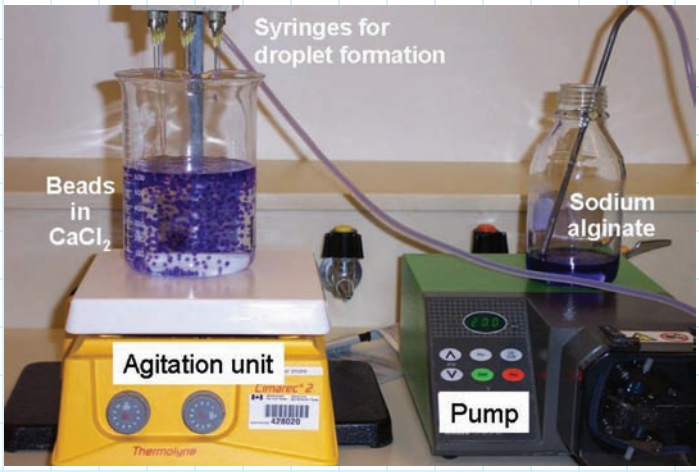

Figure 2. *Production of alginate beads. The sodium alginate solution (at right; blue color added) is pumped and added dropwise into an agitated calcium chloride solution. The Beads can subsequently be dried by free-drying or fluidized bed air drying.*

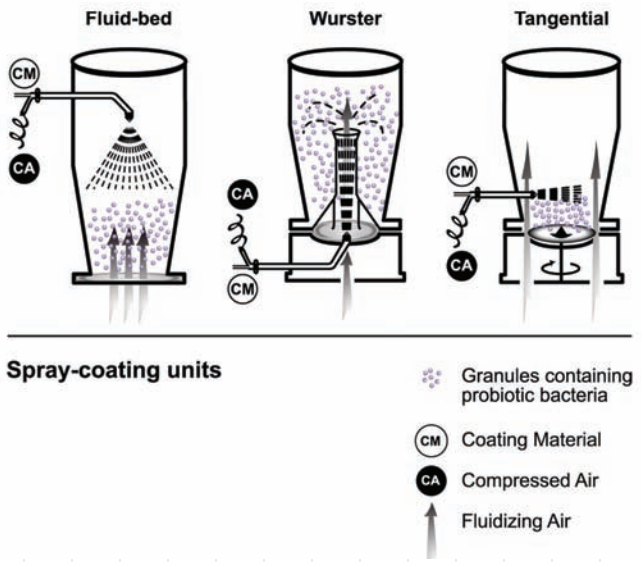

Figure 3. *Fluidized bed coating technologies which can be applied to the microencapsulation of dried probiotic bacteria.*

Although ME significantly improves stability of the cultures in the biscuit, it has simply not provided enough stability enhancement to make the product economically attractive. Thankfully, there are food matrices where probiotics are more stable, and one such example is vegetable juice (Table 1). In this beverage matrix, ME could maintain the viable count loss during storage under the 1 log threshold, while free cell inoculation could not. Therefore, it is foreseeable that ME will have economic success in foods that are not highly detrimental to probiotic viability but where viability losses with free cells are a fraction too high for economic application. It must also be kept in mind that ME products are more expensive than the original free-cell ones. Therefore, the benefits on viability must at least outweigh the increase in costs.

Probiotics: Are There Also Needs for Controlled Release?

As for most bioactive compounds, probiotics must be delivered at a site where they exert their activity. The gastrointestinal tract (GIT) is the principal target. In cases where food manufacturing or storage conditions are detrimental to cell viability, the best scenario is to prevent cell release in the food as well as in the stomach, but to allow release of the bacteria in the intestines.

With respect to the alginate beads, data show that they remain intact in dairy foods and in the stomach environment. However, they dissolve in the duodenum (5), presumably due to compounds that bind calcium, such as carbonates, which are secreted by the pancreas or epithelial cells of the GIT.

With lipid coatings, the fat that is chosen must not melt at body temperature in order to prevent cell release in the stomach. Thus, the release mechanism, or "trigger," must not be linked to temperature. Rather, the lipid coating must be selected on the basis of dissolution by bile salts or on the basis of hydrolysis by pancreas lipases. Once the cells are freed in the duodenum, they can exert their potential benefit to health.

It could even be argued that cell release at the beginning of the duodenum might be a problem because of the high levels of potentially toxic bile salts. Thus, coatings other than fat could also be used, such as protein or polysaccharides, where release of the cells would be linked to hydrolysis of the protective layer by the enzymes of the GIT further down the small intestine.

Table 1. Effect of microencapsulation (ME) in whey protein gel particles on viability of *Lactobacillus rhamnosus* R0011 in biscuits or vegetable juices. Table prepared from data in Reid et al. (7).

	Biscuits (CFU/g)		Vegetable Juice (CFU/mL)	
Time	Free	ME	Free	ME
Inoculated	1.3 × 107	1.3 × 107	2.0 × 108	2.0 × 108
1 day	< 1 × 103	4.5 × 105	1.6 × 107	8.0 × 107
7 days	< 1 × 103	< 1 × 103	1.6 × 107	5.0 × 107
14 days	–	–	1.6 × 107	5.0 × 107

Microencapsulation for Many Reasons

Food manufacturers need to keep a critical view of the benefits of ME. In many cases, the protection might be insufficient and other technological means will need to be examined (2). However, one should always consider ME in the tool box because there are cases where the economic benefits will indeed be obtained.

But even in instances where ME has only a small technological benefit or when a strain simply does not need protection to remain stable in the food product, ME might still be of use for the sole purpose of enabling a controlled release in the GIT. Indeed, improved survival to passage through the stomach is a well-documented benefit of ME (3). Thus, it can be predicted that ME of probiotics in foods will eventually be used for controlled cell release in the GIT rather than for their technological benefits.

Finally, ME might simply be attractive because of potential product differentiation. With most ME products, the particles are big enough to be seen and influence mouth feel. Most manufacturers do not wish that the addition of probiotic cultures results in changes to the sensory properties. But there might be cases what clearly "seeing" the bioactive ingredient could actually constitute a marketing benefit.

In summary, there are three reasons why ME cold be useful for the ME of probiotics: protection in the food, controlled release in the duodenum, and product differentiation. One should remain critical of ME's potential benefits, but the technology certainly warrants consideration.

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Thirsty for Knowledge and Connections? CRS's New LATTE is Your Solution!

At present, some CRS members are consultants, expert witnesses, scientific advisors, and partners in projects with industry. It is likely that many more members could be tapped for these activities if there was an easy way for interested parties to identify individuals with a specific expertise.

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LATTE is built upon specific results about the CRS member. A CRS expert participant provides essential demographic and professional data, including contact information, geographical location and affiliations, a short resume of work experience, and a short publications list. These results frame the expert in an appropriate context and serve the search functionality of LATTE.

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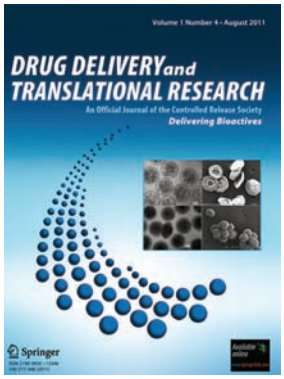
Drug Delivery and Translational Research

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



I've been thinking that summer is a good time to update everyone on the progress of *Drug Delivery and Translational Research* (*DDTR*), our society's newest journal, through this issue of the *CRS Newsletter*. Since its formal launch a year ago at the CRS Annual Meeting in Portland, *DDTR* has published four well-received issues. As you will note from the published papers in these issues, we are pleased to have fulfilled our primary aim: to provide our readers with the latest research addressing translational aspects of drug delivery. We intend to keep *DDTR* focused on providing this useful forum of drug delivery issues. As we know, clinical outcomes, in part, depend on the effectiveness of the drug treatment. Many drugs, although effective, have serious side effects or fail to reach their target site or maintain therapeutic levels. Thus, there is a strong push in the clinical and research communities to explore rationally developed drug delivery systems targeting a range of disease conditions so that patients can be more effectively treated.

Of course, designing effective drug delivery systems focused on specific disease conditions requires a broad understanding of several aspects of disease—among them, the pathophysiology of disease, the effective dosing and duration of therapy, the pharmacokinetics of drug distribution, the effective dosage form design, the means of delivery (e.g., polymers and their stability/degradation *in vivo*), and the interaction of drug delivery systems with the biological environment to ensure biocompatibility. Because of variations in the pathophysiology of different diseases, drug delivery systems need to be tailored, from simple sustained-release implants that provide therapeutic doses of a given drug over time to complex systems such as those that respond to a specific need (e.g., insulin-releasing devices that provide a precise drug dose in response to changes in blood sugar levels). Thus, drug delivery is a complex, multidisciplinary field, requiring expertise encompassing biology to polymer chemistry, pharmaceutical science, biomedical engineering, clinical pharmacology, and toxicology.

The general goals of a drug delivery system include improving the therapeutic index of the drug(s) while minimizing their toxicity, improving clinical outcomes, finding new treatments through novel drug delivery systems, and bettering the performance of devices such as implantable drug infusion pumps for chronic drug therapy. Polymeric drug delivery systems can maintain a therapeutic dose of a drug in the target tissue for an extended period of time, and this reliable sustained delivery can significantly enhance the clinical outcome and improve patient compliance in relation to complex drug therapies. In addition, specialized drug delivery systems are needed for molecules that are highly unstable in the biological environment, such as proteins and peptides, siRNA, and genes. Similarly, in the discipline of regenerative medicine, biomaterials with growth factors have been extensively investigated to facilitate the differentiation of stem cells.

Several examples show how drug delivery systems have successfully been applied to resolve clinical conditions. One important example in cardiovascular medicine is drug-eluting stents to prevent post-angioplasty restenosis. Another successful application of drug delivery is pacing electrodes that provide slow, sustained release of dexamethasone to prevent scar tissue buildup at the contact point with the heart so that the pacing threshold does not change over time. Interest in drug delivery research is steadily increasing on both scientific and corporate fronts because of its potential impact on the health of patients as well as on the economy.

The editors of *DDTR* are in the process of developing several special theme issues in the areas of nanotechnology, image-guided drug delivery, regenerative medicine, stem cells, CNS delivery of therapeutics, etc. The third issue of 2011, on Advances in Vaginal Drug Delivery, edited by David R. Friend, was a themed issue. It was very well received by the readership, as is evident from the number of articles downloaded since its publication.

As you may be aware, *DDTR* is available online to CRS members as a benefit—at no additional charge. To access this new journal as part of your member benefits, go to www.controlledreleasesociety.org and click the Publications tab at the top to get to the member access link. We are also pleased to announce the new *DDTR* Outstanding Paper Award. Please visit the CRS website for more details. I urge you to join the leading scientists who are publishing their work in *DDTR*.

Editor-in-Chief

Vinod Labhasetwar, Ph.D., is a full professor in the Department of Biomedical Engineering, Lerner Research Institute, Cleveland Clinic, and in the Cleveland Clinic Lerner College of Medicine of Case Western Reserve University in Cleveland, OH, U.S.A. He leads Cleveland Clinic's Cancer NanoMedicine Program. His research focus is on translational nanomedicine and drug delivery, particularly in the areas of cancer, stroke, and cardiovascular diseases. His laboratory also investigates biophysical interactions of nanomaterials with cells to develop unique nanostructures for efficient drug/gene delivery applications.

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Associate Editor

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Journal of Controlled Release Top 10 Downloaded Articles

Discover what your colleagues are downloading and reading. Below is a listing of the top 10 downloaded articles from the *Journal of Controlled Release* as of June 22, 2011.

1. **Biodegradable polymeric nanoparticles as drug delivery devices.** Volume 70, Issue 1-2, January 2001, Pages 1-20.
2. **Recent advances on chitosan-based micro- and nanoparticles in drug delivery.** Volume 100, Issue 1, November 2004, Pages 5-28.
3. **Nanotechnology and the transdermal route.** Volume 141, Issue 3, February 2010, Pages 277-299.
4. **The forthcoming applications of gold nanoparticles in drug and gene delivery systems.** Volume 149, Issue 1, January 2011, Pages 65-71.
5. **To exploit the tumor microenvironment: Passive and active tumor targeting of nanocarriers for anti-cancer drug delivery.** Volume 148, Issue 2, December 2010, Pages 135-146.
6. **Antibody derivatization and conjugation strategies: Application in preparation of stealth immunoliposome to target chemotherapeutics to tumor.** Volume 150, Issue 1, February 2011, Pages 2-22.
7. **New insights into and novel applications of release technology for periodontal reconstructive therapies.** Volume 149, Issue 2, January 2011, Pages 92-110.
8. **New trends in encapsulation of liposoluble vitamins.** Volume 146, Issue 3, September 2010, Pages 276-290.
9. **Gold nanoparticle platforms as drug and biomacromolecule delivery systems.** Volume 148, Issue 1, November 2010, Pages 122-127.
10. **Intravesical drug delivery: Challenges, current status, opportunities and novel strategies.** Volume 148, Issue 2, December 2010, Pages 147-159. ■

Chapter Committee Updates

Biana Godin[1] and Paolo Caliceti[2]
Chapters Committee Co-Chairs

CRS chapters are the emblematic units representing our Society around the globe. Many of the current CRS members (senior members and young scientists) got to know the Society through their initial familiarity with the local chapters which "deliver" the science of the Controlled Delivery to those members who, due to the obvious constraints, cannot regularly attend the annual meetings. Thus, the Chapters represent a tremendous opportunity to distribute the value of CRS and the research CRS members are producing to wider audience and vice versa. We are very proud of the CRS Local and Student Chapters and would like to share with the CRS community some of the Chapters Committee successes.

Starting from 2008, the Chapters Committee actively pursued the idea of globalization through bringing new chapters to the society, reviving the activities of dormant chapters and improving the communication between the chapters and the parent organization. As a result, we are delighted that during the last three years many new members joined to our Chapters "family." New Chapters were formed including Canada and China Local Chapters and University of California Santa Barbara, Hebrew University of Jerusalem, and Connecticut Student Chapters; Greek, Texas Student, and Taiwan chapters revived their activities; and the committee is currently supporting the formation of two additional student chapters. We are confident that this increase in the number of CRS Chapters will bring the awareness of the controlled delivery of bioactive materials science and the Controlled Release Society to wider international and national audience.

Our Chapters have an outstanding track of scientific activities, organizing local annual meetings and workshops, highlights of which are regularly reported to the members in the *CRS Newsletter* and News Capsule. In this communication, we would like to spotlight some of the recently formed chapters. As an example, the Canadian Local Chapter, formed in 2009, currently has more than 160 members. In May 2011, the chapter had an Inaugural Annual Meeting together with CSPT, NHPRSC, and CSPS, which was attended by 450 participants. On the side of the student chapters, the Connecticut Chapter, a consortium comprised of members from the University of Connecticut, Yale University, and the University of Connecticut Health Center established in June 2010, excelled already in the first year of its operation. The Chapter recruited 47 members and organized four scientific events. Both of the new chapters have very active websites. An interesting feature was also introduced by the Italian chapter in 2010, when the chapter webcasted its Annual Meeting to enable other chapters and the CRS global community to enjoy the great science delivered at the event.

2010 CRS Outstanding Chapter of the Year Award Recipients (left) UK-Ireland Local Chapter, and (right) Illinois Student Chapter.

"A vibrant chapter network is very important to the CRS and our ability to support the advancement of delivery science world-wide. Biana Godin-Vilentchouk has done an outstanding job over the last three years as co-chair of the CRS Chapters Committee and has played a key role in building our network of chapters including supporting the establishment of several new chapters during her term as chair. As she steps down from the Chapters Committee, Martyn Davies and I are delighted Biana has agreed to continue to serve the CRS as the new chair heading our growing webinar program. We are also grateful that Claudio Ortiz will join Paolo as co-chair of the Chapters Committee. We are very fortunate to have dedicated, experienced leaders like Biana, Paolo, and Claudio leading these important activities for the CRS," said Mark Tracy, CRS Immediate Past President.

Last year a new CRS Outstanding Chapter of the Year Award was approved by the CRS Board of Directors. The first recipients of this award were UK-Ireland Local Chapter and Illinois Student Chapter. We are very pleased to announce the 2011 Best Chapter of the Year Awardees: Australian Local Chapter and New Jersey Student Chapter. The Awards were presented to the chapters during the 38th Annual Meeting & Exposition of the Controlled Release Society.

We would like to congratulate all of our chapters and encourage them to continue the outstanding history of exceptional service and well managed events. Your hard work, continued involvement, and enthusiasm are greatly appreciated by CRS. ■

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People in the News

Compiled by Steven Giannos
Industrial Editor

Robert Langer Named Priestley Medalist

C&EN: June 13, 2011 – Washington, DC – Robert S. Langer, the David H. Koch Institute Professor at Massachusetts Institute of Technology, has been selected to receive the 2012 Priestley Medal. Langer, 62, is being honored with the American Chemical Society's most prestigious award in recognition of cutting-edge research that helped create the controlled-release drug industry and the field of tissue engineering (1).

"I'm honored—and a bit shocked—to receive the Priestley Medal," Langer says. "It's a thrill to be included among the prestigious winners of this award, not just for me, but for my lab, my fields of research, and for the chemical engineering community."

The Priestley Medal is the highest honor conferred by the American Chemical Society (ACS) and is awarded for distinguished service in the field of chemistry. Established in 1922, the award is named after Joseph Priestley, the discoverer of oxygen who immigrated to the United States of America in 1794. The ACS formed in 1876, spearheaded by a group of chemists who had met two years previously in Priestley's home (2).

To get a sense of Langer's prolific career requires looking at a few numbers: He runs one of the largest academic laboratories in the world, with nearly 100 members. He has been an author of more than 1,100 research papers. He has approximately 800 issued and pending patents worldwide that have been licensed or sublicensed to more than 220 companies. And he has had a hand in creating some 25 companies.

"Professor Langer is a talented scientist who is motivated by a sense of responsibility to help people," says longtime collaborator Joseph P. Vacanti, a tissue engineering expert and pediatric surgeon at Boston-based MassGeneral Hospital for Children. Langer is an affable person who manages to be thoughtful and gracious as he works to cross-pollinate ideas between different fields of research, Vacanti relates.

"He has an enormous gift of collaboration that gives him the ability to build successful research teams," Vacanti says. "His pioneering work, in particular in slow-release medicines, has helped millions of people throughout the world."

One of Langer's first discoveries—and one which he says is still a favorite—was that materials such as ethylene-vinyl acetate and lactic acid-glycolic acid copolymers could be dissolved, mixed with drugs, and made into materials that slowly release drugs into the body. Another defining contribution was to change the way biomedical devices were developed. "Before we became involved, researchers were primarily clinicians who adapted off-the-shelf materials that resembled the tissue or organ they were working on," Langer recalls. "We began to use chemistry and chemical engineering design principles to develop job-specific biomaterials."

A third key contribution was helping start the field of regenerative medicine and tissue engineering to address the problem of donor-organ shortages. Langer and his colleagues, including Vacanti, figured out how to make degradable polymer scaffolds that could support growth of human cells, leading to artificial skin, muscles, nerves, cartilage, bone, and organs that are now used to treat patients.

Langer never seems to run out of ideas. His group's most recent work includes contact lenses that release drugs and a polymer gel that can help people with damaged vocal cords get their voices back. His team is also reaching out in new directions, including developing substrate materials for improved growth of stem cells and lipid parcels called lipidoids to deliver short-interfering RNAs that can shut off malfunctioning genes that cause diseases.

"I have been astonished to see how successful Bob is at translating basic research findings into start-up companies without himself leaving the confines of academia," says Cornell University organic chemist Bruce Ganem, who as cofounder of intellectual property development firm KensaGroup has worked closely with Langer. "His career provides the consummate example to aspiring scientist-entrepreneurs on how to combine academic research with the necessary translational firepower to turn inventions into innovative products," Ganem says.

To name a few companies that have benefited from Langer's ideas, Seventh Sense Biosystems has a needle-free microfluidic blood extraction process to transfer blood to a collection reservoir for immediate analysis; Alkermes uses controlled-release microspheres that deliver drugs and last much longer than a pill; MicroCHIPS develops implantable biochips with sensor-controlled arrays of microreservoirs that can be opened on demand to precisely control drug release; and BIND Biosciences uses engineered nanoparticles to selectively deliver drugs to tumor cells to increase efficacy and reduce chemotherapy side effects. To create these types of applications, Langer generally focuses on developing platform technologies that lead to multiple end points, rather than one-of-a-kind products, Langer says.

The successes haven't spoiled Langer's enthusiasm for what he is doing: following his dream upon leaving graduate school to use science as a tool to change the world in positive ways. "I love working with students and postdocs to dream up technologies and then take them from the blackboard to the marketplace," Langer says. "There's still a lot to be excited about."

References

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2. http://en.wikipedia.org/wiki/Priestley_Medal

William Higuchi, Lipocine Chairman, Awarded Prestigious "Order of the Rising Sun" by the Japanese Government

Business Wire: July 6, 2011 – SALT LAKE CITY, UT – Lipocine announces that Dr. William Higuchi, Lipocine co-founder and Chairman of the Board, was awarded the "Order of The Rising Sun" by the Japanese Government for "contribution to the development of Japanese pharmaceutics and pharmaceutical chemistry, as well as to the improvement of social status of Japanese-Americans."

The conferment of this decoration, which is awarded by the Emperor of Japan to individuals worldwide, recognizes lifetime achievement and a commitment to excellence, particularly including significant positive contributions to mutual understanding and friendship between the United States and Japan.

The Japanese Government credits Dr. Higuchi with having distinguished careers at both the University of Michigan and the University of Utah and with helping their respective departments in pharmaceutics to become world-class. Through Dr. Higuchi's leadership, these training and research facilities have graduated a multitude of prominent figures in industry, academia, and government, while hosting numerous visiting researchers from Japan and many other countries. The result has been global recognition and scientific advancement in this field.

Dr. Keiji Yamamato (Vice-President of Chiba University, Japan; Post-Doctoral fellow during 1983–84 at the University of Utah) said, "Dr. Higuchi's training and teachings have had an enormous effect on Japan's pharmaceutical industry and research, and his students will never forget the kindness of Dr. William Higuchi and Mrs. Higuchi."

Dr. Higuchi's accomplishments have been felt directly in the pharmaceutical industry, especially in Utah. Prior to Dr. Higuchi's work with Lipocine, he co-founded and served as Chairman of Theratech Inc., a transdermal drug delivery company which eventually was sold to Watson Pharmaceuticals. Besides co-founding Lipocine, a specialty pharmaceutical company now developing innovative products for men's and women's health and respiratory conditions, Dr. Higuchi also is the founder of Aciont Inc., a biopharmaceutical company focusing on non-invasive therapeutics for sight-threatening anterior and posterior eye diseases.

Dr. Mahesh Patel, President and CEO of Lipocine Inc. stated, "I have been fortunate to have known Dr. Higuchi as my professor, scientific colleague, and business partner. Specifically, his scientific and business insights have been invaluable to me both personally and professionally." ■

In the News

Compiled by Steven Giannos
Industrial Editor

July 2011

Watson and Antares Announce Exclusive License Agreement for Antares' Oxybutynin Gel Product (Anturol®)

PRNewswire: July 11, 2011 – PARSIPPANY, NJ & EWING, NJ – Watson Pharmaceuticals, Inc. (NYSE:WPI – News) and Antares Pharma, Inc. (NYSE Amex: AIS) today announced an exclusive licensing agreement for Watson to commercialize Antares' topical oxybutynin gel product in the U.S. and Canada. A New Drug Application for the oxybutynin gel product is currently under review by the Food and Drug Administration (FDA). The FDA has assigned a Prescription Drug User Fee Act (PDUFA) date of December 8, 2011.

Antares' oxybutynin product is a clear, odorless topical gel that has demonstrated to be an effective and safe treatment for overactive bladder (OAB), a condition that affects more than 30 million Americans. Based on a 12-week, multi-center placebo controlled Phase 3 clinical study conducted by Antares, patients treated with 56 mg daily or 84 mg daily experienced a statistically significant decrease in OAB symptoms versus placebo, including the number of urinary incontinence episodes per day. The product was well tolerated in the study with no reported serious treatment-related side effects. Anticholinergic side effects such as dry mouth and constipation were low and no increase in CNS side effects was seen compared to placebo.

"The addition of Antares' oxybutynin gel product will strategically enhance our overactive bladder product portfolio, potentially providing patients with the dosing flexibility of two strengths, allowing for dose titration, together with a convenient novel pump delivery system," said Fred Wilkinson, Watson's Executive Vice President, Global Brands. "Additionally, this product will expand our product offerings to the Urology and OB/GYN audiences."

"We are extremely pleased to partner Anturol® with Watson, a company with a growing strategic position in urology with a well established commercialization infrastructure and a dedicated experienced sales force," said Paul K. Wotton Ph.D., President and Chief Executive Officer. "We are confident Watson will successfully market the positive attributes of this next generation OAB gel product to physicians and patients. We look forward to working with Watson and developing a strong strategic relationship between our two companies."

CytRx Receives FDA Orphan Drug Designation for INNO-206 for the Treatment of Soft Tissue Sarcomas

Business Wire: July 5, 2011 – LOS ANGELES, CA – CytRx Corporation (Nasdaq: CYTR), a biotechnology company specializing in oncology, today announced that the Office of Orphan Product Development of the U.S. Food and Drug Administration (FDA) has granted INNO-206 orphan drug designation for the treatment of patients with soft tissue sarcomas. Soft tissue sarcomas are cancers that are formed in the muscle, fat, fibrous tissue, blood vessels, or other supporting tissue of the body. CytRx holds the exclusive worldwide development and commercialization rights to INNO-206.

INNO-206 is a novel conjugate of doxorubicin, a commonly prescribed chemotherapeutic, and was designed to improve efficacy and reduce adverse events through controlled release and preferential targeting of tumors. Doxorubicin is currently the only FDA-approved drug on the market for soft tissue sarcoma, and is a standard chemotherapeutic treatment for a variety of other cancers. In April 2011, the FDA granted INNO-206 orphan drug designation for treating patients with pancreatic cancer.

CytRx plans to begin a Phase 2b clinical trial with INNO-206 in patients with late-stage soft tissue sarcomas in the second half of 2011, following completion of an ongoing open-label Phase 1b clinical trial in patients with advanced solid tumors who have failed standard therapies. The Phase 1b clinical trial, which consists mostly of patients with soft tissue sarcomas, is evaluating the safety of administering doses of INNO-206 that are more than two to four times the standard dose of doxorubicin.

"Our strategy to move quickly into a Phase 2b trial with INNO-206 in soft tissue sarcomas is further supported by the FDA's approval of orphan drug designation," said Steven A. Kriegsman, President and CEO of CytRx. "We envision a significant opportunity in this indication due to the objective clinical responses seen with INNO-206 in patients with sarcomas in an earlier Phase 1 trial as well as preclinical data."

Patients with advanced soft tissue sarcomas who can no longer be treated with surgery have a poor prognosis. Progression-free survival for this group is around six to seven months, and median overall survival is approximately 18 months with less than one-third of these patients living past three years. Combinations of the chemotherapy drugs ifosfamide and doxorubicin appear to offer the highest response rates and longest time to progression in these patients; however, these regimens have not significantly improved survival.

CytRx Corporation is a biopharmaceutical research and development oncology company engaged in the development of high-value human therapeutics. The CytRx oncology pipeline includes three programs in clinical development for cancer indications: INNO-206, tamibarotene, and bafetinib. For more information on the Company, visit http://www.cytrx.com.

June 2011

FDA Approves Lazanda® – First Fentanyl Nasal Spray – for the Management of Breakthrough Pain in Cancer Patients

PRNewswire: June 30, 2011 – READING, UK & BEDMINSTER, NJ – Archimedes Pharma Ltd., and its subsidiary, Archimedes Pharma U.S. Inc., today announced that the U.S. Food and Drug Administration (FDA) has approved Lazanda® (fentanyl) nasal spray for the management of breakthrough pain in cancer patients 18 years of age and older who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain. Lazanda marks the first FDA product approval for Archimedes Pharma. Lazanda is marketed as PecFent® (fentanyl pectin nasal spray) in Europe, where it is presently available in five countries.

"Lazanda is an important new option for patients with cancer who experience excruciating breakthrough pain," says Jeffrey H. Buchalter, chief executive officer of Archimedes Pharma. "Lazanda, which uses our patented PecSys® drug delivery system, is designed to deliver medicine in a rapid, but controlled manner, and provides patients with an effective alternative to manage their breakthrough pain."

Breakthrough pain in cancer (BTPc) is an intense, sudden pain that is often unpredictable and debilitating and occurs despite otherwise appropriate opioid therapy for background pain. BTPc has a different profile from background pain. BTPc often has high intensity, a rapid onset, usually reaching maximum intensity within five minutes, and a short duration, lasting between 30 and 60 minutes per episode. On average, BTPc affects more than half of patients with cancer and often interferes with patients' health and ability to engage in daily living activities.

"As the first fentanyl nasal spray in the U.S., Lazanda provides a new approach to managing the often debilitating and inadequately-treated episodes of breakthrough pain that many patients with cancer experience," said Donald Taylor, M.D., director at Taylor Research LLC. and clinical investigator for Lazanda. "Current treatment options typically utilize short-acting oral opioid medications that cannot provide pain relief with an onset of action or duration of effect that matches the time course of a BTPc episode. Lazanda's rapid and controlled availability is a much better match for the nature of an episode of breakthrough pain, giving physicians a new and powerful tool for treating cancer breakthrough pain."

Lazanda will be available in the second half of this year through a Risk Evaluation and Mitigation Strategy (REMS) program, which is intended to minimize the risk of misuse, abuse, addiction, overdose, and serious complications due to medication errors. Under the Lazanda® REMS program, pharmacies, distributors, and health care professionals who prescribe to outpatients are required to enroll in the program to dispense, distribute, and prescribe Lazanda.

"We fully support the FDA mandate to implement a REMS program for Lazanda as an important way to provide patients, healthcare providers, and pharmacists with the information they need about the appropriate and safe use of Lazanda," said Buchalter. "Archimedes Pharma looks forward to working closely with health care professionals to ensure safe and consistent access to Lazanda for the patients who are seeking relief from unbearable episodes of breakthrough pain in cancer."

Columbia Laboratories' NDA for PROCHIEVE® Vaginal Progesterone Gel Accepted for Filing by FDA

PRNewswire: June 27, 2011 – LIVINGSTON, NJ & MORRISTOWN, NJ – Columbia Laboratories, Inc. (Nasdaq: CBRX) and Watson Pharmaceuticals, Inc. (NYSE: WPI) today announced that the U.S. Food and Drug Administration (FDA) has accepted for filing Columbia's New Drug Application (NDA) for PROCHIEVE® (progesterone gel) for the reduction of risk of preterm birth in women with short uterine cervical length in the mid-trimester of pregnancy. The acceptance of the NDA for filing means FDA has determined that the application is sufficiently complete to permit a substantive review. The acceptance for filing does not provide any assurance that the FDA will ultimately approve the NDA.

In addition, Columbia has voluntarily withdrawn its request for priority review. Following discussions with FDA, the companies determined that a standard review would afford the agency the appropriate timeframe necessary to complete its review of the application, including empaneling an agency advisory committee, if necessary. Under the Prescription Drug User Fee Act III (PDUFA), the FDA's goal under standard review is to review and act on the NDA by February 26, 2012.

Under the terms of the Purchase and Collaboration Agreement between Columbia and Watson, acceptance of the PROCHIEVE NDA will trigger a $5 million milestone payment to Columbia from Watson. "We are pleased to achieve this important regulatory milestone and look forward to working with the FDA as they review the data package for the PROCHIEVE New Drug Application," said Frank Condella, President and Chief Executive Officer of Columbia Laboratories, Inc.

"Premature birth is a critical problem in this country and currently no therapeutic option exists for preventing preterm birth in women with premature cervical shortening, an emerging risk factor," said Fred Wilkinson, Watson's Executive Vice President, Global Brands. "The PROCHIEVE New Drug Application represents an important step in the evaluation of a potential new treatment, and if approved, could have a meaningful impact on mothers and the health of their babies, as well as a significant economic impact on the healthcare system."

Columbia submitted the NDA, which includes data from two Phase III clinical trials evaluating the use of PROCHIEVE in

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reducing the risk of preterm birth in women, as well as supportive pharmacokinetic studies, to the FDA on April 26, 2011.

Cardium Announces Plans to Acquire Transdel Pharmaceuticals Phase 3 Topical Analgesic and Cosmeceutical Business Assets

PRNewswire: June 27, 2011 – SAN DIEGO, CA – Cardium Therapeutics (NYSE Amex: CXM) today announced that it had entered into an agreement with Transdel Pharmaceuticals to acquire substantially all of Transdel's business assets including a Phase 3 product candidate Ketotransdel™ (TDLP-110), which is a topically-administered analgesic for the treatment of musculoskeletal pain. The business assets would be acquired in connection with a proposed asset purchase under Section 363 of Chapter 11 of the U.S. Bankruptcy Code, and would also include royalty-bearing license agreements for certain cosmeceutical products marketed by third parties that employ Transdel delivery technology. The completion of the asset acquisition is subject to a number of conditions, including approval of the transaction by the bankruptcy court.

Transdel is a San Diego-based specialty pharmaceutical company that developed topically-administered products, which are particularly useful for the treatment of acute musculoskeletal pain such as occurs with soft tissue injuries, and other potential pain indications. Transdel's innovative drug delivery formulation is designed to facilitate the effective penetration of a variety of drugs and other products through the skin barrier – allowing agents to be delivered directly to affected tissues. Ketotransdel™, the company's lead late-stage clinical candidate, is designed as an analgesic prescription product containing ketoprofen, which would be topically administered for the treatment of musculoskeletal pain.

Cardium would also acquire Transdel's cosmeceutical business rights, which currently include royalty-based licensing arrangements with JH Direct LLC and Jan Marini Skin Research covering the use of Transdel's innovative delivery technology for cosmeceutical products. "The proposed purchase of the business assets of Transdel Pharmaceuticals further broadens our technology and late stage product platform, and provides additional opportunities for potential commercialization, partnering, or other monetization, now that our InnerCool Therapies business has been successfully sold to Philips Healthcare," stated Christopher J. Reinhard, Chairman and Chief Executive Officer of Cardium.

Flamel Technologies and Digna Biotech Announce Multiple Product Development Agreement

Business Wire: June 27, 2011 – LYON, FRANCE & MADRID, SPAIN – Flamel Technologies SA (NASDAQ: FLML) and Digna Biotech SL today announced that the two companies have entered into a joint development agreement for the preclinical and clinical development of multiple products. The agreement has been structured to leverage Digna's groundbreaking research, preclinical, and clinical development efforts, and Flamel's formulation expertise in creating safer, more efficacious products using its innovative proprietary drug delivery platforms, Medusa® and Micropump®. Flamel will be primarily responsible for the formulation and manufacturing process development and Digna will be primarily responsible for the preclinical and clinical development. The three initial Digna products that have been identified for development under the agreement are P144, P17, and Methylthiadenosine (MTA). All of these molecules have shown significant activity in preclinical studies involving multiple indications with high unmet medical need. Both companies expect that the achievement of clinical proof of concept data under the joint development agreement will result in significant additional value creation for the parties.

P144 (Disitertide) is a Transforming Growth Factor beta-1 (TGF-beta1) inhibitor. A topical formulation of P144 has been studied in a Phase II trial involving the treatment of systemic sclerosis or scleroderma, a multisystem disorder characterized by the excessive synthesis and deposition of extracellular matrix proteins that result in the fibrosis of skin and visceral organs. The data indicated a statistically significant increase in the number of patients that noticed improvements of the treated skin area ($p<0.034$). P144 has also been successfully evaluated in preclinical animal models of organ fibrosis and macular degeneration. A Medusa-enabled formulation of Digna's P144 for controlled release via subcutaneous injection will be developed by Flamel for initial evaluation by Digna in pulmonary fibrosis.

P17 is another TGF-beta1 inhibitor which has been evaluated in preclinical studies and has shown promising activity for potential application in the treatment of cirrhosis, as well as to prevent angiogenesis and metastasis. A Medusa-enabled formulation of Digna's P17 for controlled release via subcutaneous injection will be developed by Flamel for evaluation by Digna for the potential treatment of multiple indications. The joint development agreement anticipates that clinical development of one of the two TGF-beta1 inhibitors will be prioritized based on preclinical data from the two formulations.

Methylthiadenosine (MTA) is an oral immunomodulator that has also been shown to have neuroprotective properties in a variety of animal models. These combined properties make it a strong candidate for the treatment of multiple sclerosis. A Micropump-enabled formulation, designed specifically to increase both solubility and stability of Digna's Methylthiadenosine (MTA), will be developed by Flamel for evaluation by Digna in Multiple Sclerosis.

Stephen H. Willard, Flamel's chief executive officer, stated, "This agreement has been designed to allow both companies to focus on our respective comparative advantages so that we may develop these projects further before partnering. This could generate potential greater economic returns for both companies in the three initial products we will be developing. As previously announced, Flamel is reaching out, as a complement to our core activities with large pharmaceutical companies, to identify and

partner with smaller companies with exceptional potential in early stage molecules. This can create greater value for shareholders and investors of both companies by advancing highly promising candidates into proof of concept clinical trials. We are pleased to be working with Digna Biotech in the development of these three products, which we believe may offer important advantages to patients suffering from a number of serious indications."

Pulmatrix Launches iSPERSE™, A Novel Inhaled Dry Powder Drug Delivery Platform

Business Wire: June 20, 2011 – LEXINGTON, MA – Pulmatrix, a clinical stage biotechnology company discovering and developing a new class of therapies for the prevention, treatment, and control of respiratory diseases, today announced the launch of iSPERSE™, the company's novel inhaled dry powder drug delivery platform. With completion of comprehensive proof-of-concept validation studies of the platform along with initial patent filings, Pulmatrix is now advancing a select number of proprietary iSPERSE drug formulation candidates as well as actively pursuing iSPERSE partnerships.

The iSPERSE dry powders comprise proprietary cationic salt formulations optimized for inhalation that have the unique properties of small particle size, high density, and high dispersibility. These unique attributes give iSPERSE the potential to deliver high drug payloads, low potency drugs, and large drug molecules, such as proteins and peptides. Additionally, iSPERSE's proprietary powders allow for flexible formulation with straightforward manufacturing, supporting the formulation of small and large molecule drugs as well drug combinations, including triple drug combinations or higher. This novel technology avoids the drug-loading, flow rate sensitivity and low efficiency limitations of conventional lactose blending inhalation technologies.

"iSPERSE represents a powerful new proprietary platform to deliver inhaled drugs effectively and safely, enabling the potential for best-in-class and first-in-class local and systemic therapeutic applications," said Michael Lipp, Ph.D., Vice President of Development and Intellectual Property at Pulmatrix. "Partners of our iSPERSE platform can harness the unique capabilities of iSPERSE to deliver single or combination drug formulations with a greater capacity to accommodate higher drug loadings than conventional inhaled technologies. From novel complex drug formulations to branded generics, Pulmatrix believes there are a number of significant opportunities to create inhaled drug products that meet clear and pressing market needs."

Data relating to the technical specifications and delivery capabilities of the iSPERSE technology were presented at poster sessions on June 19 and 21, 2011 at The International Society for Aerosols in Medicine (ISAM) in Rotterdam, Netherlands. In particular, Pulmatrix highlighted data on specific iSPERSE applications that have been formulated for a variety of classes and compounds including long-acting bronchodilators, long-acting anticholinergics, corticosteroid and multiple LABA/ICS and LAMA/ICS combinations. The iSPERSE platform enables the delivery of low or high potency drugs to patients across a wide range of inhalation flow rates using existing, simple-to-use, passive dry powder inhalation devices. iSPERSE can enable the delivery of small molecule drugs, drug combinations (including triple drug combinations or higher), and macromolecule drugs at doses well in excess of those achievable by traditional dry powder lactose blend technologies. Manufactured by a proven, one-step spray drying process, iSPERSE powders are small in geometric size and relatively dense, yet are highly dispersible and relatively flow rate independent with high emitted doses achieved at low flow rates. This flow rate independence provides for reliable dose delivery to patients with both normal and impaired lung function, as well as young children who might require low flow rate dosing not attainable with conventional technologies.

To support the development of its own pipeline as well as the iSPERSE partnering programs, Pulmatrix has developed a complete range of pulmonary drug formulation capabilities that are integral to the successful commercialization of the iSPERSE platform, including:

- Dry powder formulation and manufacturing
- Dry powder physicochemical properties optimization
- Aerosol characterization and method development
- Dry powder inhaler selection and testing
- Preclinical efficacy/safety testing (in vitro/in vivo), and
- Clinical program operation and management.

Phase 2 Study of SKP-1041 for Sleep Maintenance Insomnia Shows Significant Reduction of Mid-Night Awakenings without Next-Day Cognitive Impairment

Business Wire: June 15, 2011 – MINNEAPOLIS, MN – Results of a Phase 2 study sponsored by Somnus Therapeutics, Inc., add further evidence supporting the efficacy and safety of a novel bedtime therapeutic that addresses a major underserved need of insomnia patients: maintaining sleep. SKP-1041, a modified-release formulation of zaleplon, is designed to accomplish this by reducing middle-of-the-night (MOTN) awakenings without interfering with natural sleep onset and early deep sleep. At all three doses tested, SKP-1041 significantly reduced time spent awake during the night compared to placebo, with no evidence of next-morning adverse cognitive effects.

"In this study, we saw statistically significant reductions in the time spent awake during the night (WASO) for all three dosage strengths tested. For the 15 and 20 mg doses, there was a significant reduction in the number of middle-of-the-night awakenings during hours 3–7 of the 8-hour sleep period (NAASO3–7) as well as increased total sleep time for hours 3–7 (TST 3–7)," said study investigator Russell Rosenberg, Ph.D., CEO NeuroTrials Research, and the Atlanta School of Sleep Medicine. "Blood levels of zaleplon were measured over 8 hours and confirmed the release of active drug starting 2 hours after ingestion. This facilitates peak hypnotic efficacy during the hours

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when unwanted awakenings are most likely to occur. Using the Digit Symbol Substitution Test (DSST) and Digit Span Test (DST) to test for next-day effects on cognition, we saw no impairment compared to placebo at all three doses."

"The SKP-1041 formulation is engineered to deliver a short-acting agent, zaleplon, only during the time needed to maintain sleep. All of our clinical studies have confirmed that the formulation works as designed," said Gary Cupit, PharmD, Chief Executive Officer of Somnus Therapeutics. "We have seen consistent and reliable pharmacokinetics throughout our three Phase 1 studies and in the PK investigations of Phase 2. Furthermore, the formulation is well-tolerated. Adverse events in (the) more than 130 subjects included in our Phase 1 and 2 studies have been reported to be not significantly different from placebo. This is in addition to many years of safety data accumulated on immediate release zaleplon in clinical trials and over more than a decade on the market." For more information, visit the Somnus Therapeutics web site: www.somnusthera.com.

NovaBone Expands Development Capabilities for Orthopedic and Dental Bioactive Bone Graft Substitutes

Business Wire: June 14, 2011 – JACKSONVILLE, FL – NovaBone Products, LLC announces the opening of a new dedicated Research and Development facility in Gainesville, Florida. NovaBone Products develops bone graft substitutes based on advancements in biomedical engineering that meet the specialized needs of orthopedic and dental surgeons.

The new 3,500 square foot facility provides the platform for NovaBone Products to implement its product development strategy and was completed in conjunction with the recent appointment of Gregory Pomrink as Vice President, Research & Development. Prior to joining NovaBone Products, Mr. Pomrink worked at Orthovita, Dentsply, and Integra LifeSciences. "Greg has the perfect background and experience to help NovaBone Products continue to grow sales at 50+% per year," said Art Wotiz, President. "In fact, we have already seen breakthrough progress on key projects with our bioactive bone graft," he added.

NovaBone Products, LLC is a leading producer and marketer of bioactive synthetic bone graft substitutes. NovaBone is the pioneer of silicon and calcium ion controlled release products that stimulate and accelerate the regeneration of cortical and cancellous bone. The company markets on a worldwide basis from its offices in Florida, New Jersey, and Shanghai, PRC.

Since its inception in 2002, the company has developed numerous formulations and delivery systems of its patented, bioactive technology platform. The product portfolio stimulates accelerated bone growth for the repair of osseous defects throughout the skeletal system.

pSivida Announces Phase I/II Clinical Study Evaluating Bioerodible, Sustained Release Latanoprost Device in Ocular Hypertension and Glaucoma

Business Wire: June 14, 2011 – WATERTOWN, MA – Drug delivery company pSivida Corp. (NASDAQ: PSDV) (ASX: PVA) today announced the commencement of a Phase I/II clinical trial studying a new bioerodible drug delivery implant for the treatment of glaucoma and ocular hypertension. The implant is designed to provide long-term, sustained release of latanoprost, the most commonly prescribed agent for reduction of intraocular pressure in patients with ocular hypertension and glaucoma worldwide.

The product candidate is a new, compact drug-delivery implant based on the Company's Durasert™ technology system. The implant is designed to be administered by an eye care professional in a minimally invasive, outpatient procedure; it is also designed to be injected into the subconjunctival space of the eye and to be bioerodible.

The new study is a dose-escalating study designed to assess the safety and efficacy of the implant in patients with elevated intraocular pressure. If successful, pSivida plans to advance the product into a multi-center Phase II trial. Dr. Paul Ashton, President and CEO of pSivida Corp., said, "We are extremely pleased that this first application of our new bioerodible drug-delivery technology has entered clinical trials. We look forward to advancing this new delivery system both in glaucoma and potentially in other applications as well."

The insert is being developed under the recently amended Research and Collaboration Agreement with Pfizer Inc. Under the revised agreement, Pfizer will make an initial payment of $2.3 million. pSivida will, with technical assistance from Pfizer, have the right to develop this candidate for the reduction of intraocular pressure in patients with ocular hypertension or glaucoma through Phase II clinical trials. At that point, Pfizer has an option to take an exclusive, worldwide license to develop and commercialize the product candidate in return for a $20 million option exercise payment, double-digit royalty payments on sales of the product and additional development, regulatory, and any sales performance milestone payments of up to $146.5 million. If Pfizer does not exercise its option, pSivida will retain the right to develop and commercialize the glaucoma product on its own or with a partner. As part of the amended agreement, pSivida regains all rights to its intellectual property in ophthalmic applications previously included in the original Research and Collaboration Agreement, other than those related to the latanoprost product.

APR Applied Pharma Research s.a. and Labtec GmbH Announce Ondansetron Oral Dispersible Film ("ODF") is Now Available for Licensing in Europe and Selected Non European Countries, after Having Received Marketing Authorization in Most Countries of Europe

Business Wire: June 13, 2011 – BALERNA, SWITZERLAND – APR and Labtec have regained the marketing and commercialization rights of Ondansetron Oral Dispersible Film ("ODF") together with the brand name "Setofilm®" after the termination of the former license agreement with the French company BioAlliance which has refocused its activities towards other types of products. Ondansetron ODF is approved in 16 European countries and is ready to be marketed. APR and Labtec are in a position to offer marketing and commercialization rights for Ondansetron ODF in Europe and selected non-European countries, either through global, regional, or local license agreements.

"We are excited about this opportunity and we are now aggressively looking for commercial partners in the various countries of continental Europe with the right sale organization and marketing infrastructure able to maximize the product sale potential," says Paolo Galfetti, CEO of APR. "Thanks to its specific drug delivery system and dosage form, we obtained in the countries of Europe full pediatric indications for the product."

Ondansetron ODF is the first prescription product developed as an "orodispersible film" form to be registered in Europe and has been developed by APR and Labtec in collaboration with Monosol RX. The product is indicated for the prevention and treatment of Chemotherapy and Radiotherapy Induced Nausea and Vomiting ("CINV" and "RINV") in adults as well as children aged equal or above 6 months, and the prevention and treatment of Post Operative Nausea and Vomiting ("PONV") in adults and children aged equal or above 4 years.

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

Moberg Derma AB: Moberg Derma Signs Distribution Agreement in Australia and New Zealand

Business Wire: June 08, 2011 – STOCKHOLM, SWEDEN – Moberg Derma AB (publ.) (STO:MOB) has entered into a distribution agreement with OzHealth Pharma for Emtrix® – for discolored and damaged nails caused by nail fungus (onychomycosis) or nail psoriasis. Under the agreement OZ Pharma Health is granted exclusive rights to market and sell Emtrix® in Australia and New Zealand.

"The agreement is part of our international commercialization of Emtrix®, which now will be marketed in another large market. We currently have secured distributors for Emtrix® in over 20 markets," comments Moberg Derma's CEO, Peter Wolpert.

Emtrix® is a prescription-free, topical nail product and has the potential to become first-line treatment for common nail disorders. Launch of Emtrix® was initiated in the first markets in September 2010. Safety and efficacy have been demonstrated in several clinical studies including more than 500 patients. Emtrix® has a unique and rapid mechanism of action which brings visible improvements within 2–4 weeks of treatment. Nail fungus is the most common nail disease and afflicts approximately 10% of the general population and increasing with age. The estimated global market potential exceeds USD 1 billion. The untapped potential is significant since many patients remain untreated. It is generally recognized that there is a need for new efficacious and safe topical treatments. For further information, please visit: www.mobergderma.se

Halozyme and Intrexon Announce Collaboration to Develop First Subcutaneous Recombinant Alpha 1-Antitrypsin Replacement Therapy

PRNewswire: June 6, 2011 – SAN DIEGO, CA & FOSTER CITY, CA – Halozyme Therapeutics, Inc. (Nasdaq: HALO) and Intrexon Corporation, today announced the signing of a worldwide exclusive licensing agreement for the use of rHuPH20 (recombinant human hyaluronidase) in the development of a subcutaneous (under the skin) injectable formulation of Intrexon Corporation's recombinant human alpha 1-antitrypsin (rHuA1AT). Under terms of the agreement, Halozyme may receive up to $63 million, commencing with an upfront payment of $9 million and total potential future milestone payments of $54 million dependent upon the achievement of clinical and regulatory targets, plus up to 11% royalty on future sales of the combination of rHuA1AT with rHuPH20. The license provides Intrexon Corporation, a next generation synthetic biology company, with exclusivity to alpha 1-antitrypsin, for the indications resulting from A1AT deficiency. Additional terms of the transaction have not been disclosed.

Alpha 1-antitrypsin is a protease inhibitor that provides a protective effect from inflammatory cell proteases, especially neutrophil elastase. Intrexon is using its synthetic DNA platform for high-level expression of recombinant A1AT for the potential treatment of diseases resulting from genetic alpha 1-antitrypsin deficiency such as genetic emphysema. A1AT may also benefit patients with chronic obstructive pulmonary disease (COPD) and cystic fibrosis. Currently there is no A1AT recombinant protein available and, as a result, treatment for deficiency is limited and expensive. Intrexon will fund all development and commercialization expenses for the program, which is currently in the scale-up phase of process development.

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"We are pleased to collaborate with Intrexon on this exciting new endeavor for patients with A1AT deficiency," stated Gregory I. Frost, Ph.D., Halozyme's president and CEO. "The combination of Intrexon's synthetic DNA platform for high-level A1AT production with Halozyme's subcutaneous enzyme technology may enable the first recombinant human A1AT replacement therapy with a more patient-friendly administration profile."

"Halozyme's Enhanze technology is the perfect fit for our recombinant human alpha 1-antitrypsin program," stated Randal J. Kirk, CEO and chairman of the board of Intrexon and board member of Halozyme. Mr. Kirk's comment is seconded by Gerardo Zapata, Ph.D., president of Intrexon's Protein Production Division. "This collaboration allows us to utilize Halozyme's proprietary protein delivery technology with a subcutaneous recombinant human version of the A1AT protein, an innovative potential therapy for genetic emphysema, COPD, and other diseases caused by A1AT deficiency, and will facilitate our ability to bring a promising novel synthetic biologic treatment alternative to the currently available plasma-derived intravenous products," stated Zapata.

Halozyme's proprietary rHuPH20 enzyme facilitates the absorption and dispersion of drugs or fluids that are injected under the skin. When injected under the skin, rHuPH20 transiently generates channels in tissues underlying the outer layers of the skin to increase the absorption and spread of injected drugs. When combined with rHuPH20, molecules as large as 200 nanometers may pass freely through the extracellular matrix, which recovers its normal density within approximately 24 hours, leading to a drug delivery platform that does not permanently alter the architecture of the skin. Halozyme's technology platform focuses on the use of rHuPH20 to facilitate subcutaneous administration for large molecule biological therapeutics, many of which currently require intravenous administration. For additional information about A1AT deficiency please visit the Alpha-1 Foundation Web site.

ORTHOCON®, Inc. Receives 510(k) Clearance to Market HEMASORB Apply™

PRNewswire: June 1, 2011 – IRVINGTON, NY – ORTHOCON®, Inc., a privately-held therapeutic device company, today announced that the Food and Drug Administration cleared HEMASORB Apply™ for clinical use and sale in the United States.

HEMASORB Apply is a proprietary, custom-designed applicator preloaded with HEMASORB® Absorbable Bone Hemostat Matrix. The product is provided ready-to-use and enables precise application of HEMASORB to stop bone bleeding during surgical procedures and in treating traumatic injuries. Currently marketed bone hemostat products require surgeons to use their fingers or surgical instruments for application. Unlike bone waxes, HEMASORB is putty-like in consistency, does not require preparation, and is now provided in a syringe-like applicator. Furthermore, HEMASORB is absorbable, biocompatible, and water resistant.

Commenting on the significance of the HEMASORB Apply clearance, John J. Pacifico, ORTHOCON's President and Chief Executive Officer, said the following: "This regulatory clearance is an important achievement for ORTHOCON. There has been very little innovation in the bone hemostat field since bone wax was first introduced in the late 1800s. We believe that the widespread adoption of flowable surgical hemostats has created new opportunities for advanced surgical products that more efficiently and effectively control bone bleeding, and we are confident that HEMASORB Apply will help secure ORTHOCON's leadership position in this therapeutic category. Both HEMASORB and HEMASORB Apply are clearly differentiated from wax-like hemostats, and they are changing the way surgeons think about surgical hemostasis."

Since its initial market introduction in 2010, HEMASORB has been approved for sale at leading hospitals throughout the United States and has been used successfully by hundreds of surgeons. ORTHOCON is confident HEMASORB Apply will provide surgeons with an innovative and cost effective tool to assist in their management of intra-operative bone bleeding, and the company fully expects HEMASORB to become the standard of care for bone hemostasis.

May 2011

Radius, 3M Drug Delivery Systems Sign Development Agreement for Transdermal Delivery of BA058 for Treatment of Osteoporosis

PRNewswire: May 24, 2011 – CAMBRIDGE, MA & ST. PAUL, MN – Radius Health, Inc. ("Radius") and 3M Drug Delivery Systems ("3M") today announced an agreement to collaborate on the development of a transdermal delivery option of BA058, Radius' novel, proprietary PTHrP (parathyroid hormone-related protein) analog, for the treatment of osteoporosis.

The BA058 Microneedle Patch will use 3M's patented Microstructured Transdermal System microneedle technology to administer BA058 through the skin, as an alternative to subcutaneous injection. The BA058 patch is expected to combine the ease, convenience, and self-administration attributes of a transdermal patch with the speed and efficiency of a traditional injection. Terms of the agreement were not disclosed.

"Poor adherence to prescribed osteoporosis therapy is a common and serious problem. Patients who drop their treatment unknowingly place themselves at high risk of fracture, which exacts an enormous toll in terms of human and economic cost," said C. Richard Lyttle, PhD, President and Chief Executive Officer of Radius. "By providing a more convenient treatment alternative to injection that can promote improved compliance, the BA058 Microneedle Patch will be well-positioned to drive expansion of the osteoporosis market."

Radius' BA058 Microneedle Patch product is currently undergoing Phase 1 clinical studies. The company's recently concluded Phase 2 human testing of an injectable form of BA058 showed that BA058 significantly increased bone mineral density (BMD) at the lumbar spine and femoral neck (a common osteoporotic fracture site located in the hip joint) after six months of therapy, with greater BMD gains relative to Forteo®, the reference drug used in the study.

"We are pleased to partner with Radius, a company with deep domain expertise in osteoporosis," said Jim Vaughan, Division Vice President and General Manager of 3M Drug Delivery Systems Division. "This collaboration continues the validation of 3M's microneedle patch technology and provides an excellent example of how our technology adds value for promising new therapeutic agents. We look forward to merging 3M's innovative microneedle technology with Radius' promising bone-building agent to bring this important new therapy to market."

Radius Announces Closing of $91 Million Financing to Advance BA058 Injection into Phase 3 Osteoporosis Study

PRNewswire: May 24, 2011 – CAMBRIDGE, MA – Radius Health, Inc. ("Radius") today announced that the company has raised approximately $91 million in its third financing round, including $66 million in equity financing and a commitment by GE Capital, Healthcare Financial Services and Oxford Finance LLC to a $25 million multi-draw term loan facility. Five new investors, including BB Biotech AG, Brookside Capital, Saints Capital, Nordic Bioscience ("Nordic"), and Ipsen Pharma SAS ("Ipsen") joined existing investors MPM Capital, BB Biotech Ventures, MPM Bio IV NVS Strategic Fund, The Wellcome Trust, HealthCare Ventures, and Scottish Widows Investment Partnership in the equity financing. At the initial closing of the financing, Radius received gross proceeds of $22 million in equity and $6.25 million in debt, and $1.4 million of preferred stock was issued to Ipsen in lieu of a cash milestone payment. Radius will receive the balance of funds in two subsequent tranches upon written request to its investors and lenders. Leerink Swann acted as exclusive placement agent for the equity financing.

Radius will use the proceeds primarily to fund Phase 3 clinical development of the subcutaneous injection form of BA058, the company's novel, proprietary PTHrP (parathyroid hormone-related protein) analog, for the treatment of osteoporosis. Data from the study are intended to form the primary basis for an efficacy claim to support applications for marketing authorization of BA058 Injection in the United States and Europe.

In connection with the financing, Radius completed a services agreement with Nordic whereby Nordic will manage the pivotal Phase 3 clinical trial of BA058 Injection. The 18-month study will enroll 2,400 patients and will be conducted in eight countries at 11 centers operated by the Center for Clinical and Basic Research, a leading clinical research organization with extensive experience in global osteoporosis registration studies.

Serina Therapeutics Awarded Patent for Its Core Polymer Drug Delivery Technology

PRNewswire: May 20, 2011 – HUNTSVILLE, AL – Serina Therapeutics, Inc., a pharmaceutical research and development company, announced that the company was awarded a patent from the United States Patent and Trademark Office covering its polymer technology. The patent entitled "Polyoxazoline and compositions comprising the same" (U.S. Patent No. 7,943,141) covers the synthesis and composition of polyoxazolines for the delivery of different drug molecules.

The patent represents years of groundbreaking research in the development of safe polyoxazoline polymers for drug delivery. It is the first of many patents that Serina has applied for. "This patent award validates our invention and design of a novel drug delivery platform and allows Serina the opportunity to advance some of its proprietary ideas towards full development and eventually commercialization," said Dr. Michael D. Bentley, Chief Scientific Officer and cofounder of the company. "We are now in a position to build a strong pipeline of polymer therapeutic molecules." For more information on Serina Therapeutics, please visit http://www.serinatherapeutics.com

Pearl Therapeutics' Phase 2b Results Show a 50% Improvement in Lung Function with PT003 Compared to Spiriva® and Foradil® in Patients with COPD

PRNewswire: May 18, 2011 – REDWOOD CITY, CA – Pearl Therapeutics Inc. presented detailed efficacy and safety results today from the Company's phase 2b study of PT003 (GFF MDI) in patients with moderate-to-very severe COPD during a late-breaker poster session at the annual meeting of the American Thoracic Society (ATS). PT003 is a proprietary fixed-dose combination of glycopyrrolate (GP), a long-acting muscarinic antagonist (LAMA), and formoterol fumarate (FF), an established, long-acting beta-2 agonist (LABA) delivered via a pressurized hydrofluoroalkane metered dose inhaler (HFA MDI). In addition to details of Pearl's Phase 2b primary endpoint, today's poster highlights findings from secondary endpoints that reinforce the superiority of PT003 over both of its individual components as well as market-leading active comparators in patients with moderate-to-very severe COPD. Top-line results from the primary endpoint of this study were disclosed in December 2010.

The study's primary endpoint was improvement in lung function after one week of dosing, as assessed by FEV1* AUC (0-12) relative to baseline at the start of treatment. Treatment with PT003 resulted in a statistically significant improvement in mean FEV1 AUC (0-12) of 47% (or 93 mL) over Foradil® and 49% (or 95 mL) over Spiriva® after one week of dosing ($p<0.0001$ for both comparisons).
"These results demonstrate an overwhelmingly superior outcome and an even larger degree of bronchodilation than our internal benchmark of 70 mL, providing what we believe to be a clinically meaningful benefit," noted Colin Reisner, MD, FCCP,

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FAAAAI, chief medical officer, and executive vice president of clinical development and medical affairs at Pearl Therapeutics. "While current COPD medications offer some relief, a significant need still exists for many patients. I am especially optimistic that PT003 has the potential of fulfilling this unmet need for COPD patients at all stages of severity."

"The overall improvement in lung function, including the fast onset of action with higher peak improvements in FEV1 and morning trough FEV1 is a strong indicator of how PT003's twice-a-day dosing can benefit patients' disease management," continued Dr. Reisner. "To assess the full clinical potential of PT003, and ensure that we have the strongest possible regulatory package, we plan to initiate four additional Phase 2b studies in the next few weeks. These studies will further characterize the dose response of PT003 and its components, and will include extensive safety assessments."

The ATS annual meeting is being held from May 13-18 in the Colorado Convention Center in Denver, CO. A reproduction of the poster, titled "Novel Combination of Glycopyrrolate and Formoterol MDI (GFF-MDI) Provides Superior Bronchodilation Compared to its Components Administered Alone, Tiotropium DPI, and Formoterol DPI in a Randomized, Double-Blind, Placebo-Controlled Phase 2b Study in Patients with COPD," may be retrieved on the Publications page of the Pearl website. For more information, please visit www.pearltherapeutics.com.

Pantec Biosolutions Selects Oclaro Laser Diode Bars for Transdermal Drug Delivery and Tissue Ablation Systems

PRNewswire: May 18, 2011 – SAN JOSE, CA – Oclaro, Inc. (NASDAQ: OCLR), a tier-one provider of optical communications and laser solutions, today announced that its 9xx nm high-power laser diode bars have been selected by Pantec Biosolutions, the leading provider of epidermal medical applications, for use in its next generation P.L.E.A.S.E.® (Precise Laser Epidermal System) platform. This cutting-edge new laser platform represents a new era in biomedical applications by enabling an easy, painless and needle-free delivery method for drugs, as well as safe tissue ablation for skin rejuvenation.

According to Pantec, the global aesthetic market, which includes tissue ablation, is expected to grow from a $4.4 billion market in 2010 to a $7.5 billion market in 2015; while the market for transdermal drug delivery is growing rapidly and is expected to be a multi-billion dollar market by 2015. Designed for medical professionals and consumers, these new devices offer a pain-free delivery method for a variety of medical applications, such as in-vitro fertilization, vaccinations and wrinkle removal. Oclaro worked closely with Pantec to deliver a customized quasi continuous wave (QCW) sub-assembly laser diode solution that delivered the performance and reliability needed, at a price point that will enable wide-spread adoption in the consumer space. Pantec's first Oclaro-based product, which is called the P.L.E.A.S.E.® Professional, is a tabletop system that will be used for both transdermal delivery and tissue ablation. This device will initially be sold in Europe with plans to bring the product into selected markets worldwide, starting in 2011.

"This win with Pantec is yet another example of how lasers have reached the price/performance targets that enable them to be widely used in the high-volume consumer space," said Gunnar Stolze, Worldwide Sales Director of Industrial and Consumer Lasers at Oclaro. "The combination of Pantec's P.L.E.A.S.E.® platform technology with Oclaro's highly-efficient, high-volume manufacturing capabilities can deliver innovation to the consumer that revolutionizes modern day medical and cosmetic procedures such as drug delivery and tissue ablation."

"We partnered with Oclaro because it delivered the technology and reliable manufacturing excellence we needed, and also worked closely with us to design the best solution for our next generation P.L.E.A.S.E.® products," said Thomas Bragagna, CTO at Pantec Biosolutions. "As this market continues to expand, we are confident that only a world-class supplier such as Oclaro will enable us to establish a clear leadership position in a space that is poised for explosive growth in the future."

About the P.L.E.A.S.E.® Platform
P.L.E.A.S.E.® is a novel transdermal delivery method for high molecular weight drugs. It creates controlled aqueous micropores through the stratum corneum into the epidermis. Due to the special features of the device the micropores do not reach the dermis, where nerves and blood vessels reside. The first device using this new platform is the P.L.E.A.S.E.® Professional, a stationary medical laser device targeted mainly for the dermatologic and aesthetic markets. An intelligent graphical user interface, together with the CE mark and the integrated class 1 laser, guarantees simple and safe use by the medical personnel or the patient, who can use the device without supervision. At a later time, this device will then be complemented by the P.L.E.A.S.E.® Private, a battery-powered handheld medical laser device targeted mainly for drug delivery. For more information visit http://www.oclaro.com.

Arterial Remodeling Technologies ("ART") to disclose for the first time the novel design, and new data, for its potentially disruptive polymer-based bioresorbable stent - Data to be presented at EuroPCR 2011

Business Wire: May 17, 2011 – PARIS, FR – Arterial Remodeling Technologies ("ART") announced today that details of the state-of-the-art design of its potentially disruptive polymer-based bioresorbable stent platform will be revealed, for the first time, at EuroPCR 2011 from the podium tomorrow (Wednesday, May 18). The disclosure will be presented by Antoine LaFont, M.D., Ph.D., Professor of Medicine, Head Interventional Cardiology Department, Georges Pompidou Hospital (Paris); and, Past Chairman, Interventional Cardiology Group, European Society of Cardiology (ESC). Dr. LaFont is a co-founder of ART.

Additionally, on Thursday, May 19, also at EuroPCR, Dr. LaFont will make a second presentation from the podium, disclosing additional data that further validates ART's innovative approach to simultaneously balance biocompatibility, biomechanics and bioresorption in a bioresorbable PLA (polylactic acid) stent. These data will show that ART's PLA-based stent can be overexpanded by up to 25% without any problems, thus avoiding the serious medical issues caused by cracking or malapposition.

"We will debunk the myth that polymer based stents are not optimal as a bioresorbable scaffold. Indeed, we have proven that overexpansion limitations are technology related and most definitely not related to the use of polymers in bioresorbable stents. Indeed, this represents a seminal truth, that precise vessel-sizing at implantation is not necessary with our bioresorbale stent due to its crack- and malapposition-free overexpansion features," said Machiel van der Leest, CEO, who previously was a co-founder and Chief Technology Officer of Minvasys. During his career he has developed and successfully introduced 15 Class III medical devices, which required pre-market approval and a scientific review to ensure safety and effectiveness.

"ART's stent is designed to have several critically important competitive advantages over currently marketed and in-development bioresorbable stents, including that our stent is designed to have (1) faster and smoother resorption, and (2) crack- and crazing-free expansion—which are very significant competitive advantage for our bioresorbable stent," explained van der Leest.

ART's novel biopolymers have been developed in conjunction with one of the world's leading authorities in polymer chemistry, Professor Michel Vert, who is Former Director of the Research Center for Artificial Biopolymers at France's National Center for Scientific Research (Centre National de Recherche Scientifique/CNRS).

About Arterial Remodeling Technologies ("ART")
Arterial Remodeling Technologies ("ART") is developing bioresorbable coronary polymer stents that promote the natural remodeling of an injured artery after angioplasty. The Company's technology is based on intellectual property originating from three esteemed institutions: the Cleveland Clinic; the French national research institute, CNRS (Centre National de Recherche Scientifique), Montpellier, France; and, Descartes University, Paris.

DBV Demonstrates Ability of VIASKIN® to Administer Allergen via Intact Skin by Targeting Dendritic Cells for Safe Treatment of Allergic Disease

Business Wire: May 17, 2011 – PARIS, FR - DBV Technologies, an emerging biotechnology company, announced today that a study1—"Epicutaneous Immunotherapy (EPIT) Results in Rapid Allergen Uptake by Dendritic Cells through Intact Skin and Downregulates the Allergen-Specific Response in Mice"—published in the Journal of Immunology confirms the safety of the Company's VIASKIN® epicutaneous immunotherapy (EPIT) approach to desensitizing against peanut allergy via a novel and patented skin patch.

DBV is the only company in the world whose products are designed to epicutaneously (via a skin patch) deliver allergens for Epicutaneous Immunotherapy (EPIT) against food allergies such as peanut and milk. Allergen-specific immunotherapy is the only strategy that treats the underlying cause of an allergic disorder. DBV's proprietary epicutaneous patch technology — VIASKIN® — involves maintaining an allergen on the intact skin of an allergic subject for repeated and prolonged periods in order to obtain clinical desensitization to the targeted allergen.

"Since there are no known treatments for food allergies, many children and their families live with the constant fear of ingesting a life-threatening food," said Pierre-Henri Benhamou, M.D., co-founder and CEO of DBV Technologies. "VIASKIN® is designed to trigger the desired immune response while avoiding the risk of a systemic, life-threatening reaction. The evidence published in the esteemed peer-reviewed Journal of Immunology fortifies our ongoing development efforts for VIASKIN®."

DBV Technologies is the only company in the world whose products are designed to epicutaneously deliver on intact skin — via an epicutaneous patch — allergens for Epicutaneous Immunotherapy (EPIT) against food allergies. Allergen-specific immunotherapy is the only strategy that treats the underlying cause of an allergic disorder. DBV's proprietary epicutaneous patch technology — VIASKIN® — involves maintaining an allergen on the skin of an allergic subject for repeated and prolonged periods in order to obtain clinical desensitization. NOTE: VIASKIN® Peanut is only for investigational use at the moment in the USA and in Europe.

FDA Licenses Sanofi Pasteur's New Influenza Vaccine Delivered by Intradermal Microinjection

PRNewswire: May 10, 2011 – SWIFTWATER, PA – Sanofi Pasteur, the vaccines division of Sanofi (EURONEXT: SAN and NYSE: SNY), announced today the U.S. Food and Drug Administration (FDA) has approved the company's supplemental biologics license application (sBLA) for licensure of Fluzone Intradermal (Influenza Virus Vaccine). Fluzone Intradermal vaccine is indicated for active immunization of adults 18 through 64 years of age against influenza disease caused by influenza virus subtypes A and type B contained in the vaccine.
"The microinjection delivery system utilized in Fluzone Intradermal vaccine provides reliable and easy delivery of the vaccine into the dermal layer of the skin, an attractive site for immunization," said Olivier Charmeil, President and CEO, Sanofi Pasteur. "Sanofi Pasteur is proud to bring this innovation in influenza vaccine administration to the U.S., offering health-care providers a new tool that may help enhance adult influenza immunization rates."

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The new formulation of Fluzone Intradermal vaccine is the first influenza vaccine licensed in the U.S. that uses a novel microinjection system for intradermal delivery. Fluzone Intradermal vaccine features an ultra-fine needle that is 90 percent shorter than the typical needle used for intramuscular injection of influenza vaccine. Sanofi Pasteur has previously licensed microinjection intradermal influenza vaccines, marketed as Intanza® or IDflu® vaccines, in more than 40 countries including Australia, Canada and countries in Europe.

Fluzone Intradermal vaccine incorporates a new, easy-to-use, prefilled microinjection system designed to consistently deposit vaccine antigens into the dermal layer of the skin of adults. The dermal layer contains a high concentration of specialized cells known as dendritic cells, which play a key role in generating an immune response. In clinical trials, Fluzone Intradermal vaccine produced an immune response at rates similar to Fluzone vaccine administered intramuscularly.

Typically, adult influenza vaccines are administered into the muscle utilizing a needle 1 inch to 1.5 inches (25 mm to 38 mm) in length. Fluzone Intradermal vaccine features an ultra-fine needle that is 0.06 inches (1.5 mm) in length. Fluzone vaccine contains 15 mcg of hemagglutinin per strain of influenza in a 0.5 mL dose. Fluzone Intradermal vaccine contains 9 mcg of hemagglutinin per strain of influenza in a 0.1 mL dose. Fluzone Intradermal vaccine will be available to health-care providers in the U.S. for the 2011-2012 influenza season. Health-care providers wishing to reserve vaccine can do so by visiting www.vaccineshoppe.com or by calling 1-800-VACCINE (1-800-822-2463). ■

Welcome New Members

Ravindra Agarwal
Akagi Akitsuna
Josh Anderson
Bahram Asgharian
Abhijit Singh Bhatia
Eszter Julianna Biro
Anthony Blewett
Kang Bokki, Sr.
Steve Bott
Tonye Briggs
Scott A. Brown
Kevin W. Burton
Allison M. Calahan
Robert Campbell
Rick S. Chan
Hin Kin Chan
Catherine Charles
Subraman Rao Cherukuri
Jane Chisholm
Jungmin Cho
Robert John Christy
Hyejin Chung
Bob Cleek
Tansel Comoglu
Vivek S. Dave
Christopher Demerlis
Frank DeRosa
Albert Fang
Fatma Farag
Mike A. Fritschy
Yoshitaka Fujishima
Esther Furrer
Tapash Ghosh
Mauricio Gomez
Anuradha Gore
Teresa Ann Gorski
Camille Gruber
Siva Gudi
Dennis Hair
Meredith Hans
Roger Harrington
Jayne Hastedt
Asha Hegde
Bernadette Ilagan
Yalia Jayalakshmi
Xinqiao Jia
Marie Genie Jones
Michel Lonji Kalombo
Abhishek Kathuria
Jayant J. Khandare
EunJung Kim
Vijay Kumar
Kishore Kurapati
Daniel Leblanc
Seung-Young Lee
Michael Lovett
Houda Mahayni
David Maske
Christophe Massip
Keisuke Matsuo
Ryan McLemore
Andrey L. Mirakyan
Tusharmouli Mukherjee
Atish Mundada
Jared Nelson
Yemi Onakunle
Daniel Palmer
Steve Pendleton
Eric Peter
Matthew Richardson
Russell F Ross
Kevin Schmid
David Schoneker
Benjamin Samuel Schuster
John Schwartz
Joshua Sestak
Nancy E. Sever
Dinesh Shenoy
Jishu Shi
Ji-Yeon Shim
Milind Singh
Ray Sison
Anand Sistla
Paul R. Soskey
Jenny Tang
Lesheng Teng
Stewart Thompson
Goto Toshihiro
Daizo Uemura
Roberto Valducci
Rutger M.T. Van Sleeuwen
Christian Von Corswant
Xiaoqin Wang
Elizabeth Wen
Tim J. Wooster
Min Xie
Yuhong Xu
Tao Yu
Tuna Yucel
Changyou Zhan

CRS
Delivering Bioactives

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

Calendar of Events

2011

Improved Development and Regulation of Transdermal Systems
September 15–16
Arlington, VA, U.S.A.
www.diahome.org

Developing Pharmaceutical Products for Controlled Pulmonary Delivery
Sponsored by AAPS and CRS
October 23
Washington, DC, U.S.A.
www.controlledreleasesociety.org

2011 AAPS Annual Meeting and Exposition
October 23–27
Washington, DC, U.S.A.
www.aapspharmaceutica.com/meetings/annualmeet/AM11

Joint Indo-US Symposium on Nanomedicine: Prospects and Challenges
November 14–15
Mumbai, India
www.ictmumbai.edu.in/newsFiles/Indo-US-Symposium.pdf

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 15–18
Centre des Congrès de Québec
Québec City, Canada
www.controlledreleasesociety.org/main/meetings