CRS Delivering Bioactives

Newsletter

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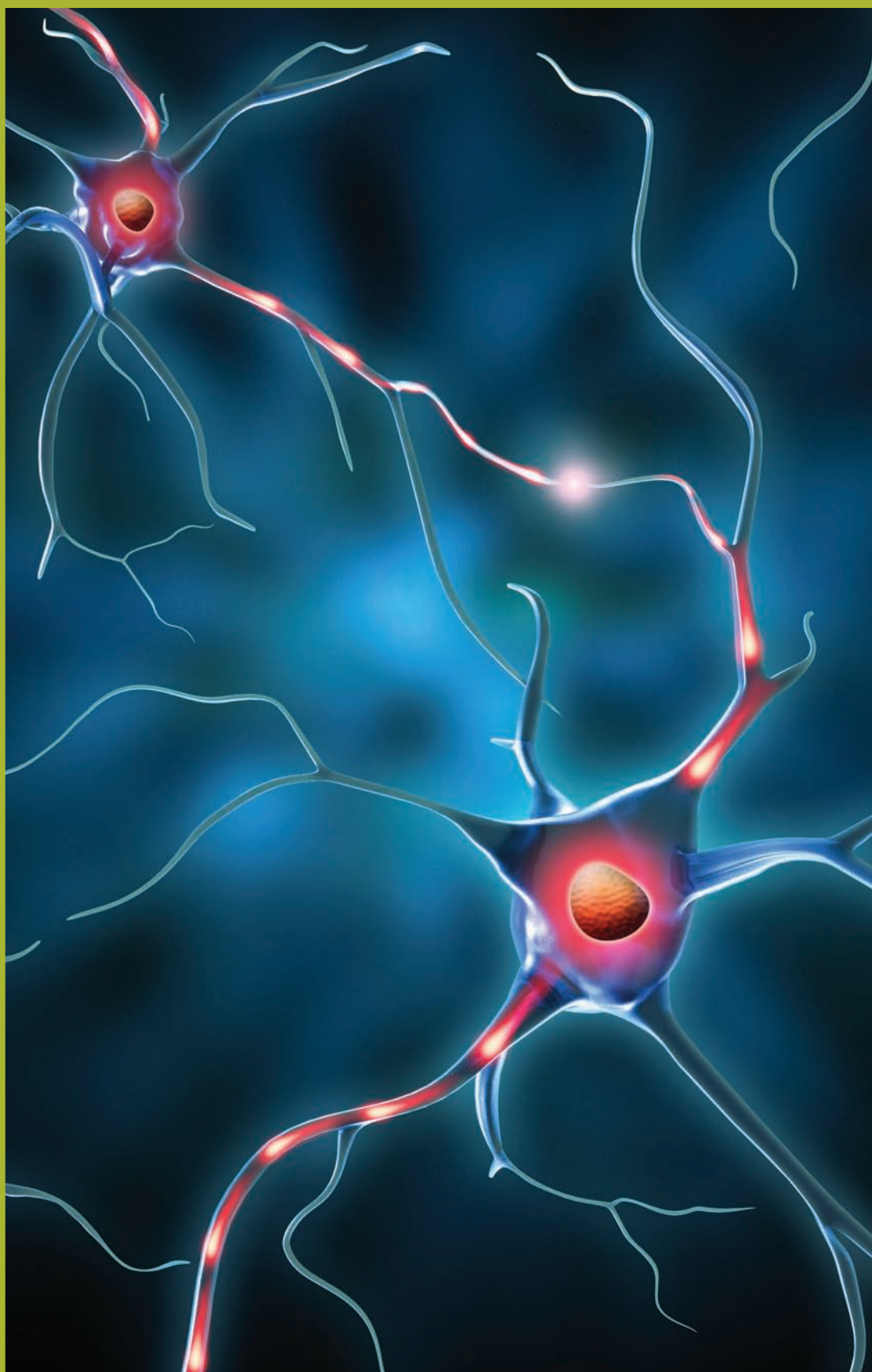
What's Inside



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CRS Newsletter

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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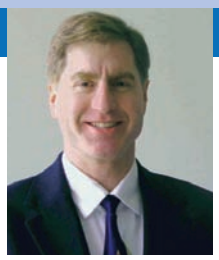

Steven A. Giannos
Chrono Therapeutics, Inc.
Quincy, MA, U.S.A.

Big Changes in Store for 2012

As we come to the end of 2011, I'm amazed by the many changes and the quantity of new initiatives that have been put into place by the industrious CRS Board, staff, and committees. It has been a busy year, filled with interesting events, new officers, a new full service website, and new priorities planned for 2012.

I hope you have taken a look at the brand new CRS website and seen the many clever features available. The website is a comprehensive center of information, community, and careers that, I think, fulfills all of our members' needs. Additionally, our CRS President, Dr. Martyn Davies, provides an excellent summary of CRS activities that occurred over the past year.

Please, don't miss the wonderful interview with Dr. Allan Hoffman in this issue of the Newsletter. Dr. Hoffman is a founding Fellow of the CRS. Here he describes his research and teaching at the University of Washington and MIT over the past 56 years. This interview is extremely informative for anyone interested in the history of the CRS and how controlled release research has grown over the years.

The interviews in the Newsletter have become one of my favorite features. Through them I've been able to get to know some of the leaders behind the CRS and those responsible for the development of controlled release and drug delivery sciences. It is always interesting to learn about how they chose their path of study in chemistry, polymer science, biology, and chemical engineering.

We have two wonderful Scientifically Speaking articles in this issue. The first article takes a look at the surface morphology of nanoparticle PLGA and its safety when used with Calu-3 cells. The second article explores QUIOSELS technology, a product composed of "raw" vesicles and a cationic polymer. These vesicles can be applied to fabrics and textiles to confer cosmetic properties to textiles.

Additionally, the CRS Foundation announces a prestigious postdoctoral fellowship for 2012, honoring Professor Sung Wan Kim, Distinguished Professor of Pharmaceutics and Pharmaceutical Chemistry and Distinguished Professor of Bioengineering at the University of Utah. The fellowship honors his exemplary service to CRS and delivery science and will be awarded to an outstanding recent postdoctoral individual at the 2012 CRS Annual Meeting & Exposition.

So, from all the Newsletter editors and me, we would like to wish all our members and friends a very happy holiday season and a great 2012.

All the best,

Steve ■

Martyn C. Davies
University of Nottingham
Nottingham, United Kingdom

As we enter "the season of mists and mellow fruitfulness" in the UK, it is time to look ahead with some anticipation to new activities and experiences. CRS is a remarkably diverse, multidisciplinary and global society that plans to continue to build on the successes of the last few years in growing our society and improving the services that we provide. Last year saw an important change in our governance structure and since the excellent annual meeting in National Harbor, MD, our new CRS Secretary Ian Tucker has been reviewing our policies and procedures, and during the year will work closely with each committee to define their role in the Society. The CRS Board has also been very active during recent months and I thought I would list some of the new Board priorities for the coming year that focus on expanding the Society's range of current member benefits:

i) Mark Tracy is leading a task force to review and update our annual CRS meeting.
ii) Claire Madden-Smith is leading a task force looking to revitalize our CRS satellite meetings.
iii) Ruth Schmid is leading a Communications Task Force to enhance communications between committees, leadership and volunteers.
iv) Susan Cady and the Foundation Board are working to provide greater visibility of the Foundation within our awards structure and finding ways to sustain its success for the future.
v) We are looking to deliver a content-rich dynamic website led by a new Website Committee chaired by Andy Lewis.
vi) Biana Godin Vilentchouk and her Webcast Committee are working hard to expand our portfolio of educational webcasts.
vii) Publications are a key mechanism of disseminating our science. In this respect,
    a. The editor Vinod Labhasetwar of our new journal *Drug Delivery and Translational Research* would like me to encourage you all to submit your innovative research to build a strong companion journal to our outstanding *Journal of Controlled Release*.
    b. Interested in editing a book in our field? Please contact our CRS Books Editor, Mike Rathbone, who is looking to expand our portfolio of books.
    c. The Newsletter Committee is also looking for new ideas for contributions to the 6 issues during the year.
viii) A task force on "Women in Science" is being led by Diane Burgess.

The Board will report on these initiatives during the year and we are very grateful to the many members who volunteer their time to ensure the CRS maintains its place at the forefront of delivery science. We are committed to expanding the opportunities that are available to CRS members to serve the Society. Please contact us should you wish to join our committees.

In these difficult economic times, I would like to reassure the membership that the Treasurer Debra Bingham and the Board are working hard to ensure the Society maintains its good financial position to weather any financial uncertainty in the coming years. However, difficult decisions may need to be made as the Board ensures that we do not spend beyond our means. In that respect, we will work to maintain and expand our delivery of a diverse range of activities as part of long term financial planning. We wish to ensure that we continue to grow the Society and provide a strategic vision that delivers innovative science and technology in our field.

Finally, I would encourage you all to submit your abstracts and attend our 2012 CRS Annual Meeting "Smart Materials – From Innovation to Translation" on July 15–18, 2012 in Québec City, Canada. Plans are well advanced to create a wonderful conference in a beautiful, cultural city. The innovative scientific program has been designed by the dedicated and committed Programme Team of Hamid Ghandehari, Dusica Maysinger, Christopher McDaniel, Arlene McDowell, Thierry Vandamme, and Teresa Virgallito. The meeting will also contain a large exposition, the ever popular CRS Innovation Sunday, workshops, talks from our award winners, and dedicated events for our different CRS groups such as those for the young scientists. We look forward to welcoming you all. ■

Interview with Dr. Allan Hoffman

Brian Kilfoyle, Ph.D. and Bozena Michniak-Kohn, Ph.D.
Ernest Mario School of Pharmacy, Rutgers-The State University of New Jersey, Piscataway, NJ, U.S.A.

Dr. Allan S. Hoffman is a true pioneer in the fields of polymer chemistry, biomaterials, drug delivery, and diagnostics. He has been actively involved in research for well over 50 years and has made numerous contributions to our field.

Dr. Hoffman attended MIT, where he received his BS (1953), MS (1955), and ScD (1957), all in chemical engineering. Upon completing his studies, Dr. Hoffman stayed in academia where he has held numerous appointments, beginning in MIT's Chemical Engineering Department: Instructor and Assistant Director of the Chemical Engineering Practice School in Oak Ridge, TN (1954–1955), Instructor (1955–1956), Assistant Professor (1958–1960), and Associate Professor (1964–1970). At the University of Washington in Seattle he has been Assistant Director of the Center for Bioengineering (1973–1983), Professor of Bioengineering and Chemical Engineering (1970–2010), and Professor Emeritus in Bioengineering (2010–present). In addition, he currently holds a position as World Class University (WCU) Distinguished Professor at Kyungpook National University Medical School in Daegu, South Korea (2009–present). He holds Honorary Professorships at Aarhus University in Denmark and Shanghai University and Wuhan University of Technology in China.

Over the past 56 years, Dr. Hoffman has taught many (15 or more) different courses at both MIT and the University of Washington. He created a number of these courses, which did not exist before he taught them. In addition, he has taught and continues to lecture in numerous short courses around the world. In 1976, he organized and taught (in French) the first course in biomaterials, medical devices, and implants in France. In 1983, he taught the first short course ever in China (in Shanghai) on biomaterials and drug delivery. In the late 1980s, he organized a short course on biomaterials, implants, and devices at the University of New South Wales in Sydney, Australia, which he taught three times in the 1980s and 1990s. Additionally, in the past several years, he has participated in short courses in Italy, the United States, Singapore, Hong Kong, India, Taiwan, and South Korea.

Dr. Hoffman has been recognized with numerous awards throughout his distinguished career. A few highlights include the Founder's Award from the Controlled Release Society (2007), election to the National Academy of Engineering (2005), the Chandra Sharma Award from the Society for Biomaterials and Artificial Organs of India (2003), the Founder's Award from the Society for Biomaterials (2000), the Alan S. Michaels Lectureship from MIT (1997), the Clemson Award for "Contributions to the Scientific Literature of Biomaterials" (1984), and a Fulbright Fellowship (1957–58). Dr. Hoffman has also given plenary addresses at numerous conferences including presentations this year at the M3 Conference of the Institute of Materials Research and Engineering in Singapore (2011) and the European Polymer Federation in Granada, Spain (2011). He gave the keynote addresses at the Society for Biomaterials Annual Meetings in 2007 and 2010, and a plenary address at the Controlled Release Society Annual Meeting in 2009. He will also be the plenary speaker at next year's World Biomaterials Congress in Chengdu, China, in June, 2012.

Dr. Hoffman is one of the four editors for the Textbook of Biomaterials Science (Elsevier), which has been adopted by every major college and university around the world where courses on the principles and applications of materials in medicine and biotechnology are taught. Dr. Hoffman has sat on numerous editorial boards throughout his career and remains involved with *Biomacromolecules* (2004–present), *J. Bioactive and Compatible Polymers* (1995–present), *Bioconjugate Chem.* (1998–present), *J. Biomaterials Sci., Polymer Edn.* (1989–present), and *Biomaterials, Artificial Cells, Molecular Biotech.* (1987–present).

Dr. Hoffman has been a member of the American Chemical Society for over 50 years. He is also a member of the American Institute of Chemical Engineers, Society for Biomaterials (President from 1983–1984; Founding Fellow, 1990s), Controlled Release Society (Founding Fellow, 2010 and member of the CRS International Advisory Board for two years), and the American

A late 1970s photo of the Hoffman research group at UW. Buddy Ratner is first on the left, Tom Horbett is third on the left, and Steve Hanson is fourth on the left.

A late 1970s photo of the Hoffman research group at UW. Buddy Ratner is first on the left, Tom Horbett is third on the left, and Steve Hanson is fourth on the left.

Institute of Medical and Biological Engineering (AIMBE) (Founding Fellow, 1992).

Dr. Hoffman has, and continues to, contribute a great deal to our understanding of biomaterials science. In between all of his travels, Dr. Hoffman took time to sit down with us to discuss his perspectives on his career, how the field has changed, and what the future holds. Now, on to the interview.

Q. What are the research interests of your group?

A. I am retired now, but more recently when I was still working full time I shared a group of students and postdocs with Prof. Patrick Stayton. Our group (now *his* group) works on numerous projects focused on the applications of "smart" (pH-, temperature-, and light-responsive) polymers for intracellular drug delivery and diagnostics. Our interest has been focused on intracellular delivery of nucleic acid drugs, especially siRNA; we're also looking at intracellular delivery of DNA, antisense oligos, peptides, and proteins. All of these biomolecular drugs are susceptible to enzyme attack in the circulation and also within cells, especially within the lysosomal vesicles. The drugs are usually delivered to the cells by combining them with polymeric nanocarriers, which protect them during circulation and sometimes target them to specific tissues and cells and enhance their uptake into cells by endocytosis. Once inside the cell and endosome, the main challenge is to design a carrier that can provide a mechanism of endosomal escape to the cytosol plus release of the drug in the cytosol in an active form. Then the drug can act at the appropriate intracellular target. A key property of the endosome is that it has a proton pump in its membrane, and the interior of the endosome rapidly becomes acidic after taking up the nanocarrier and its drug. We are currently using smart polymer nanocarriers that have pKs in the range of endosomal pHs, and become sharply hydrophobic as the pH of the endosome decreases from 6.8 and below. The hydrophobic nanocarrier can then interact with the hydrophobic lipid bilayer membrane of the endosome and disrupt it as a barrier, allowing the escape of the drug to the cytosol. The pH-responsive polymeric nanocarrier has to quickly deliver the drug to the cytosol, because within an hour or two after endocytosis in most cells the endosomes fuse with or evolve into lysosomes, which contain enzymes that are especially active at acidic pHs within those vesicles.

Diagnostics is another important current interest in our group. We have a long history (beginning back in 1983) with the thermally responsive poly(N-isopropyl acrylamide) (PNIPAAm) and its conjugates with antibodies. Now we are working with conjugates and coatings of this polymer in diagnostic systems that are designed to capture, concentrate, and assay target antigens and biomarkers in general. We have PNIPAAm-coated porous membranes, polymeric nanoparticles, magnetic nanoparticles, and gold particles, and in some cases we also surface immobilize conjugates of PNIPAAm-antibodies for different biomarkers. The diagnostic systems we are working with include lateral flow paper strips (e.g., dipsticks) and microfluidic devices. The PNIPAAm coatings enable us to collect and concentrate the PNIPAAm-capture antibody conjugates with their affinity-bound antigen biomarkers by raising temperature above the LCST, which causes the polymer chains to aggregate together, concentrating the target antigen biomarker. Later, we can cool and release them as a concentrated pulse of captured biomarker for assay. We can vary the composition and LCST of the smart polymer nanocarrier by copolymerization, and we can conjugate the different LCST polymers to different capture antibodies. This allows us to capture more than one target biomarker in any one sample. This work is sponsored by the Bill and Melinda Gates Foundation in Seattle and the NIH, and we collaborate extensively with PATH (Program for Appropriate Health Technologies), also in Seattle. Seattle is a great place for working on global health technologies. The Bioengineering department and the UW are also great places to work on such projects.

Q. What was MIT like in the 1950s?

A. I entered MIT as a freshman in Chemical Engineering in 1949. There were no bio-related activities in that department at that time or for many years thereafter. The atmosphere was pretty intense for a student. My brother was a junior in aeronautical engineering at MIT at that time and I was 2 years behind him; my father had also studied chemical engineering at MIT and graduated with a BS in 1916. So, MIT was a family affair for us. We were very much suited for MIT in our family since we are all compulsive workaholics, which is one requirement to survive at MIT. You have to like to work, and we were working there all the time as students. Furthermore, we didn't have copy machines, the internet or Google, or any of the wonderful ways available today to learn quickly about so many important topics. So we were lab and library "rats," period. The only compilation of journal publications of others that were readily available in the library was Chemical Abstracts, which we copied from by hand, as we did from the journals themselves. We went to classes and took lots of notes, and went to the library a lot, where we read and wrote a lot,

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and we used slide rules to do our calculations. Some of us (myself included) wore slide rules on our belts. There were jokes about that (we were called MIT "nerds") which circulated in the all-women's schools (called "girl's schools" in those days) in the Boston area.

I began to teach classes in the MIT Chemical Engineering Department during my graduate days, while I was working on my ScD degree. I was appointed as an Instructor in the department when I taught courses. I gave my first class (Industrial Stoichiometry) in 1955, so you could say that I've been teaching for 56 years. I really enjoyed doing that and I guess I was good at it. I also spent the academic year of 1954–55 as the Assistant Director at the MIT Practice School in Oak Ridge, Tennessee; that was also a position of Instructor on the department faculty. The Oak Ridge Practice School was for MIT grad students in Chemical and Nuclear Engineering to get practical experience in a relevant industrial setting for a semester at a time. We worked on various technical problems in the three government plants in Oak Ridge. I had a top security clearance for that, since one of the plants was for uranium isotope separation for the A-bomb, and another was for lithium isotope separation for the H-bomb. The atmosphere was always a lot of fun if you liked to work hard and think hard, and I enjoyed that. After I completed my postdoc in 1958 (I was awarded a Fulbright Fellowship to do research in Paris), the MIT Chemical Engineering Department offered me a position as an Assistant Professor. Getting rehired as an MIT faculty member was very thrilling for me, of course. So in all, I taught on the MIT Chemical Engineering Department faculty for a total of about 10 years.

The UW Biomaterials Family Tree (photo taken in 2002)—Dave Castner, Buddy Ratner, Allan Hoffman, and Tom Horbett. Buddy and Tom were Allan's postdocs, and Dave was Buddy's postdoc.

Q. You mentioned that your father studied at MIT. Who were some of the people he worked with?

A. My father was a chemical engineer in the class of 1916, and he had friendships with many fellow students at MIT, some of who became quite famous, such as Vannevar Bush, Roosevelt's science advisor during WWII who created and ran the Manhattan Project. My father introduced me to "Van" at their 50th class reunion in 1966. He also had professors at MIT who were world famous, such as Warren K. Lewis, who founded the field of Chemical Engineering at MIT by creating a curriculum of physical and organic chemistry courses combined with materials, fluid mechanics, mass transfer, and thermodynamics courses. While I was a young Assistant Professor, space was at a premium, and they put me at a desk in "Doc" Lewis's office. It was a special thrill for me, knowing that he had taught my dad. On the other hand, it wasn't so easy sharing his office, because as I sat there trying to prepare lectures, "Doc," as we called him, would often interrupt me, and tell me stories about when he consulted with Esso (Exxon now) on designing refineries. It was a special experience for me. MIT was then, and still is today, a great place to study and a great place to teach.

Q. What path brought you to the University of Washington?

A. I moved in 1970 from MIT to the University of Washington. In 1970 at MIT there was no bioengineering or anything like it in the chemical engineering department, and I had become greatly interested in combining natural biomolecules with polymers. I was offered a very seductive full professorship at UW in the Center for Bioengineering with a joint appointment in the Chemical Engineering Department. I already had good friends at UW, and my parents, brother, and sister had all moved to the west coast. The University of Washington was then and continues to be an exceptional university, and Seattle was and is a fabulous place to live. So I accepted the offer.

The University of Washington has been very good to me, and this is where I built a biomaterials group that started with myself and two postdocs (Tom Horbert and Buddy Ratner) plus the generous help of Bob Rushmer, who founded Bioengineering at UW (to my knowledge, we were also the first bioengineering activity in the world). Our activities in biomaterials grew from the three of us to several hundred involved in biomaterials research today at UW, not only in our department but also with colleagues and collaborators in other UW departments.

Q. How active do you remain in academics now that you are Professor Emeritus?

A. I will turn 80 next year but I still remain very much involved in teaching and research. For example, I'm involved in helping to organize and teach three short courses this year. The first was in June at the iNANO Center of the University of Aarhus in Aarhus, Denmark (with Ken Howard), another will be in September at Donau University in Krems, Austria (with Buddy Ratner and Dieter Falkenhagen), and another in October at the Korea Institute of Science and Technology (KIST) in Seoul, South Korea (with Pat Stayton and Glen Kwon). I also lectured in two short courses at UW in August, one run by Buddy as his annual UWEB short course, and one run by Dave Castner as the annual NESAC-BIO Surface Analysis Center course. I still share a student or two with Pat Stayton, and together we have spun off two companies in the Seattle area, one in drug delivery and the other in diagnostics.

In 2009, I accepted a part-time position in South Korea as World Class University (WCU) Distinguished Professor at

Kyungpook National University (KNU) Medical School in Daegu, Korea, where I spend a total of nine weeks a year. I occasionally teach in a short course there and give lectures to medical student classes, and I have initiated a joint research project at KNU with several Korean professors at KNU and POSTECH. I have given guest lectures in many Korean universities since I accepted that position three years ago. There are two years remaining in my WCU professorship in Korea. I am also a member of the Scientific Advisory Board of the Institute of Bioengineering and Nanotechnology (IBN) in Singapore, where we meet once or twice a year. So I continue to travel a lot to Asia.

Q. What do you regard as your most significant achievements/ contributions to science?

A. First, I would like to mention my early work in 1971 with Gottfried Schmer, an MD at UW who was in charge of the clinical diagnostics laboratory in the UW Lab Medicine department. We radiation-grafted polyHEMA hydrogels onto hydrophobic polymer surfaces used in catheters, such as silicone rubber, and then we conjugated drugs such as heparin and streptokinase (to stimulate fibrinolysis) to the PHEMA hydroxyl groups. Our concept to conjugate biomolecules such as enzymes and drugs to a modified hydrophobic polymer surface used in medical devices was novel and pioneering in the biomaterials field at that time.

Another highlight for me was to introduce smart polymers such as poly(NIPAAm) to the biomaterials field, and then to apply them for uses in diagnostic assays and drug delivery. This is one of the areas that I'm very proud of having introduced to our biomaterials community. It all started in 1982, when I began to consult with a Seattle biotech company, Genetic Systems Corp. (GSC). In 1982, a good friend recommended that I go downtown in Seattle to meet Bob Nowinski, the CEO of GSC, which was spun-off from the Fred Hutchinson Cancer Research Center (FHCRC) in 1981. Nowinski had some ideas for new products that my friend thought I could help him with by using synthetic polymers. So in the summer of 1982 I met with Nowinski and he described the situation at GSC. He had licensed about 20 monoclonal antibodies from FHCRC, mostly intended as drugs for cancer therapy, but he also wanted to use them for diagnostics, especially for screening blood in blood banks for AIDS or hepatitis, which were just beginning to be a big problem with donated blood. The main diagnostic technique was ELISA and Abbott was dominating the blood bank diagnostics business by giving ELISA plate readers to the blood banks at no charge, and selling their ELISA kits to them. Nowinski asked me if I could develop a competitive assay to ELISA "using polymers." I thought about various ways to attach polymers to capture antibodies, and then to separate them out of the solution, either on a surface or as a precipitate. It was in 1983 at the ACS meeting in Seattle that I met with Jim Guillet, a very creative polymer scientist from the University of Toronto. I asked him if he knew of any polymers that phase separated easily out of aqueous solutions and he mentioned PNIPAAm. I immediately got some monomer and we used it at GSC (with Nobuo Monji, John Priest, and Carol Ann Cole) to develop an assay that worked just as well as ELISA. Some time around 1984–85, Nowinski and I flew down to visit Applied Biosystems (AB) in the Bay Area and discussed with the scientists there what kind of equipment we needed to apply this assay commercially and how much money was needed for that development. Leroy Hood, who had founded AB in 1981 to manufacture his synthesizers and sequencers, was also there that day, and we told him that we wanted to develop a new immunoassay that was competitive with ELISA. In 1984, Nowinski and AB and others formed a diagnostics partnership and raised around $24 million. So the scientists and engineers at GSC and AB began to develop an assay based on a new design for a fluorescence-activated cell sorter (FACS) that had heating and cooling capabilities. The development was taking a lot of time, and eventually Nowinski and the partnership ran out of patience and GSC began to sell ELISA kits to blood banks, competing directly with Abbott. Bristol Myers bought GSC in the late 1980s, and they spun off the PNIPAAm diagnostics patents and the immunoassay technology IP to Sanofi-Pasteur Labs. All that IP, including the PNIPAAm patents, eventually ended up with BioRad. It was great fun and it was a great adventure for me with my new friend, polyNIPAAm.

Prof. Katsuhiko Nakamae tasting sake with Allan Hoffman and Pat Stayton, Kobe, Japan, December, 2000.

It's important to mention that some of my good friends and colleagues were also getting involved with smart polymers similar to PNIPAAm at that time, especially Sung Wan Kim, who has been a constant inspiration to me over the past 40 years with his great energy and creativity. Another person whose work with PNIPAAm strongly influenced me was Toyoichi "Toyo" Tanaka at MIT. He became my very close friend and partner at his favorite sushi bar in downtown Boston. Toyo did much beautiful work with PNIPAAm, and we lost him much too early in his life. Teruo Okano, You Han Bae, Doo Sung Lee, and my former student Tae Gwan Park have all done beautiful work with smart polymers such as PNIPAAm. Also, my long time close friend and colleague, Katsuhiko Nakamae from Kobe University, and his student Takashi Miyata (now at Kansai University) have been my great collaborators over the years in the smart polymer field. Finally, my close friend and collaborator, Pat Stayton, originally trained as a biochemist and "protein engineer," has become a

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very creative "smart polymer engineer," and he ranks with the best polymer chemists out there today.

As I mentioned, my PNIPAAm biomaterial and drug delivery work began in 1983 at the Seattle company GSC, and I also initiated my research on it at UW shortly after that; three of my earliest PNIPAAm publications were in JCR, in 1986 and 1987:

Hoffman, AS, Afrassiabi, A, Dong, LC. Thermally reversible hydrogels: II. Delivery and selective removal of substances in aqueous solutions, J. Control. Release, 4: 213-222 (1986).

Dong, LC, Hoffman, AS. Thermally reversible hydrogels: III. Immobilization of enzymes for feedback reaction control, J. Control. Release 4: 223-227 (1986).

Hoffman, AS. Applications of thermally reversible polymers and hydrogels in therapeutics and diagnostics, J. Control. Release 6: 297-305 (1987).

Q. How have recent technological advancements impacted your work?

A. Interestingly, I have learned a lot about technological advances from young people like you. However, I am still "old-fashioned" in that I have turned down all kinds of invitations to join Facebook, Twitter, LinkedIn, and so on. I am not on any of them. I fear that it could be a good way either to get a virus on your computer or to waste time, or both, and those concerns have kept me from getting involved in any of those social networks. However, I am constantly involved with the internet, especially Google's search engine, and that's my library to the world.

Q. What scientists have played an important role in your development?

A. I have already mentioned several of them above when I talked about my contributions to the biomaterials and drug delivery fields. Here are more comments about people who have played important parts in my career.

Right up front I would like to say that I have had three fantastic colleagues in the Bioengineering Department at the U of W with whom I have thrived and grown in the biomaterials field. They are Buddy Ratner and Tom Horbett, my first two postdocs and collaborators from the early 1970s, and Pat Stayton, who has been my close collaborator for the past 19 years. Buddy was an early pioneer in hydrogels, and he was especially a pioneer in bringing the importance of surface analysis to the attention of our biomaterials community (and also to me, of course) in the 1970s and 1980s. Buddy is now a world famous biomaterials scientist and in high demand as a consultant and teacher. Tom Horbett, my first postdoc who joined me in 1970, also taught me a lot about proteins and proteins at surfaces, an extremely important area in which he is a world expert. Pat Stayton has taught me a tremendous amount about cells, cell biology, and biochemistry, and I am extremely grateful to him for that. He and I, together with our students and postdocs (notably in recent times Niren Murthy, Tony Convertine, Mitsu Ebara, Mike Nash, and James Lai) have invented several novel drug delivery carriers and diagnostic assays using smart polymers. Pat and I have also co-founded two companies, one focused on development of smart carriers for intracellular delivery and another on smart capture systems for diagnostics.

At MIT I had two Chem. Eng. professors named Ed Merrill (my ScD thesis supervisor) and Alan Michaels, each of whom taught me how to visualize and use molecules, especially big ones like polymer chains. We didn't talk about proteins much in those days and we didn't have all of the beautiful modeling software that's available today, but I learned to visualize polymer molecules using CPK models and then to use them in practical applications.

Many of my students have also had a great influence on me, especially a PhD student named Tae Gwan Park, who was a

UW Biomaterials Research "Group", April 19, 2010. Faculty are kneeling in front, and students and postdocs are behind them. The original three of Buddy Ratner, Allan Hoffman and Tom Horbett, who began working together in biomaterials in 1971, are in the center of the front row. Pat Stayton is on Buddy's right.

creative thinker with great productivity. He was one of my best PhD students and continued to be both very creative and productive as a professor in Korea. He is no longer with us, and I miss him very much.

Wayne Gombotz, Liang Chang Dong, and Zhongli Ding were three of my PhD students and Guohua Chen was a postdoc, and each of them excelled in creativity and productivity. I've been very lucky over the years to have such great students and colleagues.

Q. Can you tell us how you got involved with PEGylated surfaces?

A. In the mid 1980s, a great PhD student named Wayne Gombotz suggested that I get together with Milton Harris, an expert in the PEGylation field, and that led to a successful proposal to the NIH on PEGylation of polymer biomaterial surfaces (which also funded Wayne's thesis work). Later in the 1980s Milton founded Shearwater Polymers, which was eventually bought by Nektar Pharmaceuticals (formerly Inhale). That turned out to be a very fruitful connection, and I became a "consultant/advisor" to Shearwater for many years. That interaction brought me into the PEGylated protein field. I continue to work on PEGylated polymer surfaces, PEGylated polymeric nanocarriers and PEGylated drugs to this day. One of our important contributions to PEGylated surfaces involved our explanation of the mechanism of their action. We proposed that the key to efficient repulsion of proteins and cells was the ability of the surface PEG polymer molecules to retain their water molecules of hydration (~2–3 per ether group). The major driving force for surface adsorption of molecules from a solution in any solvent, not just proteins in water, is the release of bound solvent molecules from the surface; this is especially the case when many solvent molecules are desorbed per adsorbing molecule. That represents a huge entropy gain that drives all surface adsorption processes, in my opinion. I believe that occurs with PEG molecules when the PEG MWs reach a critical level around several thousand, when they fold over to form a random, "globular" shaped "three-dimensional" coil, trapping water molecules between the PEG chain segments and not releasing them when a protein molecule tries to displace them or their water molecules. I believe that it also occurs in two dimensions with a surface assembled monolayer (SAM) when a high enough surface concentration (e.g., ~ or >50 mole %) of very short oligoethylene oxide chains (oEO) is reached. At that point they are able to share their affinity for water molecules in a horizontal fashion in the monolayer, forming a "sheet" of bound water. This helps to explain observations the Whitesides and coworkers made with their oEO SAMs.

Q. What personal attributes have allowed you to excel in your scientific career?

A. I think the most important attributes for a scientist are curiosity and a desire to learn new things. I like to listen and talk with people about their research. I try to learn something new every day, which is the key to expanding my mind and having more fun with science. I also love to think about molecules and picture them. I enjoy visualizing molecules even when I am swimming. I believe that my enjoyment of playing with molecules in my mind has definitely helped me to be successful.

Q. If you were to give advice to a recent or soon-to-be graduate, what would it be?

A. One simple word of advice would be to study biology, especially DNA and cell biology. You have to understand biology if you want to do anything in the fields of biomaterials, drug delivery, and diagnostics. Biology is the driving force in our field… it is the cutting edge now and for the foreseeable future.

Q. Outside of your research endeavors, what hobbies do you enjoy?

A. My main hobbies are traveling and swimming, which I try to do every day no matter where I am. I live on Lake Washington and I swim there in the summer, but I'm typically a lap swimmer. I go to the pool at the University or to a hotel pool. I swim for 25–30 minutes nonstop. I've been regularly swimming since 1977. I think it's been keeping me active to be quite honest.

I'm also a baseball fan. I love the Mariners (not so much this season, unfortunately) but I used to root for the Red Sox when I lived in Boston and was at MIT. In 1967, the year of the Impossible Dream, I was teaching a graduate course at MIT and there was a student in class who also loved the Sox, so I asked him to bring a transistor radio to class, and I told him he could listen to it in the back of the room as long as he raised his hand when anything exciting happened. That worked out well for most of us in the class.

Q. What do you think the future holds for controlled drug delivery? What role will polymer science play in this?

A. Eventually we will be able to assay a person's DNA and predict which diseases and which types of drugs they are going to need later in their lifetimes. Maybe we will also be able to prescribe drugs that will delay or prevent the onset of those diseases. That field of "pharmacogenetics" is already here, and it will continue to strongly evolve in the future. Polymers will always be there as nanocarriers for the new drugs, but I think that the real creative cutting edge is in the biology now and will be even more so in the future.

Q. You have received many awards in your distinguished career. What do these awards, specifically the Controlled Release Society Founder's Award (for Lifetime Achievement) mean to you?

A. I greatly cherish the two Founder's Awards I have received, one from the CRS and the other from the Society for Biomaterials. I sincerely value such high recognition by my colleagues.

I also feel especially grateful to so many colleagues who attended two conferences in Hawaii in 1992 and 2002, in recognition of my 60th and 70th birthdays. In a sense, these meetings were very special and personal "awards" for me, and they remain highlights in my career... and in my life. ■

Surface Properties Do Not Affect the *In Vitro* Toxicity of PLGA Nanoparticles Towards Calu-3 Cells

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Introduction

Application of nanoscale systems such as biodegradable nanoparticles (NPs) to health care – referred to as nanomedicine – has the potential to revolutionize the therapy of several pathologies through a controlled and targeted delivery of drugs, allowing an improvement of their therapeutic efficiency together with a reduction of side effects and toxicity (1). Among the various routes of administration, the pulmonary one has raised a large interest during the past decade. NPs are highly bioavailable after lung administration since they are well-retained *in situ* and only weakly taken up by alveolar macrophages, provided their diameter is below 250 nm (2). However, the very same properties that make NPs exciting devices in the field of nanomedicine might induce harmful effects as they interact with specific cells.

So far, most studies have focused on the toxic effects towards the lungs of manufactured NPs (3). The observed harmful effects were correlated to common biological mechanisms (e.g., inflammation and oxidative stress). However, by contrast to inorganic NPs, the lung toxicity of nanomedicines has not been extensively investigated. Most studies have assumed that, due to their biodegradability, NPs do not lead to side effects or toxicity. Nevertheless, despite their biodegradability, specific risks might arise from the NP form itself and the toxicological profile and the biological response to the different NPs is expected to be governed, at least partially, by the NP physico-chemical properties.

In the present work, the role of NP surface chemistry and surface charge on their potential *in vitro* toxicity has been investigated thoroughly. We have designed three types of surface-modified NPs: positively and negatively charged as well as neutral, and we have performed a direct comparison of the various surface coatings. NPs were prepared using Poly(lactide-co-glycolide) (PLGA), which is one of the most commonly used biodegradable and biocompatible polymers involved in the formulation of nanomedicines. NP surface chemistry and surface charge were then tuned by varying the nature of the stabilizer in the formulation. The *in vitro* cytotoxicity, cellular uptake, and inflammatory response following exposure to NPs were all assessed using a Calu-3 based model of bronchial epithelium (4). Calu-3 cells derive from a human bronchial adenocarcinoma and maintain the properties of the original submucosal glands, which are involved in the secretion of airway mucus components and mediators of the inflammatory response. Given that bronchial epithelial cells will be the first met by inhaled NPs, we considered the Calu-3 cell line to be an interesting model to investigate the potential toxicity of nanomedicines.

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Results and Discussion

NPs were prepared according to the emulsion evaporation technique. One cationic stabilizer, chitosan (CS), was used, as well as two neutral stabilizers: partially hydrolyzed poly(vinyl alcohol) (PVA) and Pluronic® F68 (PF68). PLGA/PF68 NPs exhibit a mean diameter of 100 nm while both PLGA/PVA and PLGA/CS NPs were around 200 nm. All formulations have a narrow size distribution with a polydispersity index of 0.1–0.2. These results are in agreement with TEM images (Figure 1) that show spherical NPs with a smooth surface. Zeta potential measurements confirm that stabilizers influence NP surface charge: PLGA/CS NPs exhibit a positive zeta potential ($\zeta = +32 \pm 3$ mV), whereas PLGA/PVA NPs are almost neutral ($\zeta = -5 \pm 1$ mV) and PLGA/PF68 NPs exhibit a negative zeta potential ($\zeta = -24 \pm 1$ mV). PLGA covalently linked to rhodamine was used to prepare fluorescent NPs (Rhod-PLGA NPs),

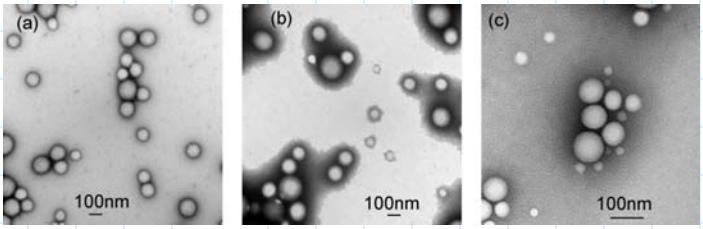

Figure 1. *Transmission electron microscopy images of (a) PLGA/CS NPs, (b) PLGA/PVA NPs, and (c) PLGA/PF68 NPs.*

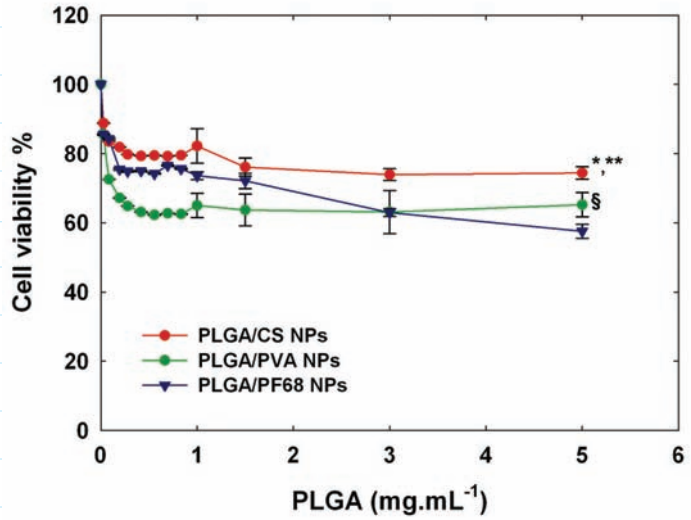

Figure 2. *Calu-3 cell viability after 72 h exposure to PLGA NPs (0.030–5 mg.mL^{-1}). Results are expressed as percentages of absorption for treated cells (± SD) in comparison with untreated control cells. The significance was indicated as $p < 0.05$, (*) PLGA/CS NP vs. PLGA/PVA NPs (0.030–5 mg.mL^{-1}); (**) PLGA/CS vs. PLGA/PF68 NPs (3–5 mg.mL^{-1}); (§) PLGA/PVA NPs vs. PLGA/PF68 NPs (0.030–1 mg.mL^{-1}).*

allowing tracking them *in vitro*. The use of Rhod-PLGA influences neither the size distribution nor the surface charge of NPs.

To assess the *in vitro* toxicity of NPs, Calu-3 cell viability was investigated as a function of NP concentration using the MTT assay. After 72 h of incubation, cell viability is always higher than 50% even at the highest concentration tested (Figure 2). Viability starts to decrease only at very high concentration, highlighting the safety of NPs independently of their chemical composition and surface properties.

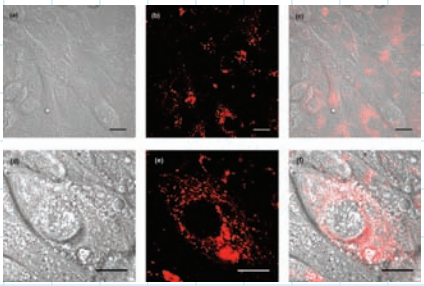

Figure 3. *Real time confocal laser scanner microscopy images of Calu-3 cells exposed to Rhod-PLGA/CS NPs for 24 h. (a) Nomarski image, (b) fluorescent image, and (c) superpostion. (d, e, f) enlarged pictures. Scale bars = 20 µm.*

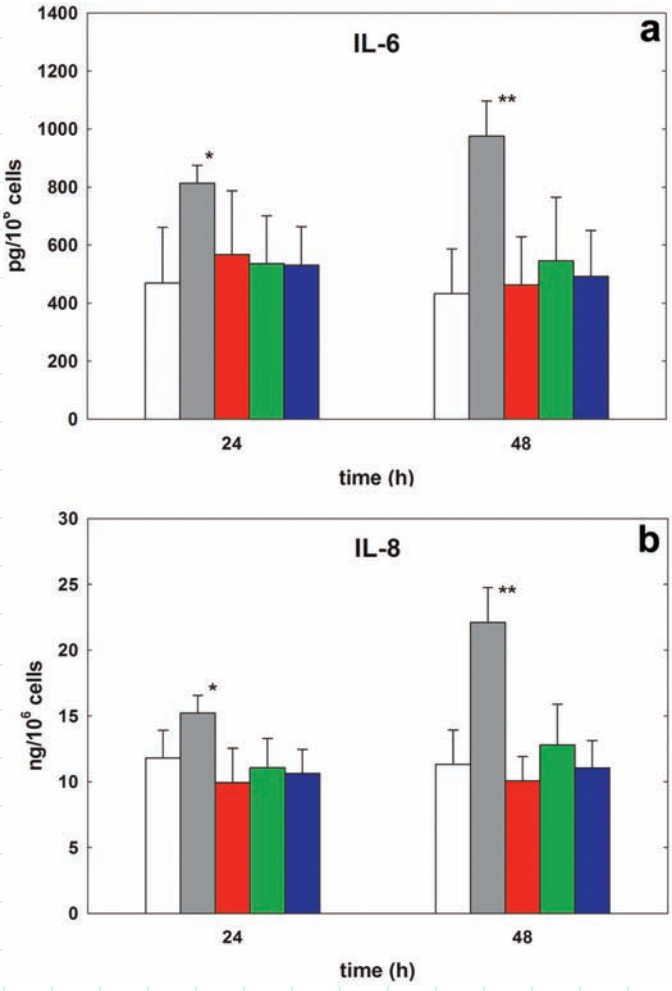

Figure 4. *(a) IL-6 and (b) IL-8 secretion by Calu-3 cells exposed for 24 h and 48 h to LPS (grey bars), PLGA/CS (red bars), PLGA/PVA (green bars), and PLGA/PF68 NPs (blue bars). White bars represent cytokine secretion of untreated control cells. Data represent mean ± SD (n = 3). *p < 0.05, **p < 0.01 (LPS-exposed vs. control and NP-treated cells).*

NP internalization was assessed on living cells by confocal microscopy (Figure 3). Confocal images show fluorescent spots within the cells and especially around the nuclei, proving the interaction of NPs with cells and their intracellular accumulation. In addition, no difference could be observed among the different NPs.

The induction of an inflammatory phenotype in the Calu-3 cells was studied as a function of NP surface properties, by assessing their effect on different markers of inflammation. Remarkably, no effect of treatment with NPs, regardless of their physico-chemical surface properties, was observed. A significant increase over time of cytokine release was only measured for the positive control (LPS) (Figure 4).

These results show that NPs made of PLGA do not cause any inflammatory activation in this *in vitro* model of lung epithelium and exclude the influence of the NP physico-chemical surface properties on the cellular inflammatory response.

Conclusion

NPs are internalized by the Calu-3 cells and induce a low toxicity even at high concentrations, regardless of their surface properties. Exposure to NPs does not promote the release of cytokines, confirming the absence of inflammatory activation potential. These *in vitro* results highlight the safety of biodegradable PLGA NPs on the bronchial epithelium and provide the first data on their potential effects and the risks associated with their use as colloidal nanomedicines (5).

Acknowledgments

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QUIOSELS™, a Redefinition of Cosmetics by Lipotec

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The QUIOSELS™ technology was presented at the annual meeting of the Controlled Release Society, National Harbor, MD, July 2011.

Introduction

Cosmeto-textiles are defined as those textiles which incorporate actives that can cause a cosmetic effect in different parts of the body when in contact with the treated fabric. Typically the actives are anchored to the fabric using various microencapsulation technologies such as polymerization reactions or by surface modifications of the fabric. However, these technologies have often been found to cause chemical modifications in the fabric or to modify the chemical structure of the active, thus diminishing its efficacy and making it difficult to transfer to the skin.

Despite the current use of microencapsulation technologies for incorporating perfumes, adequate transference of the intact active from fabrics to the skin can better be accomplished using biocompatible agents.

Results and Discussion

Structure of QUIOSELS™

QUIOSELS™ is a product composed of "raw" vesicles and a cationic polymer. In order to elucidate its structure, investigations on particle size, Z-potential, and diverse microscopic techniques were conducted. Two structures can be postulated for QUIOSELS™, a) the capsule itself is cationic, or coated with a thin cationic membrane (Figure 1, left) or b) the capsule itself is a non-cationic vesicle and is attached to the fiber via a film that has been formed by a cationic polymeric structure that binds to the fiber at several anchorage points (Figure 1, right).

Average Z-potential values for diverse samples of "raw" vesicles was found to be –4.08 mV, i.e., neutral, and for diverse samples of QUIOSELS™ was +63.44 mV, which is clearly cationic. Particle size analysis showed that "raw" vesicles had a particle size ca. 138.2 nm compared with 1,342 nm for QUIOSELS™, which is one order of magnitude larger.

Microscopic observation (TEM cryo-microscopy) of QUIOSELS™ showed the predominance of spherical mono- and bilamellar vesicles of 100–300 nm diameter (the Polyquaternium-16 chains were not observed by this technique of microscopy). This apparent contradiction of the measured particle size values by light scattering and the visualization by microscopy strongly supports hypothesis (b) as described in Figure 1. Particle size measurements are thus not compatible with a structure in which a thin layer of cationic polymer (such as Polyquaternium-16) is surrounding the vesicle, because the size of the raw liposome is one order of magnitude lower than the measured size for QUIOSELS™. So, this value can be attributed to the polymer (which is not surrounding the capsule completely).

This hypothesis was further evaluated by atomic force microscopy. Observations of the "raw" vesicles, the polymer itself, and the complete product confirmed that the polymer was able to form a film that covers and binds the vesicles to the support, where a similar binding mechanism was postulated for anchoring to the fiber.

Application Tests with QUIOSELS™

QUIOSELS™ containing LIPOREDUCTYL® CT was anchored to a fabric fiber by the exhaustion method at laboratory scale by dipping the fabric in a dilution of the product for 10 minutes without stirring. The presence of the active, caffeine (one of the anticellulitic actives contained in LIPOREDUCTYL® CT), was measured by HPLC. Evaluations were made for the freshly treated fiber and after several washing cycles using either liquid or powder detergents. Anchoring expressed as the ratio of the amount of caffeine detected in the fabric to that present initially in the application bath as determined by HPLC described a concentration-dependent curve with a positive slope. Therefore, the more concentrated the application bath, the more caffeine was anchored to the fabric. The remaining caffeine content in fabric (durability) after two and four washings by different detergents (liquid and powder) was also analyzed. The amounts of the anchored active were found to decrease with the number of washings (liquid or powder detergents), although still detectable after four washings.

In order to investigate the release of active from fiber to skin, percutaneous absorption tests were performed with a modification of the Franz Cell (1). The amount of caffeine in different layers of the skin (stratum corneum, epidermis, dermis) and the remaining active in a cotton fiber were quantified. Skin biopsy

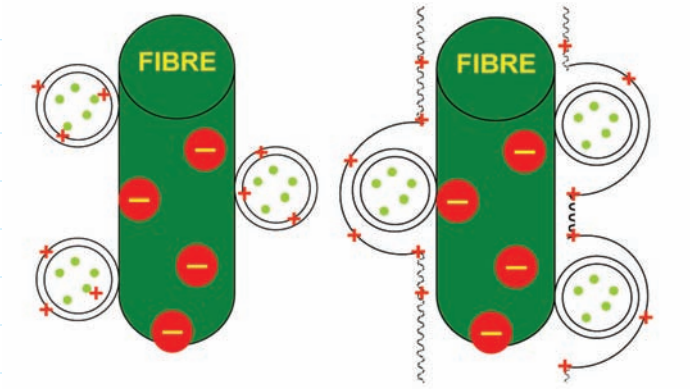

Figure 1. *Graphs showing two hypothesis for binding vesicles to anionic-charged fibre; (left) anchorage via a thin membrane surrounding the vesicle; (right) anchorage via a polymeric matrix with embedded vesicles.*

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tests showed that the amounts of caffeine transferred after 1, 2, 3, and 4 days of contact with fiber treated with QUIOSELS™ were 950, 650, 550, and 370 ng/cm^2 respectively, which is sufficient for ensuring cosmetically effective delivery of caffeine.

Conclusion

The product commercialized by Lipotec under the name QUIOSELS™ is an efficient way to confer cosmetic properties to textiles. Furthermore, this delivery system is able to interact with textile fibers and efficaciously transfer the encapsulated active to skin layers. Quantification of anchorage, durability measurement and percutaneous absorption values demonstrated an efficient transfer of the active to skin layers, thus ensuring cosmetic activity.

Acknowledgments

The authors would like to thank Dr. Juan Cebrián and his team for analysis of active anchoring and durability, and Dr. Sandra Méndez and Dr. Núria Almiñana for performing the percutaneous absorption tests, all of them from Lipotec, S.A.

Lipotec, S.A. is a global supplier of cosmetic active ingredients. It is a privately owned company founded in 1987 by Dr. José María García and Dr. Antonio Parente. The Delivery Systems line constitutes one of the most important technology platforms for Lipotec. Quiosels™ is a patent-pending technology, specially designed by cosmeto-textiles.

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Joseph R. Robinson Postdoctoral Fellowship Year Reflections

2009–2010

David Nhu Nguyen, Ph.D.
Postdoctoral Fellow, Lewis Laboratory
and Stanford Medical School

David Nhu Nguyen

I am honored to be the first recipient of the Controlled Release Society's Joseph R. Robinson Postdoctoral Fellowship, and I would like to share some insight into my experiences. Foremost, I am very grateful for the support in research and medical training that I have received as a direct benefit of this fellowship. I cannot continue to thank enough the CRS Fellowship Committee and benefactors of the CRS Foundation. My tenure has been fun and rewarding. More than just a year of training, the fellowship has connected me to many areas of research and mentorship that will serve me for the rest of my career. I was able to broaden my expertise and learn the conduct of basic biology and immunology research. I interacted daily with physician scientists. I was also able to support a year of medical training at Stanford University. Because of my year as the Robinson fellow, I have developed a more focused and sure trajectory for my future career and am looking forward with less trepidation and more confidence.

Investigating How a Novel Vaccine Adjuvant Activates Immune Responses

I joined the laboratory of David Lewis, M.D., a pediatric immunologist who focuses on neonatal T-cell development, early immune responses, and influenza vaccination. I worked on a project investigating how a novel vaccine adjuvant activates immune responses. Members of the Lewis lab had previously shown that immunization with commercially available preparations of influenza vaccine together with a cationic lipid plasmid DNA complex (CLDC) could activate both humoral and cell-mediated immune responses. However, there was much debate as to how this CLDC actually triggers greater immune responses than those with simple vaccination alone. Further, this nanoparticle complex had recently entered early phase I clinical trials, making these investigations all the more relevant and interesting.

In particular, I worked to discover the mechanism of interaction of this CLDC nanoparticle with innate immune receptors. I spent much time learning basic immunology techniques, many of which I had previously been exposed to, but working in the Lewis laboratory allowed me to develop a greater understanding of the fundamentals of these techniques. CLDC particles likely enhance vaccines through multiple mechanisms, including activation of the innate immune response. We hypothesized that the noncoding plasmid DNA in the CLDC was recognized by an intracellular receptor of DNA. Since there are multiple known and hypothesized distinct receptors of DNA, we began by showing that this CLDC does not appear to activate toll-like receptors (TLRs). A recently described pathway involves both DNA and an RNA intermediate in intracellular DNA recognition. We were able to show that, at least in part, CLDCs can trigger innate immune responses through this DNA/RNA pathway. I was able to characterize the magnitude of this response in both cultured cell lines and primary human immune cells. Currently, most of my research work has been put on hold since I have entered into the in-hospital clinical training part of my M.D. program. However, I plan to return to the laboratory this winter and spring to finish up these investigations, including *in vivo* investigations, and look forward to publishing my results.

Professional Development

As a Robinson fellow, I was able to choose any laboratory based purely on my interests and less on available funding. This allowed me to pick a laboratory in a field for which I have no formal training. During my time as a student and postdoc at MIT, I had worked extensively with developing novel materials for delivery of DNA vaccines, siRNAs, and immunostimulatory RNAs as vaccine adjuvants. I had much experience in the development of novel materials and the formulation and characterization of micro- and nanoparticles, and I also had some limited experience in characterizing innate and adaptive immune responses. Since Stanford is a world-leading expert in the field of immunology, I hoped to broaden my horizons and learn more about immunology from the perspectives of biological studies, medicine, and physiology. I believe that with a good grasp of the fundamental biology and physiology I will be more capable of engineering systems that take advantage of immune responses in my future career.

The practice of medicine and conducting laboratory-based research could readily be two careers on their own. Both require the dedication of extraordinary energy and philosophy. While both fields might antagonize each other with respect to time and resources, in the end, the goal is still the same—advancement of society by promoting health. I was able to find a lab with multiple members who are also physician scientists, splitting their time between clinical work and laboratory work. My year as the Robinson fellow exposed me to mentors and role models with career trajectories similar to my own. One of the most important aspects of career development is learning both from your own experiences and from the experiences of others. Working side-by-side with physician scientists, some established and some still in the process of establishing their careers, I have gained much insight as to how I may personally approach this daunting choice of career paths. I have come away with a greater understanding of how to align myself and my future medical training (residency and eventually fellowship) in such a manner that I will be well-situated to advance into the role as junior faculty. In short, I gained an appreciation for how to balance personal life, clinical duties, and research goals, and it is this experience that I will carry with me throughout my career as a physician scientist.

Career Aspirations
Even though my time as the Robinson fellow is up, I will continue to enjoy the benefits of this 1 year postdoc experience. In the coming 6 months, I will be applying to residency programs in internal medicine. Over 3 years of residency, and additional time in a subspecialty fellowship, I will undergo more intensive and focused medical training that will become the basis for my future practice in medicine. I currently plan to enter fellowship training in infectious diseases. It is during those years of medical fellowship training that I will have the opportunity to return to laboratory research and establish new lines of investigation.

Long term, I plan to merge my experiences in medicine with my background in nanoparticle technology and immunology. I have developed a unique set of training in materials engineering, drug delivery, immunology, and the practice of medicine. My future career will be dedicated to understanding nanotechnology in medicine and designing nanoparticle-based medicines for battling infection and controlling—activating, suppressing, or redirecting—immune responses. Our current knowledge of the safety, reliability, and function of nanoparticles *in vivo* is still limited in animal models and even more so in clinical use. As the field progresses, I will gain expertise in how nanomedicines interact with the human body. Using this knowledge, I hope to engineer new systems for delivering vaccines, investigate new vaccine adjuvants, develop novel antimicrobials, and combat autoimmunity.

Finally, I strongly believe that no matter how successful I am as a clinician or how productive I am as a scientist, my most influential role will likely be as a teacher. Like Prof. Robinson and all of my mentors, I am excited to share my cumulative experiences with future generations and look forward to embracing this role in the hospital, in the laboratory, in the classroom, or wherever else my career takes me.

The CRS Foundation's Joseph R. Robinson Postdoctoral Fellowship was presented to David Nhu Nguyen at the 36th Annual Meeting & Exposition of the Controlled Release Society in Copenhagen, Denmark, July 2009. The research was conducted in 2009 and 2010. Many thanks to the CRS Foundation donors who made this fellowship possible.

2012 Sung Wan Kim Postdoctoral Fellowship Announced

Sung Wan Kim

The CRS Foundation is pleased to announce a prestigious postdoctoral fellowship for 2012, honoring Professor Sung Wan Kim, Distinguished Professor of Pharmaceutics and Pharmaceutical Chemistry, Distinguished Professor of Bioengineering, at the University of Utah. The fellowship honors his exemplary service to CRS and delivery science and will be awarded to an outstanding recent postdoctoral individual at the 2012 CRS Annual Meeting & Exposition.

To Honor Professor Kim
As a pioneer in drug delivery research, Professor Kim has focused on hydrogels, biodegradable drug conjugates, self-regulating drug delivery, and stimuli-sensitive polymers. He has worked extensively in medical polymers, especially blood-compatible polymers. His recent research includes design of novel polymers for the delivery of protein drugs, cells, and genes. Professor Kim is highly recognized throughout the field with honors from the Controlled Release Society (College of Fellows and Founders Award) as well as the Rosenblatt Prize, AACP Volwiler Award, AAPS Dale Wurster Award, the Clemson Basic Biomaterials Award, AAPS Research Achievement in Drug Delivery, and many more. He founded the International Symposium on Recent Advances in Drug Delivery at the University of Utah, serves as a member of the NIH Study Section, and is on the editorial boards of several research journals.

Preliminary Fellowship Information
The Sung Wan Kim Postdoctoral Fellowship recipient will receive a one-year, $30,000 postdoctoral fellowship and will participate in both the 2012 and 2013 CRS Annual Meetings. More selection and application information is on the CRS Foundation web page, www.controlledreleasesociety.org/about/foundation.

Your Support Is Needed
The Sung Wan Kim Postdoctoral Fellowship is possible only through financial support to the CRS Foundation Endowment. Please contribute to build this postdoctoral fellowship. Invite your organization to match your contribution and encourage outstanding colleagues to apply. Please donate online or by contacting Cheryl Kruchten at CRS Headquarters, +1.651.994.3801. Questions may be addressed to Deborah Woodard, +1.651.994.3817, dwoodard@scisoc.org. The CRS Foundation is a 501(c)(3) charitable organization, qualified to accept tax-deductible contributions during donor lifetime or bequests by will. Donations may be tax deductible.

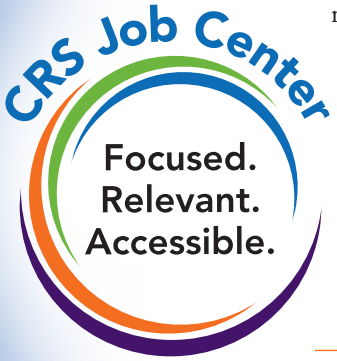
Thank you to all who have given and continue to support the CRS Foundation and future of delivery science.

New CRS Job Center—Connect with the Right Job to Reach Your Career Goals

Recently launched with the new website, the CRS Job Center exists to provide you with the tools and resources you need to identify new opportunities and to further your career. Your skill set, education, and experiences have laid the foundation of your career; now utilize the CRS Job Center to realize your career potential.

Post Your Resume

Whether you are actively searching for a job or currently employed and not actively searching, the CRS Job Center's resume system allows hiring organizations to find you. The CRS Job Center resume bank is searchable by all prospective employers, yet protects your privacy and maintains anonymity by not sharing your name or contact information. Employers can find your resume and reach out to you regarding job opportunities through a secure e-mail system. If you are interested in their job opportunity, you simply release your contact information. This tool allows you to stay connected to the employment market while maintaining full control over your confidential information.



Job Search Tip: Develop a professional resume

Posting your quality, professional resume to the CRS Job Center is the most important step in achieving top visibility to prospective employers and connecting with the right job in the areas of bioactives, consumer and diversified products, and veterinary science. Take the time to review your resume to make sure everything is concise, comprehensible, and correct.

Search for Jobs

The CRS Job Center provides you with relevant niche jobs to help focus your job search. Search by keyword, location, and job type to aid you in finding the exact job to match your career goals. As a focused recruiting site, the CRS Job Center is the best tool for finding targeted delivery science jobs that fit your career profile. This is because more and more employers are utilizing focused recruiting sites in their hiring process. Through the CRS Job Center, you will find jobs directly related to your career field and interests.

Job Search Tip: Search often

New positions are posted daily, so it is important to frequently search the CRS Job Center. The more searches you conduct, the more likely you are to find the job that will aid you in your career aspirations.

Set Up Job Alerts

The CRS Job Center provides accessibility in job searching through personalized job alerts. Setting up the job alerts tool only takes a few moments and is free of charge. Simply select your preferred criteria for job attributes and the CRS Job Center will e-mail you jobs that match those criteria. Job alerts from the CRS Job Center are the essential tool for never missing a job opportunity in the field of delivery science.

Job Search Tip: Update your job alerts

Maintaining up to date job alerts that reflect your current interests is essential for realizing the full potential of this job search tool. As your experience grows and goals change, job alerts from the CRS Job Center can develop with you. This will ensure that only those jobs matching your current aspirations will be sent to you.

.....

Employers utilize the CRS Job Center because they are looking to hire someone who is interested in controlled release and who potentially has your skill set. Upload your resume and begin your search on the CRS Job Center today for the job that will fulfill your delivery science career goals.

Covaris Demonstrates Adaptive Focused Acoustics for Nano-particle Formulations

Carl Beckett
Covaris Inc.

As a first time exhibitor at CRS, Covaris Inc of Woburn, MA, showcased their Adaptive Focused Acoustics™ (AFA) technology for formulation. Based on its proprietary focused ultrasonic technology, the Covaris equipment offers a best-in-class method for liposome formation, production of nano-suspensions, or dramatically accelerating formulation dissolution rates. The process is non-contact, isothermal, rapid, and can efficiently scale process sample volumes from 100 µL through multiple liters.

AFA is able to quickly reduce the particle size of an API to a nanometer distribution, while recovering 100% of the material due to its self-contained processing vessel. The ability to run isothermally manages the heating that might otherwise damage or degrade a sensitive ingredient. A suite of low solubility generics were processed to below 100 nm particle size in a matter of minutes.

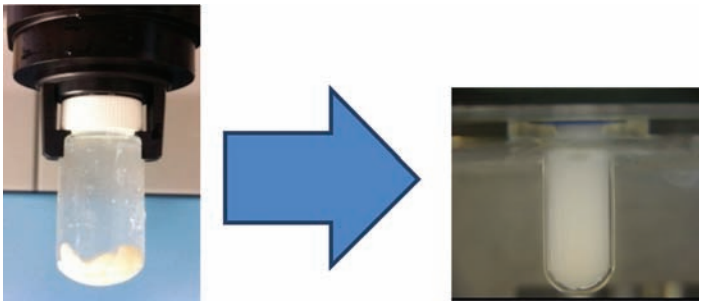
All formulations 2 mL, 0.1% SLS, 0.05% MC 5 mg/mL and measured using Malvern Zetasizer nano ZS-90.

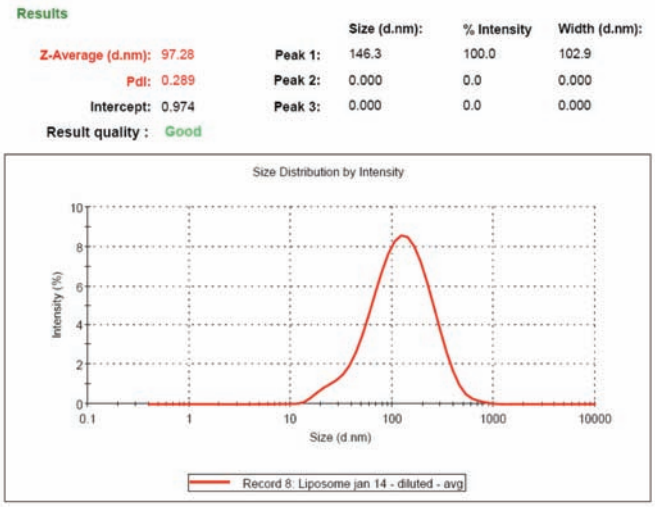
Parameters	Ibuprofen	Cinnarizine	Indomethacin	Griseofulvin
Baseline	203.67 µm	149.17 µm	239.88 µm	44.45 µm
15 minutes	110 nm	280 nm	127.4 nm	100 nm
30 minutes	97 nm	56.85 nm	20 nm	90 nm

For liposome manufacture, AFA offers a one step, simple to operate process:

Materials:

- Phospholipon 90G from Lipoid, dI water. No solvents needed!
- ~2 mL sample volume
- 30 seconds processing using AFA
- 4°C temperature

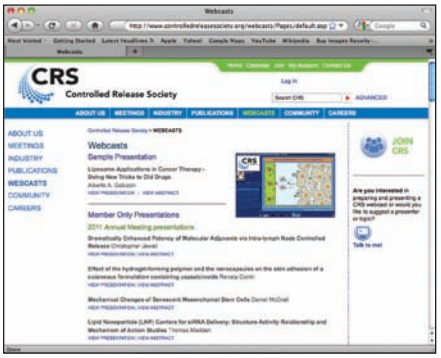




With the ability to operate on a flow-through configuration, AFA is able to generate monodisperse liposome populations in a completely continuous flow environment suitable for real time PAT feedback control and quality monitoring of the finished product.

For more information on Adaptive Focused Acoustics, please contact Carl Beckett: cbeckett@covarisinc.com, 781.932.3959 x231, www.covarisinc.com. ■

CRS's Expanding Member Resource—The CRS Webcast Library



Have you visited the ever-expanding CRS webcast library on the new CRS website? New webcasts have been added over the past few months, bringing the library to more than 60 webcasts available to members on a variety of topics within delivery science. Many of the sessions at the CRS Annual Meeting & Exposition were recorded and synced to their PowerPoint presentations, creating a full visual and audio presentation. This offers access to scientific research to those who didn't attend the meeting, and allows those who did attend the meeting to see sessions they may have missed or want to see again.

Up next for the Webcast Committee, chaired by Biana Godin Vilentchouk, is to create convenience for the user by organizing the webcasts into categories. Many additional webcasts are planned, including presentations aimed toward career development. All CRS members are invited to submit a webcast and be a part of the growing library. Suggest a webcast at www.controlledreleasesociety.org/webcasts.

This extra knowledge available through webcasts is just one of your many new and enhanced member benefits available with the new CRS website. Visit www.controlledreleasesociety.org/webcasts to learn from these important resources.

Top Webcast Downloads
What are your colleagues looking at? Here are the top three downloaded webcasts from the past five months:

#1 *Controlled release matrix tablets – Opportunities, limitations and challenges* by Christian Seiler

#2 *Studies on Liposome, Gel and Lipogelosome Formulations Containing Sodium* by Gulengul Duman

#3 *Targeting Human Prostate Cancer PC3 with Bombesin-Anti-DTPA Fab Bispecific Complexes and DTPA-polymer-drug conjugates for Molecular Imaging and Therapy* by Keyur Gada ■

Controlled Release in Oral Drug Delivery Becomes Second in the CRS Book Series

CRS has now published its second book—this time focused on oral drug delivery. Editors Clive Wilson and Patrick Crowley developed *Controlled Release in Oral Drug Delivery* by bringing together authors with a vast knowledge base, ranging from gastrointestinal tract physiology to polymer science to the mechanisms for drug release. The book delves into the subject matter and its challenges in great detail, with the support of input from academia, providers of excipients, and from those designing controlled release systems in industrial R&D and manufacturing. The contents provide a unique blend of cutting-edge knowledge, data on materials, and practical experiences. The book will be an indispensable resource for students, researchers, and industrial engineering, formulation, and manufacturing technologists, as well as those involved with quality testing and control functions.

This essential text joins the first in the series, *Controlled Pulmonary Drug Delivery*. Learn more about both books at www.controlledreleasesociety.org/publications. CRS members receive a 25% discount on these and all Springer titles when using the CRS member discount token. ■

Honor a Colleague

Submit a Nomination for the 2012 CRS Awards

Nominations are now being sought for the following CRS awards:

- Fellows
- Founders
- CRS T. Nagai Postdoctoral Research Achievement Award
- Young Investigator Award

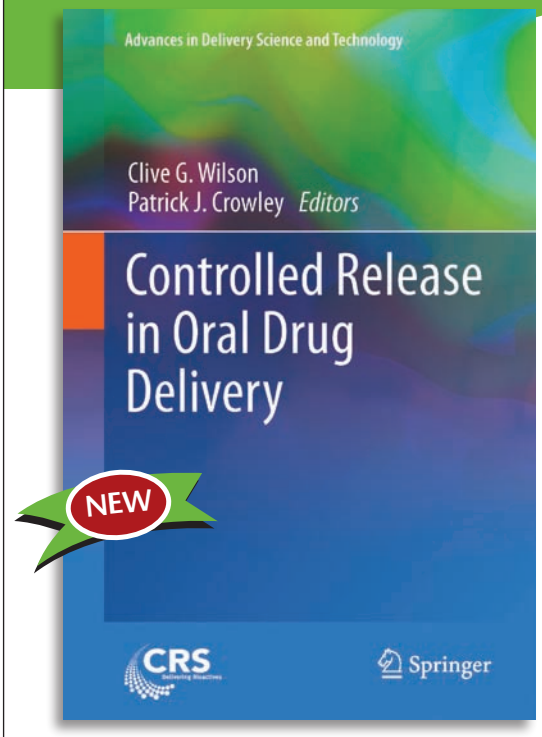
Information on the awards, eligibility requirements, and the online nomination form are available at **www.controlledreleasesociety.org/about/awards**.

CRS Delivering Bioactives

Make Your Nominations by January 31, 2012

The Latest in the CRS Book Series!

An Essential Text on Controlled Release for Oral Drug Delivery



Edited by
Clive G. Wilson and Patrick J. Crowley

2011; XIII, hardcover; 412 pages;
ISBN 978-1-4614-1003-4

$239 Regular Price

Member Price $179.25 **SAVE $59.75**

Access your token at
www.controlledreleasesociety.org/publications

Watch for more titles in the Advances in Delivery Science and Technology series
COMING SOON!

CRS Delivering Bioactives

Controlling the rate, extent, and time of a drug's delivery can optimize its performance in many ways. Such optimized design requires a broad knowledge base of topics, such as gastrointestinal tract physiology, polymer science, and the mechanisms by which drugs are released from the formulated units. This new book addresses all facets and challenges of oral drug delivery, providing a unique blend of cutting-edge knowledge, data on materials, and practical experiences.

CRS Members **SAVE 25%** on this new book, and on all Springer book titles if purchased through the Springer site. Learn more at **www.controlledreleasesociety.org/publications**.

Chapters Include:

- Introduction and History of Controlling Drug Release
- The Organization of the Gut and the Oral Absorption of Drugs: Anatomical, Biological and Physiological Considerations in Oral Formulation Development
- Controlling Drug Release in Oral Product Development Programs: An Industrial Perspective
- Animal Model Systems Suitable for Controlled Release Modeling
- In Vitro Testing of Controlled Release Dosage Forms during Development and Manufacture
- Oral Controlled Delivery Mechanisms and Technologies
- Drug-Polymer Matrices for Extended Release
- Ion Exchange Approaches to Controlling Drug Release
- Pulsatile Delivery for Controlling Drug Release
- Ordered Mesoporous Silica for the Delivery of Poorly Soluble Drugs
- Geometric Release Systems: Principles, Mechanisms, Kinetics, Polymer Science, Release Modifying Materials
- Extrudable Technologies for Controlling Drug Release and Absorption
- Coated Multiparticulates for Controlling Drug Release
- Capsules as a Delivery System for Modified Release Products
- Lipids in Oral Controlled Release Drug Delivery
- Buccal Drug Delivery
- Controlling Release by Gastro Retention
- Drug Delivery to the Colon

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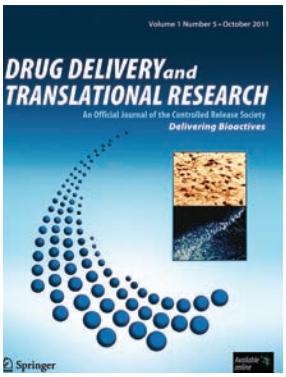
Drug Delivery and Translational Research

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



I am pleased to announce the paper published by Herzog et al. in issue #5 of *DDTR* as the editor's pick. The study describes the potential of gene therapy to address what is known as the diseases of the aging brain. Many neurological diseases—including Alzheimer's, Parkinson's, and Huntington's—affect the lives of millions. In the editorial in the same issue, the challenges in treating growing number of patients with neurodegenerative diseases are described.

Editor's Pick

Gene transfer provides a practical means for safe, long-term, targeted delivery of biologically active neurotrophic factor proteins for neurodegenerative diseases

Christopher D. Herzog, Kathie M. Bishop, Lamar Brown, Alistair Wilson, Jeffrey H. Kordower and Raymond T. Bartus* (*Corresponding author).

This paper argues that gene transfer provides the means to overcome the significant, decades-long delivery obstacles encountered as past investigators attempted to use therapeutic proteins to treat chronic CNS diseases. Several studies in rats and monkeys reported herein collectively demonstrate that one-time administration of a gene transfer viral-vector produces safe, consistent, 2-year expression of biologically-active protein, targeted to selective sites deep within the brain. Additionally, parameters for translating this success to much larger human brains were established, providing support for ongoing clinical trials in Alzheimer's and Parkinson's disease. Read more about this paper in *DDTR,* Issue #5, 2011.

Upcoming Special Issues!

DDTR is developing several theme issues on delivery science and technology with a translational focus. The primary focus of *DDTR* is to advance the science and technology of delivering actives, and provide a unique forum for publication of high quality translation drug delivery research. If you are interested in developing a theme issue, please contact the editor at labhasv@ccf.org.

Special Focus Issues

Advances in Image-Guided Drug Delivery, with guest editors Arash Hatefi and Tamara Minko from Rutgers, The State University of New Jersey.

Image-guided drug delivery (IGDD) is an emerging therapeutic approach where imaging modalities are used to guide and monitor localization of therapeutics to the site of action. Therefore, a methodical approach to IGDD entails systems for delivery, targeting, and monitoring (imaging) of the course of action. This special issue will cover various technologies that are being developed for simultaneous drug delivery validation and therapeutic response evaluation in disease conditions.

CNS Drug Delivery of Biologics, with guest editor Pericles Calias, Shire HGT.

Strategies for treating the central nervous system (CNS) manifestations of diseases have evolved well beyond the traditional size/lipophilicity paradigm. This special issue describes the challenges of developing therapies targeted to the CNS, from bench to clinical development. A review of the biological hurdles and current strategies for overcoming them will set the stage for discussions on the assessment of the product's pharmacologic effect within the CNS and regulatory considerations for the incorporation of biomarkers into product development programs.

Cancer Stem Cells with guest editor Jayanth Panyam, University of Minnesota.

There is growing evidence that cancers contain a small subset of stem-like cells (cancer stem cells; CSCs) that can self-renew. CSCs may play a critical role in cancer treatment outcomes, because they are resistant to conventional chemotherapy and can initiate tumor recurrence following treatment. The goal of this theme issue is to review the role that CSCs may play in tumor response to therapy and the strategies to inhibit CSCs.

Nasal Drug Delivery, with guest editors Elka Touitou, The Hebrew University of Jerusalem and Lisbeth Illum, Critical Pharmaceuticals, BioCity Nottingham.

The nasal route of administration for systemic action of drugs is an exciting growing field of research that opens avenues for investigation and design of new and more efficient products. This issue will focus on translational nasal drug delivery research. Reviews on the nasal administration route for systemic and nose-to-brain delivery will cover absorption pathways, delivery systems, and devices. They will be followed by papers on specific case studies on new carriers, drugs, and vaccines investigated in animals or administrated to humans.

Biomimetic and Biofunctional Materials in Regenerative Medicine, with guest editor V. Prasad Shastri, University of Freiburg, Germany.

The main objective of this themed issue *Biomimetic and Biofunctional Materials in Regenerative Medicine* is to highlight the evolution of concepts in materials engineering for inducing autologous regeneration and the challenges associated with clinical translation. In this context, material design that incorporates principles of directed-self-assembly, surface engineering, metabolic engineering, extracellular matrix mimicry, and synthetic biology, for driving functional cellular organization, and recapitulation of signaling environments in embryonic and fetal development will be highlighted.

Visit the Newly Designed CRS Website to Access DDTR

Drug Delivery and Translational Research (*DDTR*) is an official member journal of CRS providing a unique forum for publication of high-quality research that focuses exclusively on translational aspects of science and technology of delivery of bioactives. Join the leading scientists who are publishing their work in *DDTR*. It is available online to CRS members as a benefit. Members must login to the CRS website first, then click the Publications tab to get to the member access link. ■

Developing Pharmaceutical Products for Controlled Pulmonary Delivery Workshop

Over 60 attendees joined the Controlled Release Society for the October 23 *Developing Pharmaceutical Products for Controlled Pulmonary Delivery Workshop* held prior to the 2011 American Association of Pharmaceutical Scientists Annual Meeting and Exposition in Washington, DC. There has been tremendous interest in delivering controlled therapies to the lung to treat diseases such as asthma and other lung diseases. But the lung presents many barriers to controlled drug delivery systems, such as mucociliary escalator, narrow and constricted airways, and a restricted number of approved excipients.

Chairs Hugh Smyth (pictured left) and Jason McConville, both from the University of Texas at Austin, brought together nine world-class presenters to discuss formulation design and delivery systems, excipient selection, particle engineering technologies, regulatory issues, and low-cost inhalation technologies for the developing world. ■

Welcome New Members

Susan Burnett
Eduard Diviu
Inayet Dumanli
Robert A. Hoerr
Harsh Vardhan Jain
James D. Ormes
Wajira S. Ratnayake
Linda G. Richardson
Qing Wang
Daniela White

CRS Delivering Bioactives

Thirsty for Information?

Check out the new LATTE database—your link to scientific experts within CRS

LATTE—Linking Academic Technologies and Techniques to Everyone—is a searchable database designed to help you identify experts in specific areas of CRS-related technologies and techniques.

CRS Members

You are invited to create your LATTE profile and offer your expertise to the membership, and search LATTE to find the experts you are looking for.

www.controlledreleasesociety.org

Access the Latest from CRS

In the constantly and quickly expanding field of delivery, keeping up with the latest scientific research and technological breakthroughs is crucial. The Controlled Release Society (CRS) is also constantly and quickly expanding to meet *your* needs.

In addition to excellent opportunities to meet with the leaders in delivery science and view the cutting-edge research, your membership provides you access to all the products and services CRS is developing.

Access the Latest:

- The new website, with enhanced capabilities to help you advance delivery science and technology
- Find delivery science experts via the LATTE database—Linking Academic Technologies and Techniques to Everyone
- Expand your knowledge with the growing webcast library, part of the new website
- Learn about delivery science through our new books, including the first two in the series Controlled Pulmonary Drug Delivery
- Find your next position via the Job Center

All Your Member Benefits:

- Online subscription to *Drug Delivery and Translational Research* (*DDTR*)
- Reduced subscription rates to the *Journal of Controlled Release*, *European Journal of Pharmaceutics and Biopharmaceutics (APV)*, and *Biomaterials*
- Access to member-only areas of the new CRS website, including LATTE and the webcast series
- Reduced registration rates to the Annual Meeting & Exposition and select workshops/short courses
- Subscription to *CRS Newsletter*
- Member discount pricing on the book series
- International chapters and student chapters
- The mentoring program
- Ability to access the online membership directory, updated continually
- The chance to earn fellowships and awards
- Online job posting service
- Monthly member news capsules
- Opportunities to be involved through volunteering

Your Membership Matters

CRS
Delivering Bioactives

Not only does your membership give you access to these benefits and more, but your support allows CRS to create new products and services that serve the field of delivery science.

www.controlledreleasesociety.org

Montréal Hosts the First Canadian Chapter National Meeting of CRS

Jake Barralet, McGill University, Montréal

The Canadian Chapter of CRS held their inaugural national meeting in Montréal, Québec, from 24–27 May 2011. This marked a milestone in the Chapter's history, as it was the first opportunity for the 140+ members from across seven Canadian provinces to meet face to face as a national group.

As part of the larger, 500-delegate Canadian Symposium entitled "Multidisciplinary Approaches To Modern Therapeutics… Joining Forces for a Healthier Tomorrow," the meeting brought together the combined resources of four related national organizations (CC-CRS together with the Canadian Society for Pharmaceutical Sciences, the Canadian Society of Pharmacology and Therapeutics, and the Natural Health Products Research Society of Canada), with the CC-CRS providing a forum for researchers interested in topics relating to the controlled release of bioactives. Each society was responsible for organizing parallel plenary sessions, with the CC-CRS electing to recruit presenters for three consecutive sessions on the topics of bioactive delivery: "Targeting the Brain," "Targeting Nucleic Acid Therapies," and "Orthopaedics (e.g., Bone Targeting)." Among the many distinguished speakers were Dr. Mark Tracy (Senior Director, Alnylam Inc, and President of CRS), Prof. Robert Young (Simon Fraser University), Dr. Xiaodong Li (Bone and Mineral Research, Amgen), Prof. Clemens van Blitterswijk (University of Twente, Netherlands), Prof. Hasan Uludag (University of Alberta), James Hayes (Tekmira, BC), Prof. Laurent Lecanu (McGill University), and Richard Kremer (McGill University).

Furthermore, CC-CRS members contributed to the two days of poster presentations, with a dedicated section of over 20 research posters being highlighted as part of the larger poster exhibition and trade show. CC-CRS Travel Awards were awarded by the selection committee to graduate students Scott Campbell (McMaster University) and Krishna Hari Bhandari (University of Alberta) (pictured below), and CC-CRS Poster Awards were won by graduate students Diogo Lopes De Jesus (École Polytechnique de Montréal) and Ghareb Soliman (McGill University). Congratulations to our student awardees!

From left to right: Jake Barralet (Past President), Todd Hoare (Secretary), and Uwe Gbureck (Overseas attendee) at the reception.

David Basset hard at work recruiting for the Chapter.

Once again, thank you to all the speakers, volunteers, sponsors, and the boards of the Canadian Society for Pharmaceutical Sciences, the Canadian Society of Pharmacology and Therapeutics, and the Natural Health Products Research Society of Canada. Special thanks of course to Bev Berekoff and Barb Scollick of CSPS for all their help and support!

Of great importance will be next year's 2012 CRS Meeting & Exposition, which will be taking place in Québec City, in the province of Québec, Canada. The Canadian Chapter of the CRS will be pleased to participate and to once again mobilize the chapter's membership, as we help organize the delivery of workshops and plenary sessions in the historic 16th century "walled fortress" that is Québec City.

From left to right: Mark Tracy, Alnylam; Robert Young, Simon Fraser University; and Xiaodong Li, Amgen.

N'oubliez pas de rafraîchir votre français et de profiter du paysage magnifique, aller voir les baleines bleues, le Fjord du Saguenay, louez un voiture pour une visite de Montréal, allez à la Gaspé et Nouvelle-Écosse, allez voir (mais évitez) les loups et les ours, mettez vos épaisses chemises à carreaux et la section canadienne se réjouit de vous accueillir hein!

Tu te souviendras! ■

Consumer and Diversified Products

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

This article summarizes selected patents from the U.S. Patent Collection Database that were issued between January 1 and June 30, 2011. Patents were selected based on use or potential use of the technology for controlled release or delivery in a Consumer and Diversified Product area such as food, nutritional, cosmetic, household, personal care, agricultural, industrial, and other non-pharmaceutical areas. The reader is referred to the U.S. Patent Office website at http://patft.uspto.gov/ for more detail on the patents.

Pharmaceutical Compositions for Controlled Release Delivery of Biologically Active Compounds; U.S. Patent 7,964,219

This invention involves complexing a biological active containing at least one basic function with a poly-anion derived from hexahydroxycyclohexane and incorporating it into biodegradable, water-insoluble polymers for controlled release/delivery. A more stable complex with a lower initial release and more desired extended release profile is claimed.

Degradable Poly(ethylene glycol) Hydrogels with Controlled Half-Life and Precursors Therefor; U.S. Patent 7,964,217

This invention involves the use of hydrolytically degradable gels of crosslinked poly(ethylene) glycol (PEG) structures. These hydrogel materials are prepared by reacting PEGs containing functional crosslinking end groups. Materials are selected to provide hydrolytically degradable crosslinked structures with controlled hydrolysis rates. Degradation provides a means for controlled release of trapped molecules. These materials and mechanisms avoid the use of non-PEG materials common to current technology.

Orienting Polymer Domains for Controlled Drug Delivery; U.S. Patent 7,964,209

This invention provides a method for formulation of medical devices that use a field or fields to control spatial orientation of polymer domains in a release region to control release of therapeutic agents. Possible fields include electric, magnetic, mechanical shear, or a solvent gradient.

Controlled Electroporation and Mass Transfer Across Cell Membranes; U.S. Patent 7,955,827

Controlled electroporation is achieved in individual or multiple biological cells or biological tissue by monitoring the electrical impedance (current/voltage). Impedance indicates the onset of electroporation, and this feedback is used to control the intensity and duration of the voltage to assure that electroporation has occurred without destroying the cell(s). A particular method and apparatus for the study of electroporation for control of diffusive transport across cell membranes are disclosed.

Method of Controlled Delivery for Use of Electrochemical Power Source; U.S. Patent 7,943,259

A system and method are described for improving electrochemical power sources through controlled release of an encapsulated oxidizer or controlled release of organic matter from a hydrogel matrix within a galvanic electrochemical power source or microbial fuel cell.

Controlled-Release Composition for Topical Application and a Method of Delivering an Active Agent to a Substrate; U.S. Patent 7,939,570

A controlled-release emulsion composition for topical application of a bioactive material is described. The system utilizes silicone material, surfactant, and water and eliminates the need for a lipophilic solvent.

Compounds for a Controlled Release of Active Molecules; U.S. Patent 7,935,669

This invention relates to controlled delivery of perfume molecules from compounds comprised of β-oxy or β-thio carbonyl moieties. Included in the claims are perfuming compositions and perfumed articles.

Nanoporous Membrane, Process of Fabricating the Same and Device for Controlled Release of Biopharmaceuticals Comprising the Same; U.S. Patent 7,935,416

This invention claims a nanoporous membrane system for controlled delivery of biopharmaceuticals from an implant or patch. The system uses a first membrane of 10 to 200 nm thickness and 6 to 40 nm pores and a second membrane of 1 to 20 nm thickness and 4 to 30 nm pores.

Method for Controlled Gelation of Silicates; U.S. Patent 7,926,567

A process for controlled silica gel formation is described. The process uses hydrolytic organic acid or acid formation from solid polymer particles dispersed in alkaline silicate solution. The process may be used in any situation where it is desirable to achieve a controlled gelation of silicate such as grouts and sealants, the preparation of foundry moulds or other moulds and in oilfield applications. Oilfield applications may include water or gas shut off in underground hydrocarbon containing formations, control of coning, sealing of fractures or thief zones, modification of sweep profiles, temporary or permanent blocking of a wellbore. ■

Call for Papers

The 39th Annual Meeting & Exposition of the Controlled Release Society

July 15–18, 2012
Centre des Congrès de Québec
Québec City, Canada

Smart Materials—From Innovation to Translation

Québec City Convention Centre.

Share Your Research

The CRS Annual Meeting & Exposition offers the unique opportunity to share your latest breakthroughs with premier delivery scientists from around the world.

Submit your abstract by January 26, 2012.

CRS Delivering Bioactives

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In the News

Compiled by Steven Giannos
Industrial Editor

October 2011

Zynex Expands Product Line

Business Wire, October 31, 2011 – LONE TREE, CO – Zynex, Inc. (OTCBB: ZYXI), a provider and developer of non-invasive medical devices for electrotherapy, stroke rehabilitation, neurological diagnosis, and cardiac monitoring, announced that it has signed a private labeling and distribution agreement with ActivaTek, Inc. to sell and distribute a line of iontophoresis products.

Zynex will begin selling the iontophoresis products immediately through its U.S. sales force in its Zynex Medical subsidiary. The products are typically sold and invoiced directly to physical therapy clinics.

Iontophoresis is a non-invasive method of propelling high concentrations of a medication transdermally by use of a small electrical charge (an injection without a needle). This method of drug delivery is commonly used to treat site-specific inflammatory and other musculoskeletal conditions and is typically administered in a series of treatments by a healthcare provider within the clinic. The product line consists of both a self-contained patch, similar to a large band aid, as well as the more traditional clinical dose controller to drive the current through the disposable delivery electrodes. The iontophoresis market is well established, has existed over several decades and primarily allows clinics to get paid by health insurance as they treat their patients.

Zynex's CEO, Thomas Sandgaard, commented, "We are very excited about the addition of iontophoresis devices to our existing product line. We believe the iontophoresis products will not only provide opportunities for additional sales, but will also assist us in further penetrating our electrotherapy market. The iontophoresis devices will be marketed and sold directly to our already existing base of customers within the pain and rehabilitation market."

ActivaTek CEO, Jamal Yanaki, stated, "We are excited to share our most advanced and flexible iontophoresis technologies with Zynex." ActivaTek, Inc. is an innovative iontophoretic drug delivery company based in Salt Lake City, Utah. For additional information please visit: http://www.activatekinc.com.

Pulmatrix Demonstrates Superiority of iSPERSE in Delivering An Effective Multi-Drug Inhaled Dose Compared to Conventional Formulation

Business Wire: October 31, 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 that it has demonstrated that iSPERSE™, its inhaled drug platform, shows superiority in delivering an effective therapeutic dose of the active ingredients in Advair®, salmeterol, and fluticasone, compared to conventional lactose blend Advair. These data from *in vitro* studies show the potential of iSPERSE, a proprietary cationic salt formulation inhaled as a dry powder, to efficiently deliver consistent doses, which can have relevance to patients having lower or impaired lung function. Based on these and other data, Pulmatrix is now advancing a number of proprietary iSPERSE drug formulation candidates including small molecules, combinations, and biologics in a variety of therapeutic areas, including chronic obstructive pulmonary disease (COPD), cystic fibrosis, asthma, idiopathic pulmonary fibrosis (IPF), pulmonary arterial hypertension (PAH), and non-CF bronchiectasis, as well as pursuing partnerships for iSPERSE.

"These *in vitro* studies clearly demonstrate several of the key attributes of iSPERSE compared to traditional lactose blends: delivery efficiency of respirable particles, improvement of the delivered dose of active ingredients, and flow rate independence," said Michael Lipp, PhD, Vice President of Development and Intellectual Property at Pulmatrix. "We believe these iSPERSE traits will translate to improved efficacy to patients related to dose reproducibility, reduced side effect profiles, and broader applicability to patient populations with compromised lung function."

In the *in vitro* studies cited, Pulmatrix demonstrated that iSPERSE is superior to conventional inhalation drug delivery technologies in dose delivery, dose efficiency, and inhalation flow rate independence. In these studies, an iSPERSE fluticasone and salmeterol combination was matched to commercially available Advair. iSPERSE showed three times greater delivery of drug to the lungs over the lactose blend while maintaining consistent particle size over a range of inhalation flow rates. These data will be presented at the 11th US-Japan Symposium on Drug Delivery Systems, which is being held from December 16–20, 2011, in Lahaina, Hawaii.

Mike Yeadon, PhD, former Vice President and Chief Scientific Officer of the Allergy and Respiratory Unit of Pfizer and member of Pulmatrix's Scientific Advisory Board, said: "For decades, just three basic methods existed for creating inhalable drugs: nebulized solutions, lactose-based dry powders, and metered-dose inhalers. Like many in respiratory R&D, I thought that was all there could be. But iSPERSE's small, dense particle technology appears to add another and valuable option. Its potential could be huge, and not only for existing drugs. As a drug discoverer, I am aware of a number of areas of target-rich biological processes for which drugs could be invented, which may not easily fit into the existing inhalation drug-delivery

technologies. Rather than discard such candidates, or worse, the targets themselves, I'd recommend innovators take a close look at iSPERSE. If this becomes proven in clinic, it could become the new gold standard."

Additional data relating to the technical specifications and delivery capabilities of the iSPERSE technology were presented earlier this year at The International Society for Aerosols in Medicine (ISAM) in Rotterdam, Netherlands. At ISAM, 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, corticosteroids, and multiple LABA/ICS and LAMA/ICS combinations.

Arsenal Medical spins out 480 Biomedical

Business Wire: October 26, 2011 – WATERTOWN, MA – Arsenal Medical, a privately held company developing novel biomaterial-based local therapies, announced today that it has spun out 480 Biomedical, Inc. as a standalone company focused on the development of a bioresorbable scaffold for treating occlusive disease in the superficial femoral artery (SFA).

Concurrently, both Arsenal Medical and 480 Biomedical completed financings. A $15 million round for 480 Biomedical will fund clinical studies for the SFA scaffold that are being initiated in 2011, and a $3 million round for Arsenal Medical will augment considerable grant support to advance its proprietary nanofiber-based drug delivery and therapeutic foam product platforms. Both financings were led by current Arsenal Medical investors Polaris Venture Partners, North Bridge Venture Partners, and Intersouth Partners. A new strategic investor also participated in the 480 Biomedical financing.

"The formation of 480 Biomedical further validates the substantial progress made by the Arsenal Medical team in translating cutting-edge materials science and innovative engineering into therapeutic products with important clinical benefits," said Duke Collier, CEO of 480 Biomedical. "Now that our bioresorbable scaffold has reached the clinical stage, we felt it was appropriate to create an independent company to take it forward. Moreover, this new corporate structure strengthens Arsenal Medical's ability to focus on its very exciting earlier stage programs." Collier, who has been CEO of Arsenal Medical, and will continue as its Executive Chairman, previously served as executive vice president at Genzyme Corporation.

Dr. Maria Palasis, who has been leading research and development efforts at Arsenal Medical, will become the executive vice president and chief technology officer of 480 Biomedical. Prior to joining Arsenal, Dr. Palasis was a research and development director at Boston Scientific, where she managed a portfolio of strategic biotech alliances and medical device investments, and was responsible for the development of proprietary combination products.

480 Biomedical's lead product is a completely bioresorbable, self-expanding scaffold and delivery system. This scaffold is initially being developed for the treatment of SFA occlusive disease, a common form of peripheral vascular disease affecting more than 10 million people worldwide. During the post-intervention healing period, the 480 Biomedical scaffold uniquely combines mechanical strength and flexibility, similar to nitinol stents, to hold open the artery. Unlike metal stents, however, which cannot be removed, the 480 Biomedical scaffold resorbs into the body in about a year. This combination of strength, flexibility, and biocompatible resorption make the scaffold ideal for use in the SFA – a location that is subject to more complex vessel movement than coronary arteries.

"Bioresorbable scaffolding will be an important advance in the management of SFA occlusive disease, which is a very challenging anatomy to treat," said Michael Dake, MD, medical director of the Catheterization and Angiography Laboratories at Stanford University and an advisor to 480 Biomedical. "This device has the potential to provide all the benefits of traditional stenting without the need for a permanent metal implant that serves no purpose once the healing process is complete."

The company expects to begin clinical testing of the scaffold in patients with SFA disease this year. Both bare and drug-eluting versions of the 480 Biomedical scaffold are in development.

Arsenal Medical's continued focus will be on developing novel, locally acting therapeutic products built on the AxiocoreT nanofiber-based drug delivery platform and Arsenal's novel therapeutic foam technology. Preclinical studies of both Axiocore and therapeutic foams have been initiated this year, with several high-value applications being investigated. In addition to venture funding, Arsenal is also supported by $10 million in grants from the Department of Defense, National Institute of Standards and Technology's Technology Innovation Program (NIST-TIP), and the Bill and Melinda Gates Foundation.

Dr. James Barry is joining Arsenal Medical as executive vice president and chief operating officer. Barry will be responsible for advancing Arsenal's product pipeline into and through clinical development. Barry was the senior vice president of corporate technology development at Boston Scientific, where he spearheaded the TAXUS drug eluting stent development program, as well as a number of other novel local drug delivery projects.

"I am enthusiastic to be joining a very talented Arsenal team committed to improving and saving lives by developing locally-acting products and alternatives to systemic therapies," said Dr. Barry. "I look forward to taking more products to the clinic with the same focus and rigor that generated the resorbable scaffold." For more information on the two companies, please visit www.arsenalmedical.com and www.480biomedical.com.

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Flamel Technologies Announces Multi-Year Supply Agreement with GlaxoSmithKline for Coreg CR™ Microparticles

Business Wire: October 18, 2011 – LYON, FRANCE – Flamel Technologies (Nasdaq: FLML) announced today that it has entered into a multi-year supply agreement with GlaxoSmithKline (NYSE: GSK) for the production of Coreg CR microparticles. Flamel Technologies is the sole supplier of Coreg CR microparticles for GSK. Under the agreement, Flamel will receive guaranteed minimum payments to supply Coreg CR microparticles over a period of several years. The agreement defines the manufacturing relationship between the two companies following the expiration of the previous supply agreement on December 31, 2010. Pursuant to the agreement, Flamel received a payment of €1.3 million during the third quarter and anticipates a further €1.3 million payment to be paid in the next ten days, as well as the higher margin on all product produced by Flamel since January 1, 2011.

Stephen H. Willard, Flamel's chief executive officer, commented, "We welcome the conclusion of this agreement with GSK. The new supply agreement provides Flamel and its shareholders with higher margins and greater certainty. We believe that this agreement further strengthens our ability to develop both of our best-in-class drug delivery platforms."

Archimedes Pharma Launches Lazanda® – the Only Fentanyl Nasal Spray for the Management of Breakthrough Pain in Cancer in the U.S.

PRNewswire: October 17, 2011 – READING, ENGLAND & BEDMINSTER, NJ – Archimedes Pharma Ltd., and its subsidiary, Archimedes Pharma U.S. Inc., today announced that Lazanda® (fentanyl) nasal spray is now available by prescription in U.S. pharmacies. Lazanda is indicated 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. The U.S. Food and Drug Administration approved Lazanda on June 30, 2011, marking the first product approval for Archimedes Pharma in the U.S. and the first fentanyl nasal spray in the U.S.

Breakthrough pain, experienced by more than half of patients with cancer who have pain, can be debilitating to patients and interfere with their ability to engage in daily living activities. Different from the constant background pain many patients with cancer experience, breakthrough pain is described as an intense, excruciating pain with rapid onset and relatively short duration, which occurs despite taking appropriate opioid therapy for background pain.

"Even though the incidence of breakthrough pain is high in cancer patients, it is often not correctly identified nor reported," said Nash Gabrail, MD, MRCP, of the Gabrail Cancer Center and clinical investigator for Lazanda "If reported, it is typically managed by either increasing the dose of background opioids or giving an additional dose of a short-acting oral opioid – neither of which is optimal therapy. Lazanda, with its rapid and controlled availability, can provide pain relief with an onset of action and duration of effect that addresses the time course of a typical breakthrough pain episode."

Lazanda uses Archimedes' patented PecSys® drug delivery system, which allows the active ingredient to be rapidly absorbed across the nasal membrane and directly into the blood stream. Lazanda is marketed as PecFent® (fentanyl pectin nasal spray) in Europe, where it is presently available in six countries.

"As the first and only treatment option in the U.S. offering fentanyl through nasal administration, Lazanda provides clinically proven pain relief to adult cancer patients suffering from breakthrough pain," noted Jeffrey H. Buchalter, chief executive officer of Archimedes Pharma. "The availability of Lazanda also is an exciting milestone for Archimedes Pharma as it marks our first product launch in the U.S. and represents the expansion of the brand from Europe."

Lazanda will be available 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.

Noven Files Patent Infringement Lawsuit Against Watson Pharmaceuticals

Business Wire: October 13, 2011 – MIAMI, FL & NEW YORK, NY – Noven Pharmaceuticals, Inc. announced today that it has filed a lawsuit in the U.S. District Court of New Jersey against Watson Pharmaceuticals ("Watson") for infringement of certain Noven patents (the "Patents") by Watson.

The lawsuit was filed as a result of an Abbreviated New Drug Application (ANDA) submission by Watson seeking FDA approval to market and sell a generic version of Daytrana® (methylphenidate transdermal system) prior to the scheduled expiration of the Patents in 2018. The lawsuit reflects Noven's commitment to vigorously defending its intellectual property rights against infringement.

Under the Hatch-Waxman Act, because Noven filed this patent infringement lawsuit within 45 days of receiving a Paragraph IV notification letter from Watson, the FDA cannot approve Watson's ANDA for 30 months (until March 2014), unless the district court finds the Patents invalid or not infringed before the 30 months pass.

Eagle Pharmaceuticals and Flamel Technologies Announce Eagle to License Medusa Technology for Extended-Release of Tigecycline

Business Wire: October 13, 2011 – LYON, FRANCE & WOODCLIFF LAKE, NJ – Eagle Pharmaceuticals, Inc. and Flamel Technologies SA (NASDAQ: FLML) today announced that the two companies have entered into a license and development agreement for the development of a Medusa-based hydrogel depot formulation of the small molecule antibiotic, tigecycline. Following the promising results generated in the frame of an initial feasibility study established between Flamel and Eagle Pharmaceuticals, Eagle Pharmaceuticals has decided to exercise its option to pursue its partnership with Flamel. Under the terms of the license and development agreement, Flamel will receive upfront, milestone, and double-digit royalty payments. Additionally, Flamel is entitled to receive a percentage of any sub-licensing revenues received by Eagle Pharmaceuticals. All development expenses are the sole responsibility of Eagle Pharmaceuticals.

"We have been extremely pleased with the data we have seen thus far for this program," said Scott L. Tarriff, President and Chief Executive Officer at Eagle Pharmaceuticals. "We hope to offer reduced costs to hospitals and improved convenience for patients requiring this antibiotic treatment. Tigecycline is currently dosed twice-a-day by slow intravenous infusion to patients that are typically hospitalized. Flamel's Medusa platform potentially enables switching the route of administration from intravenous to subcutaneous injection through the creation of once-a-day sustained release injectable tigecycline, reducing Cmax and consequently the side effects associated with tigecycline. We anticipate this formulation may allow some patients to leave the hospital earlier and be treated at home."

Stephen H. Willard, Flamel Technologies' Chief Executive Officer, stated, "The progress we have achieved with Eagle Pharmaceuticals thus far highlights Medusa's strength with small molecules. This is in addition to our prior successes with proteins, peptides, and other biologics. We believe that our formulations can offer important improvements to patients' quality of life and demonstrate key advantages of the Medusa platform: excellent local tolerance, with a noticeable reduction of swelling, pain, and irritation at the injection site; full activity of the molecule being delivered; and applicability to a wide range of drugs. Eagle Pharmaceuticals has been an excellent partner and we look forward to expanding our work on this program, and potentially collaborating with Eagle on additional programs."

Unigene and Nordic Bioscience Combine Industry Leading Capabilities to Advance Unigene's Proprietary Peptides through Phase 2 Proof-of-Concept for the Treatment of Type 2 Diabetes, Osteoarthritis, and Osteoporosis

Business Wire: October 6, 2011 – BOONTON, NJ & COPENHAGEN, DENMARK – Unigene Laboratories, Inc. (OTCBB: UGNE) and Nordic Bioscience today announced their decision to establish a Joint Development Vehicle (JDV) to progress up to three of Unigene's internally developed, proprietary calcitonin analogs through Phase 2 proof-of-concept in humans for the treatment of Type 2 diabetes, osteoarthritis, and osteoporosis. Unigene and Nordic will each own 50% of the resulting JDV.

Morten Karsdal, Chief Executive Officer of Nordic Bioscience, said, "This exciting collaboration with Unigene is the ideal combination of Nordic's and Unigene's strengths and core competencies. Unigene is the leading company in the world for the oral formulation of peptides and Nordic within biochemical markers and clinical development. Both parties have extensive knowledge of calcitonin and entering into this Joint Development Vehicle is a rare opportunity that creates the perfect match."

In exchange for 50% ownership interest in the JDV, Unigene shall license, on an exclusive royalty-free basis, up to three (3) proprietary calcitonin analogs for development by the JDV for use in the treatment of Type 2 diabetes, osteoarthritis, and osteoporosis. In addition to the license grant, Unigene will supply the analogs selected for development by the JDV for preclinical studies and, thereafter, manufacture sufficient quantities of the selected lead analog for clinical trials. In exchange for a 50% ownership of the JDV, Nordic is responsible for conducting and fully funding all preclinical, toxicology, and clinical development through Phase 2 proof-of-concept for the Type 2 diabetes indication.

Ashleigh Palmer, President and CEO of Unigene, commented, "Our collaboration with Nordic, a preeminent drug development company with industry leading expertise in metabolic biomarkers, represents an extremely important transaction for Unigene and is clearly a strong endorsement of our peptide design, oral delivery, and recombinant manufacturing and development capabilities." Palmer continued, "Historically, our efforts have been focused on repurposing established peptide therapeutics, such as calcitonin and PTH. We have now received validation of our novel, proprietary compounds, having survived Nordic's rigorous biomarker screening. This collaboration transforms Unigene from a leading drug delivery partner to a legitimate biopharmaceutical development company. Together with Nordic, we are committed to aggressively advancing our programs focused upon multiple blockbuster markets such as Type 2 diabetes, osteoporosis, and osteoarthritis through Phase 2 proof-of-concept in humans."

Nozer Mehta, Unigene's Vice President of R&D, stated, "Nordic has published extensively on the development of calcitonin and other peptides for various metabolic diseases, including diabetes, osteoporosis, and osteoarthritis. We are extremely confident to be able to move forward with the development of our novel, proprietary analogs having received Nordic's validation following its rigorous screening of these analogs and their mechanisms of action. Our two companies working together will result in tremendous synergy and high potential value creation."

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Initial Data from Bio-Path Holdings' Phase I Clinical Trial Accepted for Presentation at American Society of Hematology Annual Meeting

Business Wire: October 4, 2011 – HOUSTON, TX – Bio-Path Holdings, Inc. (OTC BB: BPTH) ("Bio-Path"), a biotechnology company developing a liposomal delivery technology for nucleic acid cancer drugs, today announced that an abstract entitled "Safety, Pharmacokinetics, and Efficacy of BP-100.1.01 (L-Grb-2 Antisense Oligonucleotide) in Patients with Refractory or Relapsed Acute Myeloid Leukemia (AML), Philadelphia Chromosome Positive Chronic Myelogenous Leukemia (CML), Acute Lymphoblastic Leukemia (ALL), and Myelodysplastic Syndrome (MDS)" has been accepted for a poster presentation at the 53rd Annual Meeting of the American Society of Hematology (ASH) to be held December 10–13, 2011, in San Diego, California. The ASH Annual Meeting is the premier event for physicians and healthcare researchers involved in hematology to meet to learn about the latest developments to treat blood diseases.

The abstract contains a summary of the results of the first cohort in the ongoing Phase I clinical trial of Bio-Path's lead drug candidate Liposomal Grb-2 being evaluated in patients with blood cancers. The lead author for the abstract is Jorge Cortes, MD, Professor of Leukemia at The University of Texas M.D. Anderson Cancer Center and Principal Investigator for the Phase I clinical trial.

"We are extremely pleased and honored that this abstract has been accepted for presentation at this important meeting of physicians and researchers in the field of hematology," said Peter Nielsen, President and Chief Executive Officer of Bio-Path. "The abstract accepted for presentation is a summary of results from a very early stage in our Phase I program. We believe the inclusion of these early results at the ASH annual meeting indicates that the reviewers see the potential importance of our drug candidate Liposomal Grb-2 as a new and novel way of treating AML, CML, ALL, and MDS blood cancers."

Bio-Path is developing a neutral lipid-based liposome delivery technology for nucleic acid cancer drugs (including antisense and siRNA molecules), a delivery technology that forms microscopic-sized vehicles to safely deliver these drugs to their intended target cancer cells.

Bio-Path's drug delivery technology involves microscopic-sized liposome particles that distribute nucleic acid drugs systemically and safely throughout the human body via simple intravenous infusion. The delivery technology can be applied both to double stranded (siRNA) and single stranded (antisense) nucleic acid compounds with the potential to revolutionize the treatment of cancer and other diseases where drugable targets of disease are well characterized. Bio-Path also anticipates developing liposome tumor targeting technology, representing next-generation enhancements to the Company's core liposome delivery technology.

InSite Vision Announces Positive Phase 2 PK Results for BromSite™ (ISV-303) for the Reduction of Pain and Inflammation After Cataract Surgery

Business Wire: October 4, 2011 – ALAMEDA, CA – InSite Vision Incorporated (OTCBB: INSV) today announced positive top-line results from a Phase 2 pharmacokinetic (PK) clinical study comparing the tissue penetration profile of InSite Vision's BromSite (ISV-303) with ISTA Pharmaceuticals' Bromday (bromfenac ophthalmic solution) 0.09%. BromSite combines a lower dose (0.075%) of the non-steroidal anti-inflammatory drug (NSAID) bromfenac with InSite Vision's DuraSite drug delivery technology and is intended to reduce the pain and inflammation associated with ocular surgery.

The randomized, double-masked, two-arm study evaluated the aqueous humor concentration of once-daily doses of BromSite versus Bromday in 58 subjects. Subjects were dosed two days before and the morning of the day of cataract surgery. Study results showed that the mean concentration of bromfenac in the aqueous humor of patients in BromSite's group was more than twice greater compared to those patients in Bromday's group with a P-Value of p=0.0032.

The Phase 2 PK clinical study was fully enrolled in six weeks using three sites in the United States under the direct supervision of the InSite Vision clinical department without the use of a contract research organization. BromSite and Bromday were both generally well tolerated and there were no safety concerns or serious adverse events related to either agent. InSite Vision intends to present a final analysis of the BromSite Phase 2 PK clinical trial in conjunction with a future scientific meeting.

In March, InSite Vision reported positive results from a Phase 1/2 clinical trial of BromSite which showed statistically significant superiority compared to vehicle (p=0.0016) for its primary endpoint (the absence of cells in the anterior chamber of the eye at day 15 post surgery). The results of the Phase 2 PK study and the earlier Phase 1/2 clinical trial hold the promise that BromSite may be a commercially superior NSAID for ocular surgical use. The company plans to initiate discussions with the U.S. Food and Drug Administration (FDA) on the design of the pivotal Phase 3 program for BromSite. Patent protection for BromSite is expected to extend into 2029.

"We are delighted that the study confirmed the superior penetration of BromSite against the current market leader, Bromday," said Dr. Kamran Hosseini, Vice President and Chief Medical Officer of InSite Vision. "Most physicians believe that a higher penetration of bromfenac into the ocular tissues of the eye may reduce the risk of cystoid macular edema, or CME, as a result of ocular surgery. CME is a relatively rare but extremely serious adverse event in ocular surgery that can lead to blindness. We are looking forward to working with the FDA to finalize the design of the Phase 3 program for BromSite and currently expect to begin pivotal trials in early 2012."

Cataract surgery is the most frequently performed ocular surgery in the United States, with more than three million procedures annually. Both before and after surgery, anti-inflammatory eye drops are typically prescribed to reduce pain and inflammation and to enhance healing. Anti-inflammatory eye drops are currently used as prophylaxis against CME.

InSite Vision is advancing a second product candidate, known as ISV-101, that utilizes a low concentration of bromfenac enabled by DuraSite for the treatment of dry eye disease. In January 2011, InSite Vision announced it had filed an Investigational New Drug (IND) application for ISV-101 with the FDA. The company is positioned to initiate a dose-ranging Phase 1/2 clinical trial in late 2011 or early 2012 to evaluate the safety and efficacy of ISV-101 when administered to patients suffering from dry eye disease. Patent protection for this drug candidate is also expected to extend into 2029.

NanoViricides Inc. to Present at the Partnership Opportunities in Drug Delivery (PODD) Conference in Boston Today

Business Wire: October 4, 2011 – WEST HAVEN, CT – NanoViricides, Inc. (OTC BB: NNVC) (the "Company") announced that its President, Dr. Anil R. Diwan, will present at the "Partnership Opportunities in Drug Delivery (PODD)" Conference being held at the Omni Parker Hotel in Boston, MA, today. Dr. Diwan is invited to present in the "Track 2: Large Molecules and Biologics Delivery".

He will focus on the building-block-based tailor-made customization capabilities of the nanoviricide® platform technology that has enabled (1) rapid development of highly active drug candidates against many diseases, by using its direct-"address" targeting to the virus particle, and (2) rapid development of different formulations for administration. The Company has developed skin cream and lotion, eye drops, ophthalmic gels, and injectables based on this platform with very little formulation development needed.

In addition, he will present a summary of the nanoviricides® platform technology, the Company's drug pipeline, its recent successes with animal studies for the Company's influenza therapeutic FluCide™, and progress towards the initial FDA submission.

In particular, the Company reports that it is on course to submit its pre-IND application on the influenza clinical drug candidate to the US FDA as soon as the draft is finalized in consultation with its regulatory expert consultants including the Biologics Consulting Group (BCG), engaged by the Company to help in the regulatory submissions process.

The Company has recently announced that it is working on enabling cGMP ("current Good Manufacturing Practices") capability for producing its drug candidates. cGMP manufactured materials will be required when the Company is ready to file an Investigational New Drug (IND) application to the US FDA.

The Company has chosen a clinical candidate, NV-INF-1, in its anti-influenza drug program (FluCide™) to develop for regulatory submissions both domestically and internationally. This is a single drug that the Company believes will be effective against most if not all Influenza A viruses. The Company believes that a single course therapy easily administered by a medical office is feasible for out-patients. The Company believes that in most instances no follow-on treatment would be necessary. This expectation is based on the following results from its animal studies: (1) the extremely high treatment effectiveness in inhibiting the cycle of infection, virus expansion, and spread of infection and, (2) the significantly long lasting effects of the drug treatment after the drug is discontinued.

The Company has also recently announced significant successes in its anti-HIV drug program, viz. HIVCide™. The best HIVCide candidate in a recent SCID-hu Thy/Liv mouse model study showed effectiveness against HIV-1 similar to a three drug HAART (highly active anti-retroviral therapy) cocktail even when HIVCide was administered at a much lower total dosage. What is more significant, this nanoviricide drug candidate continued to work to suppress HIV viral load for at least 28 days beyond last drug administration. These data along with previous similar successes in anti-HIV drug development indicate that HIVCide may provide a "functional cure" of HIV/AIDS either alone or in combination with other drugs.

Mission Pharmacal Partners with TriLogic Pharma on Drug Delivery Platform

Business Wire: October 3, 2011 – SAN ANTONIO, TX – Mission Pharmacal Company announced today that it is developing a new drug delivery system utilizing technology developed by TriLogic Pharma. The delivery system will be based upon TriLogic's proprietary drug delivery platform TRI-726 and will be licensed to Mission Pharmacal for future drug development.

"Mission Pharmacal's growth over the last 60 years has been the result of good relationships with other innovative pharmaceutical companies. We look forward to working with TriLogic and its new technology," stated Terry Herring, president of Mission Pharmacal's Commercial Operations.

Jim Harwick, president of TriLogic Pharma, said, "We are excited to partner with Mission Pharmacal on the development of a new drug delivery system. We continue to be pleased with the versatility of TRI-726 and the wide range of therapeutic classes and actives that can be developed with our novel delivery platform."

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September 2011

MicroDose Therapeutx Begins Phase 1 Trial of MDT-637 for Treatment of Respiratory Syncytial Virus

Business Wire: September, 27, 2011 – MONMOUTH JUNCTION, NJ – MicroDose Therapeutx, Inc. today announced that the first human subject has been dosed in a Phase 1 clinical trial of MDT-637, MicroDose's inhalable small molecule antiviral fusion inhibitor for the treatment of respiratory syncytial virus (RSV). This Phase 1 trial follows the reactivation of the United States IND for MDT-637 as re-formulated for delivery using MicroDose's proprietary dry powder nebulizer.

The Phase 1 clinical trial is a U.S.-based, single ascending dose, randomized, placebo-controlled trial studying the safety, tolerability, and pharmacokinetics of MDT-637 in 48 healthy adult subjects.

MDT-637 is a fusion inhibitor that has been shown to block RSV infection in preclinical testing. The product is formulated for inhaled delivery via MicroDose's proprietary dry powder nebulizer, a novel device, which allows for the rapid delivery of dry powder medications via tidal inhalation to the site of infection in the respiratory tract.

"We are pleased to announce first subject dosing as we initiate clinical testing for MDT-637," said Robert Cook, PhD, Senior Director, Product Commercialization Group, at MicroDose. "This study will provide important safety and pharmacokinetic data for assisting dose selection in subsequent clinical development."

MicroDose is developing MDT-637 in collaboration with Gilead Sciences, Inc. under an agreement announced April 20, 2011. As previously reported, MicroDose is responsible for the development of MDT-637 through Phase IIa clinical trials.

Celator® Pharmaceuticals Granted U.S. Patent Covering Lead Cancer Product

Business Wire: September 21, 2011 – PRINCETON, NJ – Celator Pharmaceuticals today announced that U.S. Patent No. 8,022,279 was issued by the United States Patent and Trademark Office on September 20, 2011, and that two related patents in Japan have been granted as well. These patents add to the intellectual property surrounding Celator's lead anti-leukemia drug, CPX-351.

U.S. Patent No. 8,022,279 covers the key composition features of CPX-351, a liposome formulation that co-encapsulates cytarabine and daunorubicin at a synergistic 5:1 molar ratio. In addition to this patent, Celator has also been notified that patent claims broadly covering the CombiPlex® method of developing drug combinations as well as claims covering the Company's metal-based drug loading technology have been allowed by the Japanese Patent Office. Both of these patents also provide protection of CPX-351 and were previously allowed in the United States.

Cytarabine and daunorubicin have been a standard of care for the treatment of patients with acute myeloid leukemia (AML) for more than 30 years, and CPX-351 has demonstrated marked improvements in efficacy versus the conventional administration of the same two drugs in a randomized phase 2 clinical study in elderly patients with newly diagnosed AML.

"We're pleased to receive these patents which increase the depth of intellectual property protection for CPX-351 in the United States and expand the protection of Celator's broader technology platforms into Japan," said Scott Jackson, chief executive officer of Celator Pharmaceuticals. "The positive results for CPX-351 in a previously reported phase 2 clinical trial have supported the planning for a pivotal phase 3 registration trial. With the Patent Term Adjustment, the U.S. patent provides protection until September 2027 which, should we be successful in gaining regulatory approval, significantly extends market exclusivity for CPX-351 in the United States."

Liposomes Block HIV Infection in Early Tests; Could be a Cost-Effective Preventive for Developing Countries

PRNewswire: September 19, 2011 – BOSTON, MA – HIV vaccines are in their infancy, and effective microbicides to prevent sexual transmission of HIV still don't exist. Protection is especially needed for women, who make up nearly half of all global cases. Researchers at Children's Hospital Boston envision a new way for women to protect themselves before sex: an applicator filled with specially formulated fatty particles called liposomes.

In tests led by Daniel Kohane, MD, PhD, director of the Laboratory for Biomaterials and Drug Delivery at Children's Hospital Boston, liposomes inhibited HIV infection in cell culture and appeared safe in female mice when injected intravaginally. The findings are reported in the November issue of the journal Biomaterials, published online September 19.

Liposomes are spherical particles with a double outer layer of lipids (fats) and hollow centers. They are relatively easy and cheap to engineer, and thus present a viable option for developing countries, where the cost of anti-HIV drugs bars access for most people.

Liposomes can be filled with drugs or other compounds, but in this case, Kohane and colleagues found, to their surprise, that the liposomes alone were effective in blocking infection.

"We had been planning do much more complex things, like putting ligands on the surface to increase binding to HIV," says Kohane. "It was a surprise that liposomes alone worked so well. Simplicity is always better – if liposomes work by themselves, we may not need anything else, and it would be cheaper and potentially much safer."

Kohane and colleagues hope to conduct further tests to better understand how the liposomes are blocking infection. They bind to HIV, perhaps interfering with the virus's ability to fuse with cell membranes, the first step in infection.

"The idea, simplistically, is that liposomes look like cell membranes," says Kohane, "so maybe we could use them as decoys to prevent HIV infection."

Kohane and colleagues formulated a range of liposomes using various naturally occurring and synthetic lipids and screened them systematically in cell cultures. Several formulations showed a good therapeutic profile, protecting the cells from HIV infection without being toxic. Especially effective were liposomes containing cardiolipin, a fat that was first found in animal hearts; performance was further improved by adding a synthetic phospholipid.

Tested in female mice, these formulations caused little or no inflammation, which can compromise the vaginal lining and increase the risk of HIV transmission. Imaging confirmed that the liposomes remained in place or left the body, but did not travel beyond the vagina.

"This research makes an important contribution towards creating a safe and effective form of HIV prevention for women," says Nikita Malavia, PhD, the study's first author, who worked in Kohane's lab and in the lab of Robert Langer, ScD, of MIT. "Women in areas such as sub-Saharan Africa often cannot control their male partners' use of condoms, making them three times more likely to be HIV-positive than men. This technology could enable women to take control in their own hands."

Though some intravaginal compounds are in the pipeline, none are available yet. The advantage of using liposomes is that they are inexpensive, easy to formulate into ointments or gels, and stable for long periods of time, making them a particularly good option in resource-poor settings. Kohane hopes to get further funding to test liposome formulations in other animal models. The study was funded by the Grand Challenges in Global Health initiative and the National Institutes of Health.

Unigene's Industry Leading, Proprietary Oral Delivery and Recombinant Manufacturing Technology Platforms are Further Validated with Positive Phase 3 Safety and Efficacy Data for OSTORA™

Business Wire: September 19, 2012 – BOONTON, NJ – Unigene Laboratories, Inc. (OTCBB: UGNE) a leader in the design, delivery, manufacture, and development of peptide-based therapeutics announced today that its licensee, Tarsa Therapeutics (Tarsa), presented positive Phase 3 data from its ORACAL trial of OSTORA™ during the annual American Society for Bone and Mineral Research (ASBMR) 2011 meeting on September 18. The data demonstrated that OSTORA achieved all of the efficacy endpoints in the trial and indicated that the safety profile of OSTORA did not substantially differ from nasal calcitonin or placebo.

Developed by Unigene and licensed to Tarsa, OSTORA™ is an oral recombinant salmon calcitonin tablet in development for the treatment of postmenopausal osteoporosis.

Ashleigh Palmer, Unigene's President and Chief Executive Officer, commented, "The results from the ORACAL Phase 3 trial presented at the ASBMR, including data showing that OSTORA demonstrated superior efficacy to nasal calcitonin, provide robust validation of Unigene's leading proprietary oral peptide delivery and manufacturing technologies. In particular, the success of the study clearly illustrates how Unigene's Peptelligence™ platform is pioneering oral peptide production and delivery, having successfully overcome the often mission critical challenges of Phase 3 clinical development and could potentially be the first oral natural peptide to market."

The ORACAL study was a Phase 3 multinational, randomized, double-blind, double-dummy, placebo-controlled trial of OSTORA™ compared to placebo and to commercially available, synthetic salmon calcitonin administered by nasal spray. The data demonstrated that OSTORA achieved all of the efficacy endpoints in the trial and indicated that the safety profile of OSTORA did not substantially differ from nasal calcitonin or placebo, and that OSTORA also appeared to be significantly less immunogenic than nasal calcitonin spray. The primary efficacy endpoint was the percentage change in lumbar spine bone mineral density (BMD) after one year of treatment. The trial enrolled 565 postmenopausal women with established osteoporosis in six countries.

Dr. Nozer Mehta, Vice President, Biological Research and Development stated, "The strong Phase 3 results establish Unigene's leadership position in oral peptide drug delivery. Not only is Unigene responsible for originating and developing what could potentially be the first oral calcitonin to reach the market, which it licensed to Tarsa at the start of Phase 3, but our Peptelligence™ platform has also led to the advancement of several additional oral peptide programs for other partners currently in ongoing feasibility studies as well as an oral PTH compound in Phase 2 clinical testing that Unigene is co-developing with GlaxoSmithKline."

Palmer concluded, "Given the strength of the clinical results and performance of our technology combined with our intellectual property, Unigene is supremely positioned to provide our current and future partners with a means of administering their peptides orally. Unigene can provide the solutions to companies that are faced with the challenges of limited potential for their products due to route of administration, approaching the end of their patent life with the threat of generic competition or development stage peptides with questionable commercial viability. I truly believe the opportunities are tremendous for Unigene, and we look forward to multiple events that could fundamentally change the Company over the next 6–9 months."

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Unigene Laboratories, Inc. is a leader in the design, delivery, manufacture, and development of peptide-based therapeutics. The Company is building a robust portfolio of proprietary partnerships in this expanding drug class based on its Peptelligence™ platform. Peptelligence encompasses extensive intellectual property covering delivery and manufacturing technologies, unsurpassed research and development expertise, and proprietary know-how representing a genuine distinctive competence. Core Peptelligence assets include proprietary oral and nasal peptide delivery technologies, and proprietary, high-yield, scalable, and reproducible *E. coli*-based manufacturing technologies.

Unigene's technologies have extensive clinical and partner validation. The Company's first product to market, Fortical®, a nasal calcitonin product, received FDA approval in 2005 and is marketed in the U.S. by Upsher-Smith for the treatment of postmenopausal osteoporosis. Unigene licensed its oral calcitonin program to Tarsa Therapeutics and expects an NDA filing with the FDA before year end. The Company has a worldwide licensing agreement with GlaxoSmithKline for its parathyroid hormone product candidate currently in Phase 2. In addition, Unigene has a manufacturing license agreement with Novartis, which is completing three Phase 3 studies of oral calcitonin for the treatment of osteoporosis and osteoarthritis. For more information about Unigene, please visit http://www.unigene.com. For information about Fortical, please visit http://www.fortical.com.

Licensing Agreement for Pharmaceutical Disposal Technology Between Teikoku Pharma USA, Inc. and Verde Environmental Technologies Inc.

PRNewswire: September 14, 2011 – SAN JOSE, CA – Teikoku Pharma USA, Inc., ("TPU") is pleased to announce an exclusive license agreement with Verde Environmental Technologies Inc. ("Verde"), a company aimed at developing environmentally responsible solutions for pharmaceutical disposal. Verde is a privately held company, founded by former executives of TPU and Travanti Pharma, Inc.

Verde obtained rights to develop products, which are designed to adsorb and inactivate the active ingredients in pills, tablets, capsules, and topical patches, in a convenient and environmentally responsible manner, based on patented technology developed and owned by TPU.

"We are very pleased that these new product ideas that were generated from our research led to this important new development, stated TPU CEO, Masahisa Kitagawa. TPU, located in San Jose, California, is the U.S. operations of Teikoku Seiyaku Co., Ltd., one of the world's largest manufacturers of medicated patches based in Japan, and its product, Lidoderm, is a leading global brand.

"The products being developed by Verde will address the growing issue of pharmaceutical contamination of groundwater supplies. By providing an effective means of adsorbing the active ingredients, this will help keep waste pharmaceuticals from appearing in the water supply," stated Verde Chairman and CEO, Dr. Andrew Korey. "In addition, these developments will provide anti-abuse features, and improved safety, by diminishing the risk of accidental poisoning from active pharmaceuticals disposed in trash." For more information about Teikoku Pharma USA, Inc. please visit http://www.teikokuusa.com

Moberg Derma AB: Moberg Derma Has Completed Recruitment for MOB-015 Phase II Clinical Study

Business Wire: September 12, 2011 – STOCKHOLM, SWEDEN – Moberg Derma AB (OMX: MOB) has successfully completed the recruitment of 237 patients with nail fungus (onychomycosis) to participate in the ongoing MOB-015 phase II study. MOB-015 is the company's second-generation topical treatment for nail fungus.

The purpose of the study, which includes 237 patients, is to confirm the validity of the MOB-015 product concept and to provide the basis for a phase III program as well as licensing. Patients will be followed up during 12 months and the endpoints normally accepted by FDA, EMA, and other relevant authorities for nail fungus will be used.

"We are very pleased that patient recruitment has been successfully completed and that the study is proceeding according to plan. MOB-015 has the potential to be the future market leader for the treatment of nail fungus," said Peter Wolpert, CEO of Moberg Derma.

MOB-015 is a new topical treatment for nail fungus (onychomycosis) with fungicidal, keratolytic, and emollient properties. Moberg Dermas patent-pending formulation technology facilitates high concentrations of a fungicidal substance to be transported in and through nail tissue. In pre-clinical studies on human nails, more than tenfold concentrations of the antifungal substance have been detected, compared to the concentrations measured in the nail with successful oral treatment. As MOB-015 is applied locally, the side effects associated with oral treatment are avoided.

Nail fungus is the most common nail disease and afflicts approximately 10% of the general population, increasing with age. The estimated global market potential exceeds $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.

Diamyd Medical: Diamyd Awarded Three Million Dollar Grant and Expands the NTTDS Portfolio

Business Wire: September 12, 2011 – STOCKHOLM, SWEDEN – Diamyd Medical AB (STO: DIAMB) (Pink Sheets: DMYDY), with collaborators, has received a three million dollar grant from the U.S. National Institutes of Health to develop the Company's patented Nerve Targeting Drug

Delivery System (NTDDS) for prevention of Chemotherapy Induced Peripheral Neuropathy. The grant allows Diamyd to expand the NTDDS technology to also target neuropathy, in addition to the Company's development portfolio for the treatment of pain.

The three-year grant funds the development of a NTDDS-based drug candidate, engineered to deliver a neurotrophic factor to nerve cells. It is hoped that use of NTDDS to deliver such a neurotrophic factor to cancer patients prior to initiating chemotherapy will prevent peripheral neuropathy, which is a common side effect of chemotherapy. Typical symptoms of peripheral neuropathy are numbness, pain, tingling, or burning sensations in hands and feet.

"Expanding the application of the NTDDS technology from pain therapy to include the treatment and prevention of neuropathy is something we have foreseen for a long time," says Peter Zerhouni, President and CEO of Diamyd Medical. "With the non-dilutive funding provided by the grant, we can take this step earlier than anticipated."

The grant covers the costs for advancement of the new drug candidate through preclinical efficacy, toxicology, and biodistribution studies, manufacturing, and filing of an Investigational New Drug application with the U.S. Food and Drug Administration (FDA). The grant is awarded to David Fink, MD, Professor and Chairman, Department of Neurology at the University of Michigan, and Darren Wolfe, PhD, President of Diamyd, Inc., as principle investigators.

"Building off our clinical development of NTDDS for the treatment of pain, this grant will allow us to accelerate the critical steps in translating our preclinical findings in Chemotherapy Induced Peripheral Neuropathy into human therapy," says Darren Wolfe. "Chemotherapy Induced Peripheral Neuropathy represents an important unmet medical need that we have identified as an attractive market opportunity for our unique NTDDS technology."

"Chemotherapeutics are invaluable tools in the fight against cancer," says Dr. David Fink, a long-term collaborator doing research with Diamyd Medical's NTDDS technology. "Unfortunately, they also produce serious side effects, such as peripheral neuropathy, which often prevents administration of higher, more effective chemotherapy doses. Treatment with NTDDS delivering a neurotrophic factor may not only prevent the development of Chemotherapy Induced Peripheral Neuropathy, but may also allow more effective chemotherapy doses to be administered to the patient."

Neurotrophic factors are a class of small proteins that were originally identified by their role in brain development and their ability to prevent specific cell death of nerve cells during development. In the adult nervous system, neurotrophic factors promote the survival, growth, connectivity, and proper function of nerve cells and aid in recovery of nerve function following injury. Targeted delivery of neurotrophic factors to nerve cells could lead to treatments for central and peripheral neurodegenerative diseases. Further information is available on the Company's website: www.diamyd.com.

FierceBiotech Names Pearl Therapeutics a 2011 Fierce 15 Biotech

PRNewswire: September 6, 2011 – REDWOOD CITY, CA – Pearl Therapeutics was named by FierceBiotech today as one of 2011's Fierce 15, designating it as one of the most promising private biotechnology companies in the industry. This is FierceBiotech's ninth annual Fierce 15 selection.

"Pearl's veteran team has done a super job of raising the funds and doing clinical research to advance PT003 – an inhaled LAMA/LABA combination therapy – toward the market," says Ryan McBride, the executive editor for FierceBiotech. "I believe the company is positioned well to gain marketing partners for the treatment."

Chuck Bramlage, Pearl's chief executive officer continued, "Earlier in 2011, following our $69 million Series C financing, we were named by FierceBiotech to the list of 15 top venture capital deals in biotechnology. Today's Fierce 15 award speaks not only to our fundraising ability, but also to the commitment, expertise, and passion with which the Pearl team pursues product development. I look forward to continuing to work with this exceptional team in our development of our lead COPD candidate, PT003, and living up to the 'fierce' moniker in fighting major respiratory ailments."

An internationally recognized daily newsletter reaching more than 90,000 biotech and pharma industry professionals, FierceBiotech provides subscribers with a quick, authoritative briefing on the day's top stories. Every year, FierceBiotech evaluates hundreds of private companies for its annual list, which is based on a variety of factors such as the strength of its technology, partnerships, venture backers, and a competitive market position.

The Fierce 15 celebrates the spirit of being "fierce" – championing innovation and creativity, even in the face of intense competition. A complete list of "Fierce 15" companies – the online newsletter's ninth annual selection – is available online at www.fiercebiotech.com.

Pearl Therapeutics is a privately held company developing combination therapies for the treatment of highly prevalent respiratory diseases, including chronic obstructive pulmonary disease and asthma. Pearl is rapidly advancing a pipeline of products including PT003, an inhaled, fixed-dose combination bronchodilator product comprised of a long-acting muscarinic antagonist (LAMA) and a long-acting beta-2 agonist (LABA) delivered via a metered dose inhaler (HFA MDI); and PT010, a triple-combination product that combines the LAMA and LABA components of PT003 with an inhaled corticosteroid (ICS) for twice-daily administration from an HFA MDI for the

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treatment of severe COPD. Both PT003 and PT010 are developed with Pearl's proprietary porous particle cosuspension technology, which allows the formulation of multiple products in the MDI format, with highly stable, robust, and aerodynamically efficient drug delivery. Founded in 2006, Pearl Therapeutics is privately held and backed by 5AM Ventures, Clarus Ventures, New Leaf Ventures, and Vatera Healthcare. For more information, please visit www.pearltherapeutics.com.

Berlin Pharmaceutical and Acino Pharma of Switzerland Sign Partnership Agreement to Market a Wide Range of Acino Products in Thailand

PRNewswire: September 5, 2011 – BANGKOK, THAILAND – Berlin Pharmaceutical Industry Co., Ltd. and Acino Pharma AG (SIX: ACIN) signed a long term partnership agreement under which Berlin will market a wide range of the Swiss company's current and future products in Thailand.

"The new products will complement our current line of therapies as well as significantly expand our presence into new areas," said Amal Naj, Chief Executive Officer of Berlin. "We are very excited about this association with Acino and the high quality products we will bring to our patients at affordable prices," he said.

Peter Burema, CEO of Acino Group, said, "We are very pleased to partner with one of the leading pharmaceutical companies in Thailand to introduce our products in the market. We see great opportunities for our products there and rest of Asia and other emerging markets."

Acino, based in Basle, Switzerland, specializes in the development, registration, and manufacture of generic and innovative pharmaceuticals using advanced drug delivery technologies, for which it also holds patents. With a focus on solid oral dosage forms with modified release of the active ingredient, transdermal therapeutic patches, and biodegradable, subcutaneous implants, Acino supplies leading pharmaceutical companies throughout Europe.

Mr. Naj said the vast majority of the Acino products Berlin will introduce in Thailand are for the treatment of urological disorders, cancer, and pain. The company's current products are prescribed mainly for the treatment of cardiovascular and metabolic diseases and gastro-intestinal disorders.

Mr. Naj said a number of Acino products are innovative, and they will help strengthen Berlin's market presence in the highly competitive market. Berlin currently manufactures most of its products in GMP-approved (Good Manufacturing Practice) and ISO-certified facilities, and imports active pharmaceutical ingredients (API) as well as finished products from Canada, France, and India.

The Acino Group is headquartered in Basle, and currently employs approximately 380 staff. Acino Holding Ltd., the Group's parent, is listed on the SIX Swiss Exchange (SIX: ACIN). ■

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Calendar of Events

2012

14th Annual Conference on the Formulation and Delivery of Bioactives
February 16–17
Hutton Theatre, Otago Museum
Dunedin, New Zealand

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

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

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

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

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

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