CRS Leading Delivery Science and Technology

Newsletter

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CRS Leading Delivery Science and Technology

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CRS Newsletter

Leading Delivery Science and Technology

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

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Arlene McDowell
University of Otago
New Zealand

Keeping It Real

When was your first CRS conference? For me it was 2004 in Hawaii. Our 2013 annual meeting will again be held in Honolulu in beautiful Hawaii. The dates are July 21–24, and the CRS website (www.controlledreleasesociety.org) has lots of great conference information. And as you can read in this issue, the website is a wonderful resource for other valuable information—including archives of the *CRS Newsletter!*

So this year I will be going back to Hawaii, where my association with CRS really began. Prior to attending my first CRS Annual Meeting in Hawaii, I had been on the committee of the New Zealand Local Chapter. I started as a postgraduate representative and have worked my way up to my current position as president of NZCRS. Being part of this committee has been great and valuable for my career. I have met many fantastic people, learned to organize and host successful events, and travelled. The CRS Board has an initiative to enhance involvement of the CRS membership in committees and to ensure those who volunteer gain from the experience, and I have been asked to help facilitate this process. You will hear more from me about this later, but in the meantime, if you are interested in being on any of the committees within CRS, please contact me (arlene.mcdowell@otago.ac.nz).

I can't say that I am a tweeter, but I recently learned about the Twitter hashtag #overlyhonestmethods. This is worth a look, as it's a collection of realistic tidbits about how the way we do science is often determined by practicalities rather than strict convention. Creativity may also be the key to secure a £500 prize from UKICRS. The UKICRS chapter is calling for essays on the topic of drug delivery science in 2050 (see Chapter News). Why not let an article in this *CRS Newsletter* be your inspiration? It seems likely that "nano" will feature in our future, and this topic was discussed in New Jersey at the Nanomedicine and Drug Delivery Symposium (NanoDDS'12) featured in this issue. Congratulations to a great leader in nanomedicine, Prof. Robert Langer, who was recently awarded the National Medal of Technology and Innovation (see People in the News).

On behalf of the editorial team of the *CRS Newsletter,* I wish you a happy, healthy, and successful 2013.

Best wishes,
Arlene McDowell ■

Kazunori Kataoka
University of Tokyo
Tokyo, Japan

Feeling the Aloha Spirit Already

There are many things I am looking forward to in 2013, but in particular I am excited about the CRS Annual Meeting to be held in Honolulu, Hawaii, U.S.A. I feel a deep connection with the 2013 meeting, beyond having the honor to be the president during this time.

I was privileged to have served as the chair of the programming committee alongside Dave Grainger when CRS was in Honolulu in 2004, and am eager to return to the paradise that is Hawaii, which provided an excellent backdrop to scientific learning and business opportunities.

There are two sessions at the 2013 CRS Annual Meeting that are of great personal interest to me, and I am extremely pleased to share them with my delivery science colleagues from around the world. The Japanese Society of Drug Delivery System (JSDDS) will present the mini-symposium "Breakthrough Technologies in Drug Delivery Systems from Asia," highlighting emerging papers from Asia in cutting-edge fields such as gene delivery and regenerative medicine. In addition, "Rising Suns in Asia" will honor the talented young researchers from Asia. Also sponsored by the JSDDS, this session will allow young scientists to present their research and encourage them to be the next generation of leaders in the society. I hope you are able to make it to both important sessions while at the meeting.

To add one more personal connection to this meeting and the beautiful island of Hawaii, I would like to share that Japan and Hawaii have a unique cultural link. The colorful Hawaiian clothing I hope to see many of you wearing during the CRS Annual Meeting has its roots in the Japanese kimono. Early immigrants to Hawaii from Japan used colorful leftover kimono cloth to create work shirts, which became early precursors to the modern Hawaiian Aloha shirts.

There is much more to be excited about regarding this year's annual meeting. The program committee has pulled together an excellent selection of scientific sessions around our theme of "Emerging Challenges for Global Delivery," providing a comprehensive view of current delivery science breakthroughs and issues. Plenary lectures will include successful launching of new technology in immunology, the application of nanotechnology, and insights from the venture capital world (visit page 13 for more details). Five mini-symposia and 20 technical sessions will cover the areas of bioactives, industrial pharmaceuticals, preclinical sciences and animal health, and consumer and diversified products. Five workshops will offer additional knowledge in select areas pertinent to delivery science. From interspecies variability in drug targeting to challenges around brain delivery to nutraceuticals, there will be educational opportunities of interest to anyone in delivery science.
CRS Innovation Sunday will offer more than 25 industry presentations that focus on needs and solutions in the business of delivery.

Finally, on a presidential note, I wanted to share that the new bylaws regarding the creation of the Treasurer-Elect position have been passed. This was done to ensure that the important position of Treasurer received sufficient training to understand the society's needs, and it ultimately led to a decrease in the number of At-Large Directors by one person. Thank you to all who took the time to review the changes.

Kazunori Kataoka ■

The Academic Journey of Dr. Joachim Kohn, Professor at Rutgers University

Vishwas Rai, Ph.D.[1]

Kohn Lab members crowd the staircase in their new Life Sciences Building home at Rutgers Busch Campus in the summer of 2010. Kohn is fifth from bottom on the right.

"I worked at Rutgers University for the last 28 years, but I feel as if I've had four completely different jobs during those 28 years," said Joachim Kohn when I asked him about his academic journey. He continued: "I had a wonderful career in academia, full of challenges but always very exciting. But now I see a lot of change, and I expect that the lives of all the young scientists who are only now starting out will be very different from the experiences I had over the last 30 years of my academic journey."

Today, Joachim Kohn is widely recognized as a leader in biomaterials science. Probably the best-known theme of his laboratory is the exploration and commercial development of tyrosine-derived resorbable polymers, one of which is now used in an FDA-approved medical device that has so far been implanted in over 30,000 patients. He holds the position of Board of Governors Professor of Chemistry in the Department of Chemistry and Chemical Biology at Rutgers University, serves as the director of one of the two branches of the Armed Forces Institute of Regenerative Medicine (AFIRM), and is the founding director of the New Jersey Center for Biomaterials.

Kohn was born in Germany a few years after World War II. He grew up in Munich, which he describes as "one of the most wonderful cities" in Germany. He obtained his Ph.D. in chemistry and biophysics in 1983 from the Weizmann Institute of Science in Israel, working on the immobilization of enzymes and the development of chemical reactions that allow the attachment of biologically active ligands to polysaccharide beads. Kohn recalls: "My thesis adviser was Dr. Meir Wilchek. Dr. Wilchek is an extremely bright and productive scientist. He not only instilled the love of science in me, he truly influenced my life."

Kohn was fortunate to have had another great scientist as a mentor: after completing his Ph.D., Kohn joined the laboratory of Prof. Robert Langer at MIT in 1983. At that time, he was one of the first postdocs in the Langer lab, and he joined just when Prof. Langer's laboratory was about to make some major breakthroughs in drug delivery and tissue engineering. This was an extremely productive time but also a seminal experience that undoubtedly contributed to Kohn's own career development. He advises young scientists to be very picky when choosing a laboratory for postdoctoral training.

Q *Can you share some of your memories from the time you were a postdoc in Prof. Langer's laboratory at MIT?*

A I read with great interest the recently published interview with Allan Hoffman (CRS Newsletter 28[6], 2011), who described what life was like at MIT in the 1950s. That's about

[1] Chrono Therapeutics, Waltham, MA, U.S.A.

30 years before my time, but it is easy for me to point out some common experiences: It was intense! We worked extremely hard. And it almost seems that I could have saved myself the rent for my apartment—I spent so much time in the lab. But perhaps my most important memories relate to how stimulating and exciting my postdoctoral experience really was. I had no clue, back at that time, that I was witnessing history in the making. I met a lot of young, exciting people, all more or less at the beginning of their careers. My friendship with Nicholas Peppas (a former CRS president) started when I met him during one of his visits to Bob Langer's lab. Likewise, I meet Jorge Heller, the inventor of poly(ortho esters); Henry Brem, the brain surgeon who helped commercialize the first biodegradable drug delivery system; and Howard Rosen, who became the president of the ALZA division of Johnson & Johnson. Some of my peers were Mark Salzmann (today at Yale University), Kam Leong (today at Duke University), Elazar Edelman (today at Harvard/MIT), Margaret Wheatley (today at Drexel University), Edith Mathiowitz (today at Brown University), Ronald Siegel (today at the University of Minnesota), and many others. I am sure that many readers of this interview will instantaneously recognize these names. I think that, as a group, these early "lab rats" from the Langer lab have changed the fields of drug delivery and tissue engineering, and it was a unique and unforgettable experience to be part of this group back in the 1980s.

Just to add one fun memory: I met John Godfrey, the inventor of zinc lozenges, which later became a huge commercial success and are commonly known as Cold-Eeze. John had just cooked up his first zinc lozenges in his kitchen (see http://pabook.libraries.psu.edu/palitmap/ColdEEZE.html) and wanted me to taste them and to help him commercialize this product.

Q *You mentioned that you've really had four jobs while working at Rutgers for 28 years. Can you elaborate?*

A I can see four very distinct stages in my career development. After my postdoctoral training at MIT, I started as an assistant professor at Rutgers in 1986. Being a professor was my first "real" job.

In 1992, I started to develop the New Jersey Center for Biomaterials (NJCBM), and I became an administrator of a major collaborative team of scientists. In my experience, there are huge differences between being an individual faculty member and being the leader of a collaborative team of scientists. I regard my directorship of the NJCBM as my second job.

Then, for one full decade, starting approximately in 1999, I became an entrepreneur. This was my third job. I founded start-up companies, participated in commercial fund-raising efforts, and became an expert in the pros and cons of academic technology transfer and commercialization.

Finally, for the last five years, I've served as one of the two civilian directors of the Armed Forces Institute of Regenerative Medicine (AFIRM). In this capacity, I was the principal investigator of a national research team of over 100 scientists in more than 20 institutions, a team that received about $60 million in research and clinical trial funding from the U.S. Department of Defense. I regard this as my fourth job, distinctly different from anything I had ever done before.

Q *Let's talk a bit more about your first job, being a professor. What insights can you give to our readers?*

A When I joined Rutgers as an assistant professor, 100% of my effort was devoted to teaching, science, and service. This is what professors are doing. For me, teaching involved standing in front of some very large classes, as the Rutgers Chemistry Department has to teach over 9,000 students annually. I remember having over 400 students in one of the organic chemistry classes. Four hundred people looking at the professor can be an exciting or a frightening experience, depending on one's attitude toward lecturing. Some of my students were about the same age I was—therefore, gaining control over the class and motivating the students to learn chemical formulas was a really interesting challenge. Here's a piece of advice for the younger readers thinking about an academic career: it is not likely that you'll get a lot of help from your senior faculty colleagues. Standing in front of a large class is a very personal learning experience. I certainly made my share of beginner's mistakes, but over time, I also gained confidence in addressing large crowds.

Then, there is the science component. Starting a lab is a wonderful opportunity. My chairman handed me a $250,000 check, smiled, and said jokingly, "Spend it wisely—I'll see you again, once you have the Nobel Prize." Then he walked out, and I was left with a huge amount of money to spend and a 500 square foot empty room. My next challenge was to find good students, define projects, and hunt for grant support.

Here, I think, is a key difference between my experience and the experience of younger faculty: back in my time, the national funding rate was still over 30%. That means, on average 1 in 3 grant proposals to the NIH or NSF was actually funded. Today the proportion of funded proposals is apparently closer to 10%—and the grants being awarded are much smaller (in real dollars) than the awards I got back in the 1980s. Therefore, my experience is probably no longer typical for younger faculty: my very first proposal was funded, and within 9 months of starting at Rutgers, I was able to supplement my shrinking "start-up funds" with my first independently funded project. I remember this moment of getting a call from the program director at the NIH telling me that my proposal would be funded. I still didn't have an office, and the call came in on a payphone in the hallway. But, these minor details not withstanding, the sense of pride, satisfaction, and joy was truly overwhelming.

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The third component in a professor's portfolio of activities is "service." Faculty are supposed to sit on various governance committees, evaluate other people's work as part of the peer review system, and do some general societal good. I remember that all of these activities were very rewarding, and I always felt that I gained a lot in terms of experience and exposure through these service activities.

Q *Aren't you still a professor? Have there really been major changes in your life?*

A Yes, I am definitely still a professor, but I can really differentiate four phases of my career development. Therefore, what I call my "four jobs" are really four different levels of professional development while I continued to work at Rutgers.

A big change came when Dr. Stanley Bergen, the president of the neighboring medical school (University of Medicine and Dentistry of New Jersey, UMDNJ), called one day and asked me to work with him on the establishment of a biomaterials center in New Jersey. I agreed, not exactly knowing how significantly this decision would affect my life. A few weeks later a $300,000 check from UMDNJ arrived with the requirement to start a biomaterials program. Overnight, I turned from a professor to an administrator, from someone who begs others for research funding to someone who has research money to give out. I define my second job as my directorship at the New Jersey Center for Biomaterials, which started in 1992. My life really changed. I'll just mention a few amusing tidbits: I used to be late for meetings. Jokingly, like most professors, I thought that 15 minutes late is within the academic norm. Before 1992, it never mattered that I was late, since the meetings usually started just fine without me. But that changed in 1992: suddenly, everyone would wait for me to show up. Now, my being late became very noticeable, and I had to change my habits. Also, people took me much more seriously. As a professor, I used to joke that so few students would pay attention to what I was saying in class that it really didn't matter if I occasionally misspoke. Once in a leadership position, I learned very quickly that I had to be very careful about what I said, because people would actually listen. And finally, the amounts of money I was responsible for dramatically increased. As a professor, one usually deals with support for a single laboratory that is measured in the hundreds of thousands of dollars. As a center director, my first successful grant was a huge $3.6 million. Over time, the New Jersey Center for Biomaterials developed a highly visible and successful program of academic and industrial research. But, on the downside, I ended up spending less time in the laboratory. Therefore, my advice for younger scientists is to avoid taking on highly demanding administrative positions too early in one's scientific career.

Drug-eluting, fully degradable coronary stent made of polymers invented by Kohn and his associates. Image courtesy of REVA Medical ©2007 REVA Medical Inc.

Perhaps the most significant insight from my "second job" was the realization of how difficult it really is to get collaboration and cooperation from individual faculty. Faculty have to spend so much time looking for funding for their own laboratories that it is really difficult for most professors to find value in being a smaller player in a larger enterprise. In addition, the rules of academic recognition and professional standing tend to favor faculty members who are principal investigators of many small grants over faculty who are making huge contributions as collaborators on a larger team. Since finding solutions for our major societal and scientific challenges requires large, interdisciplinary, and often interinstitutional teams of many great minds, the old rules of academia are not fully in line with the needs of modern science.

Q *As you developed the New Jersey Center for Biomaterials, what role was played by entrepreneurship and interactions with industry?*

A This is a very good question, and one I actually love to respond to. I always felt that there is an unspoken societal contract between the scientific community and the taxpayers: taxpayers support our work, and in return we not only generate knowledge but also contribute to enhancing the life and health of all people. I feel that we scientists are very good at generating knowledge, but it takes an extra effort to translate this knowledge into products that enhance the lives of people. I feel that too few scientists make this extra effort.

My advice for young assistant professors is to focus initially on developing their scientific careers and building a body of scientific work and patents. But, at some point, when a "critical mass" of intellectual property has been generated, faculty should start thinking about commercialization.

In my case, by 1996, I had about 10 issued U.S. patents. That's when I started to think seriously about industry. I had participated in founding a first start-up company, which promptly failed. Rather than giving up and being discouraged, the failure of my first start-up company provided me with the expertise to try again. And this time it worked: my second start-up company was TYRX, a New Jersey based company that developed drug-eluting coatings for a series of innovative product concepts. Today, the products made by TYRX are used by over 30,000 patients. Quickly thereafter, I helped Rutgers enter into additional licensing agreements with

several other companies. Here, I would like to highlight REVA Medical (a coronary stent company in San Diego, CA), Lux Biosciences (a company developing ophthalmic drug delivery systems in Jersey City, NJ), and finally, Trident Biomedical (a company developing orthopedic implants in Bridgewater, NJ).

One thing is clear: these entrepreneurial activities are extremely time and energy consuming. Today I fully appreciate why so few faculty are willing to go down this road—and I do respect their decision not to engage in serious commercialization activities.

For me, dealing with four companies was a difficult learning experience. There is a constant need to balance one's limited time, to avoid legal pitfalls, and to stay clear of complex conflict-of-interest regulations. And, while there are books and the occasional workshop, it is impossible to really learn how to manage academia-industry interactions without practical experience. Therefore, I regard the decade from about 1995 to 2005 as my third job.

Q *In hindsight, do you believe that it was really worthwhile to engage in technology transfer and commercialization?*

A I want to make sure that I leave you with the notion that all of this extra effort in the end pays off in many ways. TYRX was able to bring two products to the market: one is an antimicrobial sleeve to prevent devastating (and sometimes fatal) infections among recipients of pacemakers and other coronary assist devices. So far, about 30,000 patients have been implanted with this device, and based on the significant drop in the infection rate seen in these patients, the polymer we developed and licensed to TYRX has already saved many lives. I regard this as my most important achievement. I am convinced that many academic researchers, from students to postdocs and faculty, are seriously thinking about commercializing their inventions, and I hope that the path toward commercialization will become easier over time.

Q *I assume that your fourth job was being involved with the Department of Defense and the Armed Forces Institute of Regenerative Medicine (AFIRM)?*

A You are correct. It was a huge step when we were awarded about $60 million to guide the work of a group of over 100 scientists in 15 major academic institutions and several companies. Our vision was to create regenerative therapies that can alleviate the human pain and suffering caused by crude bombs, often called improvised explosive devices (IEDs). Our key mission was to focus on the treatment of burn injuries, injuries to the musculoskeletal system, and injuries to the face. The Army asked us to develop therapies that can restore the body's form and function after massive injuries. Many people are not aware that military doctors had found ways to save the lives of many seriously injured war-fighters. As a consequence of highly efficient rescue

Das Bolikal (left) and Joachim Kohn (right) in the laboratory around 2000. Dr. Bolikal is a key member of the lab, a polymer chemist and a coinventor of many inventions coming from the Kohn Lab.

operations, the mortality rate of the wars in Iraq and Afghanistan was the lowest of any war so far. But, on the other hand, our ability to save lives on the battlefield had outgrown our ability to deal with the horrific injuries sustained by the survivors. There are about 5,000 veterans of Iraq and Afghanistan who have lost arms and/or legs or who are seriously disfigured. AFIRM was created to find medical solutions for these most seriously injured members of our armed forces. In addressing this need, drug delivery, tissue engineering, biomaterials science, cell and stem cell biology, and clinical practice were combined to make a number of major breakthroughs.

As one of the civilian directors of AFIRM, I had a glimpse into the future of science, in terms of how scientific work may be solicited by the government and how teams may be organized and managed. I think the term "megascience" is sometimes used to describe the establishment of very large collaborative teams that address major societal problems. I really believe that government support for individual investigators will shrink over the next few years and that we will see more AFIRM-like efforts that encourage a wide range of experts to collaborate toward a major common goal.

Q *Could you focus on the interests of CRS members and tell us what aspects of drug delivery were important in your AFIRM work?*

A Regenerative therapies rely in part on the release of biologically active agents, either systemically or locally. A good example are the bone morphogenic proteins BMP-2 and BMP-7, which are powerful activators of bone regeneration. Other growth factors were used to support the regeneration of

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Lux Biosciences and the Kohn Lab jointly developed an insertable drug delivery device for the long-term treatment of inflammatory diseases of the eye. This specific device will deliver a proprietary new calcineurin inhibitor for the treatment of uveitis and dry eye syndrome.

cartilage. A project that proceeded in our lab was addressing the serious problem that partial thickness (2nd degree) burns can progress after the injury occurred to full thickness (3rd degree) burns. When that happens, medical treatment becomes more complicated and costly, and the formation of scars can lead to lifelong disability. Together with Dr. Richard Clark, a leading burn injury expert from Stony Brook University, we worked on developing a burn wound dressing that is impregnated with P12, a proprietary peptide that can prevent burn injury progression. Formulating an appropriate release system for P12 as part of a wound dressing turned out to be a major challenge. We finally settled on incorporating P12 into a nanofiber mat made of a uniquely designed polymer that provided the required seven-day release profile for P12. These are just a few examples of the important role drug delivery technologies play in the implementation of regenerative therapies.

Q *Finally, can you tell us about past and current research work in your laboratory?*

A I am very excited about the successful development of a new "discovery paradigm" for revolutionary biomaterials using combinatorial and computational methods to optimize the composition and properties of biomaterials for specific applications. Briefly, we started to look at the way the pharmaceutical industry is discovering new lead compounds for drug development. We realized that new biomaterials were usually discovered (or invented) based on serendipity rather than as a consequence of a rational design approach. That meant there was a lack of bioactive polymers specifically designed for advanced applications such as tissue engineering and drug delivery. As a first demonstration of the utility of this approach, we applied a systematic design paradigm to discover an optimized polymer for use in a fully degradable cardiovascular stent. Our polymer enabled a new stent design, which is now being tested in clinical trials in Germany and Brazil. Additional examples of our use of a combinatorial biomaterials design approach are the development of optimized polymers for Lux Biosciences (ophthalmic applications) and for Trident Biomedical (orthopedic applications).

Much of our recent work builds upon our invention of pseudo-poly(amino acids), amino acid-derived, degradable polymers in which individual amino acids are linked by nonamide bonds. While most conventional poly(amino acids) have poor engineering properties, pseudo-poly(amino acids) can be designed to exhibit outstanding engineering and physicomechanical properties, as well as a high degree of biocompatibility. For example, tyrosine-derived polycarbonates were shown to be promising materials for implantable drug delivery systems and orthopedic implants, copolymers of the natural amino acid L-lysine and poly(ethylene glycol) were successfully used as drug carriers, and polymeric conjugates of *cis*-hydroxyproline were prepared and found to exhibit powerful antifibrotic activity. These insights allowed us to develop computational models that can predict many important polymer properties, based simply upon the knowledge of the chemical composition of the polymer.

Q *To conclude, can you share with us your connections with CRS?*

A CRS was the first major scientific society I joined as a postdoc back in 1984. I have vivid memories of my very first international travel to give my first public lecture at the CRS meeting in Geneva, Switzerland, in 1985. At that time, I made my first professional connections, and some of these contacts became part of my professional life for years. CRS was definitely an important part of my professional development. We didn't use a lot of e-mail prior to 1990, and at that time the personal contact with colleagues, friends, and scientific competitors was very important. The CRS Annual Meetings were the highlights of my travel calendar. Then, in 1992, I was the recipient of the CRS Young Investigator Award—a very important event in my professional life, as it came right around the time I was coming up for the critical tenure decision and promotion to associate professor. I still display my CRS award prominently on my desk.

In spite of the advance of e-mail, internet, and smart phones, the need for personal interactions remains as strong as ever; therefore, I am sure that professional societies like CRS will continue to provide a vital service to the scientific community. I also hope that CRS continues to occupy a central role in the professional development of young scientists today. My final thought is directed toward the leadership of CRS: I hope that CRS will continue to provide mentorship opportunities and other opportunities to grow to our younger members. ■

Intracellular Delivery of Bioactive Molecules Using Liposomes Surface-Modified with Cell-Penetrating Peptide Octa-arginine for Improved Anticancer Activity

Swati Biswas and Vladimir P. Torchilin[1]

Introduction

Intracellular delivery of bioactive molecules is important to achieve maximum therapeutic benefit. Unlike small-molecule drugs that cross the cell membrane by diffusion, nanosized drug delivery systems (DDS) translocate into the cellular cytoplasm via energy-dependent endocytosis, which is often the rate-limiting step for achieving the required therapeutic action of the loaded cargo of the DDS. Apart from this passive transport mechanism, active transporter-mediated uptake has been considered as a promising approach to enhance the intracellular transduction of nanocarriers.

Over the last two decades, various short peptide sequences have been identified that promote active transport of a variety of cargo across the plasma membrane to deliver their payload intracellularly. These short peptide sequences, referred to as cell-penetrating peptides, contain less than 20 amino acids and are highly enriched with basic residues. The majority of cell-penetrating peptides are the short stretches of the protein domain that are primarily responsible for their translocation ability. One of the most frequently used cell-penetrating peptides, TAT peptide, is the peptide sequence (48–60) derived from the 86-mer transactivating transcriptional activator (Tat) protein encoded by human immunodeficiency virus type 1 (HIV-1).[1]

In our previous work on intracellular delivery of DDS, we demonstrated that TAT peptide on the surface of the liposomes afforded their efficient intracellular delivery.[2] In another study, TAT-peptide modification of the paclitaxel-loaded micellar system enhanced the cytotoxicity *in vitro* and *in vivo* compared with unmodified drug-loaded micelles, indicating that the enhancement of drug action resulted from the efficient intracellular delivery of the drug-loaded DDS.[3]

In our present study, the modification of PEGylated liposomes using a relatively unexplored, short synthetic peptide, octa-arginine (R8), has been carried out for the purpose of efficient intracellular delivery of the liposome-incorporated chemotherapeutic drug doxorubicin (Dox) in cancer cells. PEGylated liposomes have long systemic circulation, advantageous for getting accumulated in the tumor site via the enhanced permeability and retention (EPR) effect. However, polymer coating on the liposome surface hinders their cellular internalization. In this work, we have modified the surface of PEGylated doxorubicin-loaded liposomes using an R8-conjugated PEG-phosphatidylethanolamine (PEG-PE) polymer. The delivery efficiency has been investigated in a murine breast cancer model *in vitro*.

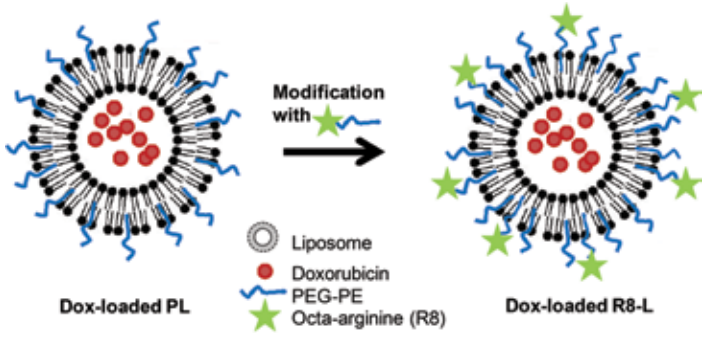

Figure 1. *Schematic representation of the preparation of octa-arginine-modified doxorubicin-loaded PEGylated liposomes (R8-L).*

Experimental Methods

The octa-arginine-modified amphiphilic polymer R8-PEG-2K-DOPE was synthesized as follows.

R8 (7.4 mg, 5.6 μM) was added to the solution of activated acid-functionalized poly(ethylene glycol)-dioleoyl phosphatidyl ethanolamine, pNP-PEG-2K-DOPE (10 mg, 3.9 μM), in phosphate buffered saline (PBS), pH 8.4. The reaction mixture was stirred at 4°C overnight, dialyzed using cellulose ester membrane (molecular-weight cut-off 2 kDa) against water, and lyophilized. The white fluffy solid was dissolved in methanol (5 mg/mL) and stored at –80°C for further use.

Dox-loaded PEGylated liposomes, commercially available as Doxil®, were purchased from Sun Pharmaceutical (Gujarat, India). Doxil was modified by a micelle transfer technique. A lipid film of R8-PEG-2K-PE/PEG-2K-PE (2 mole % of the total lipid in the liposome) was hydrated with Doxil suspension and stirred overnight to prepare Dox-loaded PL and R8-L. The

[1] Center for Pharmaceutical Biotechnology and Nanomedicine, Northeastern University, U.S.A.

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liposomes were subjected to gel filtration chromatography to remove the unincorporated R8-PEG-PE/PEG-PE. Liposome size and size distribution were measured in triplicate by dynamic light scattering (DLS) using a ZetaPlus instrument (Brookhaven Instruments, Holtsville, NY, U.S.A.). Size distribution was confirmed through transmission electron microscopy (JEM-1010, Jeol, Tokyo, Japan).

For confocal microscopy studies, the murine mammary carcinoma 4T1 cells were grown on cover slips in six-well cell culture plates. The cells were incubated with liposomes for 1.5 hr before washing with PBS. The cells were stained with Transferrin Alexa Fluor 488 at 10 mg/mL for 20 min, followed by Hoechst 33342 at 5 mg/mL for 5 min for visualization of the endosomal compartments and the nuclei, respectively. The cover slips were mounted on Fluoromount-G and visualized under the Zeiss LSM 700 confocal microscope. The pictures were analyzed by ImageJ software.

For the determination of antitumor efficacy of Dox-loaded PL and R8-L, the 4T1 cells were incubated with liposomes at different Dox concentrations, diluted serially from the maximum dose of 25 mg/mL, for 4 hr. The cells were incubated in the complete media for an additional 48 hr before analyzing the cell viability with Thiazolyl blue tetrazolium bromide (MTT assay).

Results and Discussion

We anchored R8 on the surface of the liposomes by using the R8-PEG-PE copolymer, the lipid part of which was buried in the liposomal lipid bilayer (Figure 1). The size of R8-L was in the range of 75–115 nm (same as without R8-polymer insertion; Figure 2). To assess the intracellular delivery of Dox, liposome-treated 4T1 cells were visualized under the confocal laser scanning microscopy, and z-stacked images were obtained (Figure 3). The images clearly showed that Dox-loaded R8-L had a significantly higher cellular internalization compared with PL. A colocalization analysis using a nuclear stain and endosomal marker (Figure 4) demonstrated that the treatment with R8-L caused a marked accumulation of Dox in nuclei, as indicated by the bright purple color of the nucleus (resulting from colocalization of the blue and red signals). PL failed to deliver Dox to the nuclei in 1.5 hr. Strong green fluorescence in Figure 4A indicated that the liposomal Dox was entrapped in the endosomes. A clear improvement in the intracellular delivery efficiency of Dox-loaded R8-L led to a more efficient drug action compared with Dox-loaded PL (Figure 5).

Conclusion

R8 modification of the liposomal surface enhanced the intracellular delivery of the payload, which resulted in improved Dox activity against cancer cells compared with unmodified liposomes.

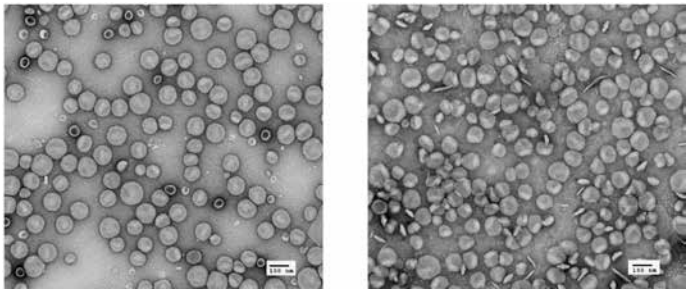

Figure 2. *Transmission electron micrograph of Dox-loaded PL and R8-L.*

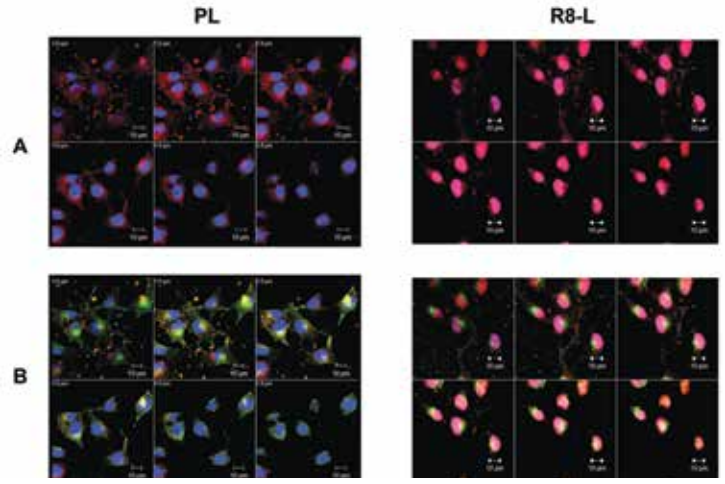

Figure 3. *Confocal laser scanning micrograph of Dox-loaded PL and R8-L-dosed 4T1 cells, stained with Hoechst 33342 for nuclei and Transferrin Alexa 488 for endosome visualization. Cells were imaged using z-stacking. Z7–12 were presented to visualize the vicinity of the nuclear zone. The signals from Dox, Hoechst 33342, and Transferrin Alexa 488 were visualized using rhodamine, UV, and fluorescein isothiocyanate (FITC) channels. (A and B) Merged pictures of UV/rhodamine and UV/rhodamine/FITC channels, respectively.*

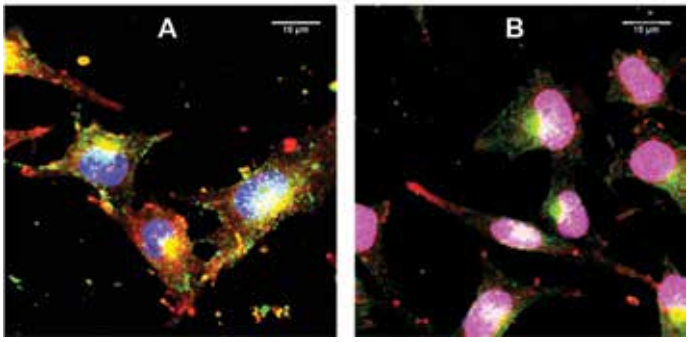

Figure 4. *Intracellular fate of Dox delivered by Dox-loaded R8-L (B) compared with Dox-loaded PL (A). The yellow signal indicated the colocalization of Dox and endosomes, whereas purple spots indicated the accumulation of Dox in the nucleus.*

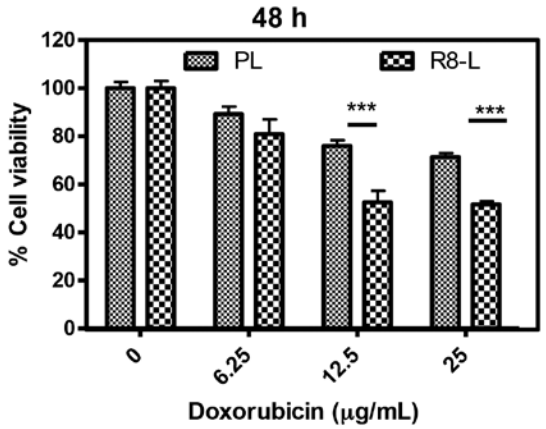

Figure 5. *Cell viability of 4T1 cells treated with liposomes at Dox concentration range of 0–25 μg/mL for 4 hr, followed by incubation for 48 hr. *** indicates $P < 0.001$, analyzed by Student's t test.*

Acknowledgement

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3. Sawant, RR, Torchilin, VP. Enhanced cytotoxicity of TATp-bearing paclitaxel-loaded micelles *in vitro* and *in vivo*. Int. J. Pharm. 374: 114-118 (2009). ■

As the 2013 CRS Annual Meeting & Exposition approaches, the *CRS Newsletter* will highlight some of the top science, business, and networking opportunities from the meeting. Here is what to expect on the science of bioactives during this year's meeting in Honolulu. Watch for the next issue of the *CRS Newsletter* for a preview of other research.

Discover the Technical Program at the 40th CRS Annual Meeting & Exposition, Honolulu, HI, U.S.A.

Annual Meeting Planning Committee

The Annual Meeting Planning Committee (AMPC) is excited about the scientific sessions shaping up for this year's CRS Annual Meeting & Exposition. Committee Chair Mark Saltzman (Yale University, U.S.A.), Deputy Chair Ick Chan Kwon (Korean Institute of Science and Technology, Korea), and committee members Marcel Bally (British Columbia Cancer Agency, Canada), Marcus Brewster (Johnson & Johnson, Belgium), Sarah Eccleston (Aptuit, United Kingdom), Chuck Frey (Coating Place, U.S.A.), Justin Hanes (Johns Hopkins University, U.S.A.), Hideyoshi Harashima (Hokkaido University, Japan), Nicole Papen-Botterhuis (TNO, The Netherlands), Joshua Reineke (Wayne State University, U.S.A.), and Christian Seiler (Merck Sharp & Dohme, United Kingdom) have been working since early September 2012 to organize an engaging program that encompasses a comprehensive scope of current controlled release and delivery science with contributions from world-class scientists.

The theme of this year's meeting is "Emerging Challenges for Global Delivery." Headlining the program are plenary lectures on the successful launching of new technology in immunology, the application of nanotechnology, and insights from within the venture capital world. These lectures offer a high-level look at technology and/or paths to bringing technology to practical use.

The preliminary program includes five mini-symposia and 20 technical sessions covering the areas of bioactives, industrial pharma, preclinical sciences and animal health, and consumer and diversified products (C&DP). Mini-symposia are arranged around new focal areas of specialized interest and include the following topics:

Breakthrough Technologies in Drug Delivery Systems from Asia (compiled by the Japanese Society of Drug Delivery System)

Drug Combination Products (explores positive and negative drug–drug interactions in combination products)

Energy: Problems Within the Industry That Controlled Delivery Can Solve (a C&DP session on controlled release technology employed in energy production and conservation)

Hybrid Groups—Bridging the Gap Between Industry and Academia (addresses the challenges to bridging the gap between industrial and academic philosophy and needs)

Nanoparticles and Cancer (examines positive or negative aspects of nanoparticle therapies)

Bioactive technical sessions are focused on various aspects within the extensive scope of controlled release and delivery, including drug targeting, development strategies, prediction, particle design, molecular structure or size, material characterization, manufacturing, and demographic formulation constraints. The sessions are rounded out with a veterinary session on the drug targeting variations between species and C&DP sessions capturing food, nutrition, diet, personal care, home care, agriculture, aquaculture, and building/construction materials.

The CRS AMPC has taken a close look at the popularity of topics/sessions of past annual meetings and has taken this and current or future areas of interest, along with suggestions from the CRS Board of Scientific Advisors, into consideration when compiling the program for the 2013 meeting. Oral controlled release is one area where the AMPC felt the need to increase its investment, hence the two scientific sessions associated with this topic, since it is a core area of CRS and has historically attracted a high number of abstract submissions. The following is a full list of the preliminary sessions. More detailed descriptions, including the invited speakers, can be found on the CRS website at www.controlledreleasesociety.org/meetings/annual/program/pages/ScientificSessions.aspx:

- Challenges Around Brain Delivery: Sampling Site Issues and Interspecies Extrapolations
- Drug Delivery for Developing Countries/Global Challenges
- Drug Targeting, Pharmacokinetics, and Biodistribution: Differences Between Species
- Emerging Technologies

- Food, Nutraceuticals, and Personalized Diet
- Imaging and Characterization Techniques for Drug Delivery: Systems and Targeted Drug Delivery
- Micro- and Nanoparticle Design
- Modern Agriculture and Aquaculture
- Oral CR – Pharmaceutical Formulations, Technologies, and Development Strategies
- Oral CR – Predictive Tools *(In Vitro/In Vivo/In Silico)*
- Parenteral Sustained Release Drug Delivery
- Peptide and Protein Delivery
- Personal and Home Care
- Processing Technology/Manufacturability
- Regional Delivery: Challenges in Ocular Delivery and Pulmonary Delivery
- Rising Suns in Asia
- RNAi and DNA Delivery
- Smart Building and Construction Materials and Coatings
- Solubilization Technology – A Key Enabler for the Delivery of Poorly Soluble Drugs
- Topical/Transdermal Drug Delivery

In addition to the oral presentations, there will be the poster presentations within these same categories.

The CRS Annual Meeting & Exposition offers a comprehensive snapshot of the current state of controlled release and delivery science with the opportunity not only to see what is being accomplished and how problems are being solved but also to be a part of the conversation and direction of this work. Make plans to engage in this rewarding experience July 21–24, 2013, in beautiful Honolulu, Hawaii! ■

Plenary Speakers to Cover Nanotechnology, Immunology, and Venture Capitalism

The 2013 plenary speakers offer expert presentations on innovative and cutting-edge areas of delivery science and technology, providing up-to-the minute insight into our unique field or sharing outside perspectives on our science. This year's plenary speakers will provide a greater understanding in a variety of relevant areas.

Plenary speaker **Paula Therese Hammond** is the Koch Professor of Engineering and Executive Officer with the Department of Chemical Engineering and Koch Institute of Integrative Cancer Research at Massachusetts Institute of Technology. Her research program focuses on the self-assembly of polymeric nanomaterials. The core of her work is the use of electrostatics and other complementary interactions to generate functional materials with highly controlled architecture. Hammond holds many distinguished titles and awards, including Scientist of the Year at the Harvard Foundation's Albert Einstein Science Conference and being featured as one of the Top 100 Materials Scientists by Thomson Reuters (based on citation and overall impact), and she has published over 200 papers in refereed journals. Her plenary session is titled "Electrostatic Nanolayer Delivery Platforms: From Macro- to Nanopharmacies."

Chairman and founder of Evec, Inc., and Professor Emeritus at Hokkaido University, **Kenzo Takada** has studied molecular mechanisms of oncogenesis by Epstein-Barr virus for 40 years. He is the author of over 150 peer-reviewed publications and received the Minister of State for Science and Technology Policy Award and the Hokkaido Science and Technology Award, and he was appointed as Director of the Institute for Genetic Medicine, Hokkaido University, from 2002 to 2006. Evec, Inc., is one of the most successful bio venture companies, having its head office in Sapporo, Japan. Takada will deliver a plenary on "Human B-Lymphocytes as a Source of High-Affinity, Really Fully Human Antibodies."

Josh Wolfe is a cofounder and managing partner of Lux Capital Management, focusing on investments in the physical and life sciences. He is a columnist with *Forbes*, editor of the *Forbes/Wolfe Emerging Tech Report*, and host of a show on the Forbes Video Network. Wolfe has been an invited guest to the White House and Capitol Hill to advise on nanotechnology and emerging technologies; a lecturer at MIT, Harvard, Yale, Cornell, Columbia, and NYU; and a frequent guest on CNBC and CNN. In addition, Wolfe has published AIDS-immunopathology research in *Cell Vision* and the *Journal of Leukocyte Biology*.

Full descriptions of the speakers and their subjects can be found at www.controlledreleasesociety.org/meeting. In addition to these fascinating presentations, the 2013 CRS Annual Meeting will feature the always popular roundtables, mini-symposia, CRS Innovation Sunday, and Exposition of 100 companies in the industry, along with nearly 1,500 of your colleagues.

Plan now to join the top scientists in delivery science and technology at the CRS Annual Meeting & Exposition in Hawaii. ■

Articles and Websites of Interest in Animal Models of Disease, Cross-Species Comparisons, and "One Health"

Professor David Brayden[1] and Dr. Terry Bowersock[2]

The Preclinical Sciences & Animal Health (PSAH) Division provides a platform for exploring the development of drugs, formulations, and novel delivery systems intended for use in veterinary species or studied in veterinary species to support the development of novel therapeutic technologies for the human patient. Consistent with this objective, PSAH will be providing regular distillations of relevant papers and website materials that describe the use of animal models in pharma discovery and delivery programmes. Here is a sample of five recent publications showcasing how animal data can be used to model human conditions in unexpected ways:

1. Piglets are being used as a new model for human microbiome research. Research reported in *Science* suggested that pigs inoculated with human gut microbiota are being used to examine whether the range of human microbes that affect health can be established in this species. This has great potential for investigating probiotic research and colonic drug delivery, given that the piglet is an excellent model of the human gastrointestinal tract. See Hvistendahl M. Pigs as stand-ins for microbiome studies, Science 336: 1250 (2012).

2. Zebrafish articles are on the increase. Zang *et al.* established a protocol using gluten particles as a carrier to orally administer fluorescently labelled chemicals to adult zebrafish. They conducted a pharmacokinetic study of oral administration of felbinac and confirmed that it was successfully delivered into the blood of zebrafish. The pharmacokinetics of drugs given by oral administration were also compared with those of chemicals given by alternative administration routes such as intraperitoneal injection. See Zang, L, Morikane, D, Shimada, Y, Tanaka, T, Nishimura N. A novel protocol for the oral administration of test chemicals to adult zebrafish, Zebrafish 8:203-210 (2011).

3. An interesting comparative study on mucus thickness in the intestines of postmortem rats, rabbits, and pigs has been carried out by the Basit group at University of London. This is very relevant for oral delivery using mucoadhesive polymers. Interspecies variability in mucus thickness along the gut was demonstrated and suggests that the pig resembles more closely the mucus pattern of humans. This may be relevant when preclinical animal models are used in oral drug absorption studies. See Varum, FJO, Veiga, F, Sousa, JS, Basit, AW. Mucus thickness in the gastrointestinal tract of laboratory animals. J. Pharm. Pharmacol. 64: 218-227 (2012).

4. Mouse models of colitis are widely used to assess predictive drug efficacy for human inflammatory bowel disease, none more so than the dextran sodium sulphate (DSS) model, whereby mice drink spiked water for five days. Until now, the etiology of the inflammation development *in vivo* was a mystery and could not be mimicked *in vitro*. Laroui *et al.* discovered that the key is the formation of nanocomplexes in the colon between DSS and medium-chain fatty acids including C12, which then attach to the colonic epithelia and deliver the dextran moiety to the cytoplasm to cause inflammation. The authors concluded that the distal colon targeting concept of DSS can be developed further but without the ensuing damage. See Laroui, H, Ingersoll, SA, Liu, HC, Baker, MT, Ayyadurai, S, Charania, MA, Laroui, F, Yan, Y, Sitaraman, SV, Merlin, D. Dextran sodium sulfate (DSS) induces colitis in mice by forming nano-lipocomplexes with medium-chain-length fatty acids in the colon, PLoS One 7(3): e32084 (2012).

5. According to a recent paper, a live vaccine containing new *Lactococcus lactis* strains generated mouse data that may provide a basis for the development of an inexpensive and

[1] University College Dublin.
[2] Pfizer Animal Health, U.S.A.

safe oral live vaccine against a parasite that infects humans, Leishmania. Hugentobler *et al.* made *L. lactis* strains expressing the protective Leishmania antigen LACK along with the coexpressed adjuvant IL-12. This construct partially protected BALB/c mice against subsequent *Leishmania major* challenge and was accompanied by mucosal immunity. See Hugentobler, F, Di Roberto, RB, Gillard, J, Cousineau, B. Oral immunization using live *Lactococcus lactis* co-expressing LACK and IL-12 protects BALB/c mice against *Leishmania major* infection. Vaccine 30(39): 5726-5732 (2012).

In addition, there exist numerous disease states shared by humans and animals. In these situations, there is the opportunity for the development of shared therapies. To cover some of these examples, the cochair of PSAH, Dr. Marilyn Martinez of the FDA, has an excellent public resource page on the links between human and animal therapeutics. Hosted by AAPS, it contains many useful videos, articles, and websites with some fantastic material on the "One Health" theme. See http://aapsblog.aaps.org/human-and-veterinary-therapuetics. A recent professionally made four-minute video on tuberculosis transfer between dogs and humans caught our attention, as it arose from a collaboration between pathologists from the University College Dublin veterinary school and the local film school. See www.youtube.com/watch?v=SiJk1LegLIM.

Prof. Sean Callanan, University College Dublin (UCD) Veterinary School, and Shane Kelly, Dun Laoghaire Institute of Art and Design Technology (IADT), Dublin. UCD and The National Film School IADT Science Expression Short Film Dependence.

Our intent is for the PSAH website to provide a unique and valuable resource that links timely and pertinent information describing the shared opportunities that link human and animal health. ■

The 10th International Nanomedicine and Drug Delivery Symposium (NanoDDS'12) in New Jersey Succeeds Despite Sandy's Delay

Robert Prud'homme presents on "Nanoparticle Targeting and Treatment for TB— Scaleup of Nanoparticle Production."

Despite a nearly six-week delay caused by the devastating Hurricane Sandy, more than 100 scientists from academia, industry, and the health science sector participated in the 10th International Nanomedicine and Drug Delivery Symposium (NanoDDS'12) held on December 6–7, 2012, in Atlantic City, New Jersey, U.S.A.

Signs of the devastating storm were still apparent along the city's famed boardwalk, just outside the symposium venue's front door, but the hotel was running smoothly again in time for the meeting, which was chaired by Professors Tamara Minko and Arash Hatefi from Rutgers University. Tamara Minko chairs the Department of Pharmaceutics in the Ernest Mario School of Pharmacy, and Arash Hatefi is an assistant professor.

The overall objective of NanoDDS'12 was to gather internationally recognized experts in the area of nanoscale-based drug delivery systems. The symposium was specifically focused on nanocarriers of different composition, architecture, size, and charge and their use for treatment and imaging. The advances in nanomedicine and bioimaging research have been discussed at several scientific conferences and meetings of well-established professional societies. However, the NanoDDS series of symposia is very different from conferences discussing problems in nanomedicine and bioimaging. The series started in 2003 and has been established as a medium-size, internationally recognized series of symposia closely focused on various aspects of nanomedicine related to drug delivery and imaging.

Jindrich Koopecek (University of Utah), Alexander Kabanov (University of North Carolina, Chapel Hill), and Abraham Rubenstein (Hebrew University, Jerusalem) delivered the first three of the symposium's 26 lectures, speaking on "Novel Nanostructures and Nanomaterials." The morning session ended with a presentation on "Nanosphere-Based Formulations of Highly Hydrophobic Drugs for Topical Delivery" by Joachim Kohn of Rutgers University. Presenters talked about the design of drug-free macromolecular therapeutics, the state of the art and future of drug delivery, the development of biomarkers for real-time diagnostics of malignancy, and the many challenges they encountered in bringing technologies to market.

Julia Ljubimova (Cedars-Sinai Medical Center), Diane Burgess (University of Connecticut), Ram Mahato (University of Tennessee), and Robert Prud'homme (Princeton University) delivered their lectures in the second morning session that focused on "Nanosystems for Theranostics and Diagnostics." Afternoon sessions focused on "Engineered Nanosystems and Nanomaterials" and "New Technologies in Nanomedicine and Drug Delivery." Professors Andrew Mackay, David Putnam,

NanoDDS'12 cochairs Tamara Minko (left) and Arash Hatefi (right).

Prabhas Moghe, Chun Wang, Zheng-Rong Lu, Thomas Anchordoguy, Richard Gemeinhart, and David Oupicky shared their new findings with colleagues. The symposium's second day was mainly focused on "Multifunctional and Multicomponent Nanosystems for Drug Delivery." Both new investigators and leaders in the field, including Adah Almutairi, Vinod Labhasetwar, Jayanth Panyam, Tatiana Bronich, Mark Tracy, and Oleh Taratula, presented very interesting, original, and novel results in the session.

Along with many discussions of novel materials in the area of nanotechnology, a noteworthy aspect of the science presented was the role of nanomedicine in translation research. "It's not only about new technology but clinically based research, from bench to clinic with more collaboration with clinicians," Dr. Minko said. "This was our intent—not simply focus on new technology but hear from speakers who took the next steps and tried to use their new technologies on the clinical level, including clinical trials in the delivery of drugs and testing in animal models."

Researchers in academia and industry from across the United States, as well as England, India, Iran, Japan, Switzerland, and Russia presented more than 60 posters at the symposium. Subjects included nanozymes for treatment of stroke, assembly of anticancer drugs into well-defined nanostructures, and "Synthesis and Application of Biodegradable Janus Particles for Combination Therapy."

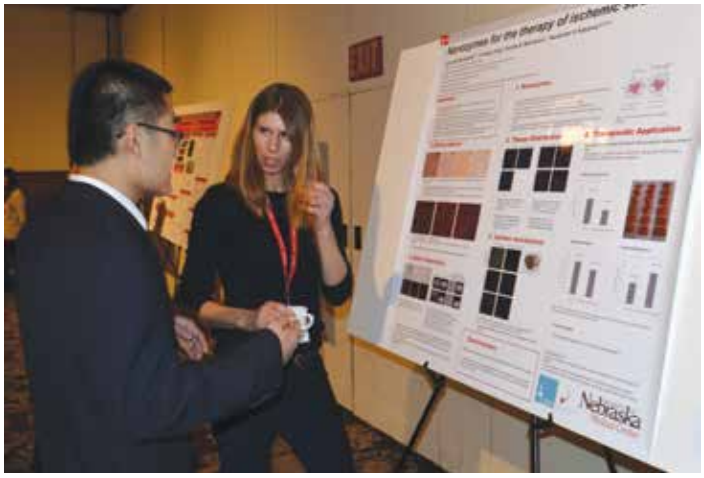
The feedback from participants was very positive, according to Dr. Minko. She credits "extremely high quality" of the presentations and posters, coupled with the considerable engagement of those at hand: "We were pleased to see many questions from the audience and good discussions, particularly among the young scientists."

Steven Zullo of the National Institute for Biomedical Imaging and Bioengineering and Yali Fu of the National Cancer Institute conducted a special session on "NIH Grantsmanship in Nanomedicine and Nanotechnology Areas." James Li and Amy Rubenstein of NIH/CSR gave a brief overview of the NIH peer review process, particularly the nanomedicine study sections.

"We felt hearing from NIH representatives, people who are responsible to review proposals and get funding to scientists, hearing them discuss funding possibilities, would be very valuable," Tamara Minko said. "It's certainly a very complicated area, and there was a high degree of interest among participants, who asked a lot of questions. After all, as we all know, it's a matter of life and death for scientists."

Researchers' presentations and posters at the symposium covered the use of novel materials in nanotechnology, such as new approaches for delivery of drugs to the brain, which Dr. Minko noted is a considerable challenge for scientists. She also pointed out that because of its format, the symposium showed the high efficiency of bringing together new investigators and students along with well-known, world-recognized scientists from academia and industry. The relatively small number of participants encouraged young investigators to discuss their research with recognized specialists in the field and helped them to establish network connections for further collaborations and employment. The specific objectives of the symposium were (1) to facilitate translational research by enhancing discussion, fostering exchange of opinions, and establishing collaborations between academic scientists, industrial researchers, and clinical researchers; (2) to provide a forum to discuss theoretical and applied problems in nanomedicine and drug delivery; and (3) to allow students, postdoctoral researchers, and young investigators to present and discuss their research in front of world-recognized established scientists.

Although postponed and slightly truncated, the symposium was successful, Tamara Minko feels, because of the range and quality of information discussed, which she predicts will lead to new collaborations in the future, new avenues of research, and valuable new discoveries. ■



Anna M. Brynskikh discusses her poster.

The Eighth Annual Meeting of the CRS Israeli Local Chapter (ICRS)

Dr. Ayelet David[1] and Prof. Ronit Satchi-Fainaro[2]

The eighth annual meeting of the Israeli Local Chapter of the Controlled Release Society was held on September 5–7, 2012, at the Hacienda Forestview Hotel in Maalot Tarshiha. We had 200 participants, which included 148 scientists from academia (of which 99 were students), 44 scientists from industry, 5 clinicians, and 3 representatives from governmental offices. The ICRS8 conference brought together people from different disciplines related to drug delivery systems and controlled release of bioactive materials—from basic, applied, industrial, and clinical research—enabling them to interact with each other and hopefully to seed some new collaborations.

The ICRS8 program focused on four main lines of discussion, with the goals of reflecting the latest developments in the field of drug delivery systems, fostering multidisciplinary collaborations between materials science and life science and between academia, clinic, and industry, and encouraging young scientists to take an active part in this research and training conference.

The program consisted of four keynote lectures, invited talks, short oral student presentations, and poster presentations.

The first session, on "Nanomedicines for Cancer Therapy," opened with the keynote presentation of Prof. Ruth Duncan (Cardiff, United Kingdom, and CIPF, Valencia, Spain), a leading expert in the field of nanomedicine, who reviewed the use of polymer therapeutics for clinical use and clinical development. She discussed the lessons learned from three decades of clinical studies and the emergence of new technologies in the design and development of polymer therapeutics and nanomedicines. Dr. Avi Schroeder (Technion) described the design of programmed nanorobots for cancer treatment. Dr. Ayelet David (Ben-Gurion University) discussed novel polymer-drug conjugates that can be activated by external stimuli to trigger intracellular and intratumoral drug penetration. Prof. Simon Benita (Hebrew University of Jerusalem) reported the development of new targeted nanoparticles toward the implementation of a combined drug and radioisotope delivery system for cancer therapy. Prof. Itai Benhar (Tel Aviv University) discussed the principles in the design for bispecific antibodies for human therapy.

Prof. Simon Benita receives the Outstanding Achievements in Controlled Release Prize from Prof. Ronit Satchi-Fainaro.

The second session, on "Targeting Stem Cells and Regenerative Medicine," included the presentations of Prof. Marcelle Machluf (Technion) on unique vesicles produced from the cell membrane of mesenchymal stem cells for drug delivery into solid tumors, Dr. Tal Dvir (Tel Aviv University) on delivering instructive cues and imaging biomolecules to 3D engineered tissues, and Dr. Boaz Tirosh (Hebrew University of Jerusalem) on unfolded protein response as a regulator of drug-induced liver injury.

Twelve short (five-minute) student oral presentations of selected posters from submitted abstracts concluded the first day's scientific program.

The second day of the meeting opened with a keynote lecture by Prof. Vladimir Torchilin, a distinguished professor and director at the Center for Pharmaceutical Biotechnology and Nanomedicine, Northeastern University, U.S.A., who described new opportunities in intracellular drug delivery with subsequent organelle targeting; he illustrated the specific targeting of lysosomes and mitochondria with multifunctional drug delivery systems.

The third session, on "Nano-Particulated Drug Delivery Systems," included the presentations of Prof. Chezy Barenholz (Hebrew University of Jerusalem) on PEGylated nanoliposomes for successful systemic treatment of animal models for rheumatoid arthritis, multiple sclerosis, cerebral malaria, and cancer. Prof. Alberto Gabizon (Shaarei Zedek) presented on a novel liposomal formulation coencapsulating alendronate and doxorubicin for cancer therapy, Prof. Dan Peer (Tel Aviv University) on gagomers as novel safe particle clusters for systemic delivery of therapeutic payloads, and Prof. Rimona Margalit (Tel Aviv University) on encapsulated drugs with or without biomaterial-based bioadhesive polymer to improve clinical outcomes in acute and chronic inflammations.

In the industrial session on "Industrial View on Controlled Release of Bioactive Materials," Dr. Aharon Schwartz, vice president of innovative ventures for Teva Pharmaceutical Industries, discussed the concept of targeted therapy versus personalized medicine. Gal Ehrlich (Ehrlich & Fenster, patent

[1] Ben-Gurion University, Israel.
[2] Tel Aviv University, Israel.

First place winner, sponsored by Teva Pharmaceuticals: Prof. Marcelle Machluf's student, Naama Furman, receives the award from Prof. Ronit Satchi-Fainaro, Dr. Ayelet David, and Teva's representative, Dr. Sigal Blau.

attorneys) discussed intellectual property strategy for drug development, and Dr. Noam Emanuel (PolyPid) described a novel lipid- and polymer-based drug delivery system with anti-infection activity.

The fourth session, on "Drug Delivery Issues in Infectious and Rare Diseases," included the presentations of Prof. Shula Michaeli (Bar-Ilan University) on the potential of two types of nanoparticles building on a core of silica (SiO_2) or CAN-maghemite (CAN-Fe_2O_3) functionalized with a thin layer of polyethyleneimine (PEI) for gene silencing in various cancer cells and trypanosome parasites. Prof. Yechiel Shai (Weizmann Institute of Science) presented on targeting and lysis of bacteria, fungi, and cancer by host-defense-like membrane active peptides and nanoparticle lipopeptides. Prof. Avi Domb (Hebrew University of Jerusalem) presented on crystallization and release of rapamycin from metallic stents, and Dr. Meital Reches (Hebrew University of Jerusalem) presented on self-assembly of biomolecular necklaces. Eight short student oral presentations of selected posters concluded the fourth session.

A fifth session, on "Selected Routes of Drug Administration," concluded the scientific program of second day. In this session Prof. Avri Rubinstein (Hebrew University of Jerusalem) described the mucosal targeting of biomarkers for real-time diagnostics of gastrointestinal malignancy by drug delivery tools. Prof. Yoav Livney (Technion) described quadrugnostic nanoparticles for cancer therapy. Prof. Gershon Golomb (Hebrew University of Jerusalem) demonstrated the effect of liposomal bisphosphonate formulation in inhibiting restenosis, and Dr. Sigal Blau (Teva) described recent results using gastric retentive oral dosage forms. Four short oral presentations of selected posters concluded the fifth session.

The sixth session on the third day was devoted to "Theranostic Nanotechnologies for Personalized Medicine." This session was opened with a keynote lecture by Prof. Rainer Haag (Institute of Chemistry and Biochemistry–Organic Chemistry, Frei University Berlin, Germany), who reviewed the use of dendritic polymers as highly functional polymeric supports for DNA and drug delivery mimicry of functional biomacromolecules and protein-resistant material surfaces. In this session Prof. Rachela Popovtzer (Bar-Ilan University) described gold nanoparticles as computed tomography imaging contrast agents, and Prof. Thomas L. Andresen (Technical University of Denmark) demonstrated liposome imaging agents for personalizing treatment with nanocarriers. Prof Eylon Yavin (Hebrew University of Jerusalem) described the use of peptide nucleic acids for detection of endogenous mRNA and noncoding RNA in living cancer cells for cancer diagnosis. Dr. Galia Blum (Hebrew University of Jerusalem) described the development of photodynamic quenched activity-based probes and nonquenched control probes for simultaneous detection and therapy of cancer.

The last session of this meeting addressed "Novel Biomolecular Self-Assembled Systems for Drug Delivery." In this session Dr. Niv Papo (Ben-Gurion University) described a protein engineering method to generate proteins with desired binding specificities and properties for applications in drug and gene delivery as well as in medical diagnostics. Yael Shaked (Dr. Golik) discussed the benefits of different characterization techniques for drug delivery application. Dr. Roey Amir (Tel Aviv University) described hybrid PEG-dendritic scaffolds as nanocarriers for drug and gene delivery, and Prof. Ehud Gazit (Tel Aviv University) concluded the meeting by discussing the mechanism of association and technological applications of self-assembled peptide nanostructures.

Prof. Simon Benita was awarded the ICRS Prize for Outstanding Achievements in Controlled Release, in recognition of his pioneering work in the field of targetable nanoparticulate drug carriers.

With the aid of the generous sponsorships, we awarded one Barenholz Prize to Hadas Skaat, whose work was selected from nine excellent applications submitted by Ph.D. students, and a total of six poster prizes (one first place sponsored by Teva

Invited speakers Prof. Ruth Duncan, Prof. Vladimir Torchilin, and Prof. Rainer Haag with the organizing committee

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Pharmaceuticals presented to Naama Furman; one second place sponsored by Dexcel Pharma presented to Shiran Ferber; three third places sponsored by Unipharm presented to Roni Azaguri, Nour Kara, and Yossi Kam; and one third place sponsored by Silicol presented to Galia Tiram), which were selected from 86 outstanding posters.

The social part, which included the everyday meals, cocktail hour, and gala dinner, were all a lot of fun, especially as all participants were so cooperative, Business Time Scanorama people were so efficient and kind throughout the whole process, the Hacienda Forestview Hotel and Conference facility were comfortable, and the food was superb!

We had a wonderful group of sponsors that helped to make this conference a success. Their contribution enabled a record number of students to register for the meeting. More details on the presentations can be found in the abstract book published in the ICRS website (www.icrs.org.il) under the Meeting 2012 link. ■

2012 CRS Italy Local Chapter Workshop

Prof. Gennara Cavallaro, University of Palermo, Italy

Paolo Caliceti, president of the CRS Italy Local Chapter, welcomes conference attendees.

The annual CRS Italy Local Chapter workshop "Biomaterials: From Drug Delivery to Tissue Engineering" was held in Palermo during November 8–10, 2012. The workshop was financed by CRS Italy Local Chapter and some industries, which allowed us to invite outstanding foreign scientists as well as to support the participation of young researchers.

Over the years, the annual workshop has become an important scientific event for the Italian pharmaceutical and drug delivery community. The number of participants was about 100 this year, and the multidisciplinary approach of the workshop attracted people from different disciplines, including clinicians and materials engineers.

Prof. Gennara Cavallaro (University of Palermo) opened the workshop by welcoming the participants. The chapter president, Prof. Paolo Caliceti (University of Padua), illustrated the upcoming international activities of CRS and the opportunities offered to CRS members. Attendees were warmly invited to join the annual international CRS meeting on "Emerging Challenges for Global Delivery" (Honolulu, Hawaii, U.S.A., July 21–24, 2013).

The workshop program started with "A General Strategy for the Obtainment of Biodegradable Microparticles with Ultrasound Contrast Agent and Drug Delivery Properties," delivered by Prof. G. Paradossi (University of Rome "Tor Vergata"). Dr. De Rosa (Federico II University of Naples) described bioactive physical chitosan-based gels for wound healing. Dr. Fiorica (University of Palermo) reported on hyaluronic acid-graft elastin-based scaffolds for potential tissue engineering applications. Then, in a relaxed atmosphere, a cocktail party was offered to welcome participants.

Prof. Sheila MacNeil (University of Sheffield) opened the first session of the second day concerning biomaterials from tissue engineering with an excellent invited lecture: "Developing Tissue Engineering Materials from the Lab to the Clinic to the Commercialization." Prof. Tanzi (University of Milan) reported on "Pectin and RGD-Grafted Pectin Microspheres for Cell Delivery and Tissue Regeneration." Afterward, a lecture on "Characterization of Processing-Induced Changes in Drugs Morphology" was delivered by Dr. Coletti (TA Instruments).

Dr. Benjamin Nottelet (University of Montpellier) opened the second session dedicated to biomedical applications of biomaterials with an invited talk focused on novel degradable copolyesters and their use for drug delivery and tissue engineering. Dr. Pietro Matricardi (University "Sapienza" of Rome) contributed to the session with a talk concerning polysaccharide nanohydrogels as drug delivery platforms, and Dr. Adriana Trapani contributed a talk on nanoparticles of chitosan and glycolchitosan for the systemic delivery of heparin. Dr. Santoliquido (Alfatest) presented an innovative technique for the separation and characterization of complex nanosystems.

The session concerning biomaterials for bone applications was opened by Prof. Benazzo (Policlinico of Pavia) with an excellent invited lecture concerning the state of the art and future needs of tissue engineering in orthopedic surgery. Dr. Dorati

(University of Pavia) contributed to the session with a talk concerning the combination of biomaterials with bovine bone substitute to guide bone regeneration, and Dr. Carmisciano (University of Palermo) contributed a talk concerning nonadherent clonogenic adipose-derived stem cells and their growth and differentiation within a bovine collagen scaffold.

The last session of the second day was opened by Dr. Bonzi (University if Padua), reporting the synthesis and characterization of a bone-targeting antitumor drug-polymer conjugate containing a cathepsin-sensitive spacer. Next, Dr. De Gioia reported on lung localization of aerosolised nanoparticles loading beclomethasone dipropionate for anti-inflammatory therapy. At the end of the session, Dr. Pluss (Buchi) presented a new apparatus to produce beads based on a spray dryer and encapsulator.

The day ended with a social dinner, a traditional event of all CRS workshops. This year it took place at Istituto Professionale di Stato per i Servizi di Enogastronomia e Ospitalità Alberghiera di Palermo "Pietro Piazza." During the dinner, the scientific and enogastronomic discussions were capably combined by participants, thanks to the excellence of the banquet prepared by the chef and students of the Istituto Professionale.

On the last day, Prof. MacNeil gave her second invited lecture concerning biomaterials and tissue engineering for wound healing. Then the modelling approach of drug delivery from swellable matrices was given by Prof. Lamberti (University of Salerno), and Dr. Franzè (University of Milan) presented on the role of the conformational profile of polysaccharides on skin penetration. The last talk of the session was given by Dr. Triolo (University of Palermo) concerning new amphiphilic copolymers based on polyhydroxyethylaspartamide for coated gold nanostars to be used as antimicrobial agents activated by NIR irradiation.

In the last session, Prof. Roberta Cavalli gave her contribution on nanosponges based on cyclodextrin used as antiviral agent delivery systems. Dr. Scaturro (University of Palermo) talked about a conjugate of dopamine-amino acid able to cross the blood-brain barrier, and Dr. Sutera reported the preclinical evaluation results and evaluation of animal behaviour effects of the same molecule. Next, Dr. D. E. Santis (Sigma Tau) gave her contribution on Avidinox-driven delivery of biotinylated cells. Finally, Dr. Battaglia (University of Turin) talked on solid lipid nanoparticles obtained through the coacervation technique, and Dr. Abadessa (University of Chieti) talked about some new derivatization of poly(D,L-lactide-*co*-glycolide) for protein delivery.

Attendees listen intently to a presentation.

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

Prof. Cavallaro's concluding remarks underlined once again the multidisciplinary nature of the workshop, which brought basic and applied research closer and highlighted the young scientists, either in chairing sessions or podium presentations and discussion.

Podium presentations of speakers who authorized the posting of their talks have been uploaded to www.itcrs.it/itcrs2 and www.unipa.it/giomo/crs. ■

What Does the Year 2050 Hold for Drug Delivery?

Share Your Thoughts with UKICRS

As part of a new initiative to promote scientific communication and creative thinking within the general arena of pharmaceutical sciences and drug delivery, the United Kingdom and Ireland Local Chapter of the Controlled Release Society (UKICRS, www.ukicrs.org) is holding an essay competition. Essays of up to 2,000 words are now invited that address the following general topic: "Fast Forward: Drug Delivery in the Year 2050." Entrants are encouraged to address the topic and the essay in whatever manner they see fit. For example, the technologies could be extrapolated from current systems or be entirely speculative. Essays must be submitted by May 15, 2013, using the online form (www.ukicrs.org/essay.php). The essay competition is open to all. The winning entry, as judged by a panel composed of UKICRS committee members, will be awarded a cash prize of £500, and the essay will be published in the 2013 edition of the *UKICRS Newsletter*. Full details are available at www.ukicrs.org/resources/Essay.jpg. ■

Drug Delivery and Translational Research

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

You may have noticed that *Drug Delivery and Translational Research* (*DDTR*), an official journal of CRS, has a new online look. The content platform has been rebuilt from the ground up. In addition to the new layout, the overhauled site features new functions designed to aid research discoverability, including a fast search with auto-suggest, a "Look Inside" feature (just like on Amazon), flexible search filters, and easy downloading. It has also been optimized for smart phones and tablets. Visit the new *DDTR* online today!

DDTR is growing and is poised to become one of the leading journals to cover advances in science and technology of delivering bioactives. Visit the *DDTR* website to glance through research articles, reviews, editorials, and special issues published in *DDTR*. CRS members get free access to the journal contents as a membership benefit. Members must login to the CRS website first and then click the Publications tab to get to the member access link.

V. Prasad Shastri (chair) of the University of Freiburg, Germany, and Elka Touitou (cochair) of the Hebrew University of Jerusalem, Israel, are heading the committee to select the 2012 *DDTR* Outstanding Research Paper Award recipient. The award will be presented during the 2013 CRS Annual Meeting, to be held July 21–24, 2013, in Honolulu, Hawaii, U.S.A. Join the leading scientists who are publishing their work in *DDTR* and compete for the 2013 *DDTR* Outstanding Research Paper Award.

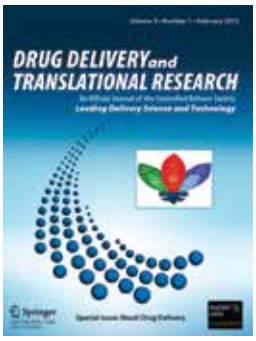
Editor's Pick (Vol. 2, Issue 6)

Evaluation of new bi-functional terpolymeric nanoparticles for simultaneous *in vivo* optical imaging and chemotherapy of breast cancer

Alireza Shalviri, Ping Cai, Andrew M. Rauth, Jeffery T. Henderson, and Xiao Yu Wu

In this paper, the authors have developed self-assembled bifunctional nanoparticles as nanotheranostics and evaluated their efficacy *in vivo* with a murine model of breast cancer using doxorubicin as a therapeutic agent. The bifunctional nanoparticles conjugated with both near-infrared dye, which helped evaluate biodistribution and tumor targeting efficiency of different formulations via imaging, and doxorubicin to achieve tumor growth inhibition.

Special Issue on Nasal Drug Delivery



For the first issue of 2013, guest editors Elka Touitou (Hebrew University of Jerusalem, Israel) and Lisbeth Illum (IDentity, Nottingham, United Kingdom) developed the theme issue covering various aspects of intranasal drug administration: factors involved in the design of a nasal drug product for actives of various physicochemical characteristics including small-molecular-weight drugs, peptides, proteins, nucleic acids, and vaccines; strategies used in overcoming low drug absorption from the nasal cavity; and an overview of existing nasal delivery devices and their pros and cons. Visit the *DDTR* website to read reviews, research articles, technological developments, and preclinical and clinical studies in this special issue on nasal drug delivery.

About the Guest Editors

Elka Touitou is a professor emeritus of pharmaceutical sciences at the School of Pharmacy, Hebrew University of Jerusalem, Israel. She is the head of the Dermal, Transdermal, and Transmucosal Drug Delivery Group. An internationally recognized authority in the field of drug delivery, she was a visiting professor at several universities in Europe and Asia and spent two full sabbatical years in the United States at Hofmann La Roche and American Cyanamid. Prof. Touitou has more than 200 scientific publications including research papers, reviews, book chapters, and the books *Enhancement in Drug Delivery* (2006) and *Novel Cosmetic Delivery Systems* (1999). She pioneered leading technologies in drug delivery, some of which evolved into startup companies. She served on the Board of CRS and was recently honored as a CRS Fellow. She received the Jorge Heller Outstanding Paper Award and the Kaye Award for

Innovation. Elka Touitou has broad experience in collaborating with the pharmaceutical industry in the design of new systems for efficient drug delivery. Her group is actively involved in the design and development of novel carriers for enhanced drug delivery for nasal, transdermal, and dermal administration.

Prof. Lisbeth Illum was the founder and for 12 years the managing director of DanBioSyst UK (sold in 1996), a company specializing in drug delivery systems. She was the managing director of Phaeton Research (sold in a management buyout in 2005) and through 2011 the CEO of Critical Pharmaceuticals. She is now director of IDentity (part of Eurocage Ltd.), a company specializing in pharmaceutical consultancy, patent litigation, and expert reports. She is associated with Nottingham University as a special professor. She received her M.Pharm, Ph.D, and D.Sc. from the Royal Danish School of Pharmacy in 1972, 1978, and 1988, respectively. Her research expertise covers novel drug delivery systems for difficult drugs such as polar small-molecular-weight compounds, peptides, and proteins. She has studied novel approaches to the delivery of such drugs using transmucosal routes. She has published about 350 scientific papers and is among the top 100 most cited scientists on pharmacology (*h*-index factor of 57). She coedited four books, filed nearly 50 patents on novel drug delivery systems, lectured around the world at conferences and workshops, has been elected a fellow of AAPS and CRS, and serves on the editorial boards of seven scientific journals. In 2008–2009, she was the president of CRS. ■

Make the Most of the CRS Website: Find the Science

One of the most important benefits of being a member of CRS is access to the cutting-edge science that is being produced by other members and top delivery scientists from around the world. The CRS website is your gateway to that research.

Be sure to log on to the CRS website to ensure your full access to *Drug Delivery and Translational Research* (*DDTR*). As a member, you automatically receive access to *DDTR*; visit www.controlledreleasesociety.org/publications/Pages/DDTRAccess.aspx for your member link to the journal. *DDTR* is CRS's journal exclusively focused on translational aspects of drug delivery. *DDTR* provides a unique forum for publication of high-quality research on topics such as designing and developing novel drug delivery systems, preclinical and clinical data related to drug delivery systems, short-term and long-term biocompatibility of drug delivery systems, host response, image-guided drug therapy, nanomedicine, and many others.

View the online webcasts, which are available to members only. Presentations cover a large variety of topics, from interspecies extrapolation to nanomedicine to blood-brain barrier issues and much more. These presentations include PowerPoint slides and voiceovers from the original presenters.

The *CRS Newsletter* archives give you access to past issues, including "Scientifically Speaking" articles. These are concise and informative articles detailing the science behind techniques, technological advances, or commercial products that are of relevance to delivery science. Read the "Patent Watch" articles for the latest innovations and "In the News" for news on product introductions, company announcements, collaborative study notifications, and much more.

View abstracts from past CRS Annual Meetings online as well, and see the science presented at each meeting. Visit "Meeting" and "Annual Meeting Archives" to access abstracts from 2010 to 2012.

Want to access the people behind the science? Try using LATTE (Linking Academic Technologies and Techniques to Everyone). This database provides a rapid mechanism to locate individual academic CRS members who are recognized experts in specific areas of CRS-related technologies and/or who use specific techniques in their research efforts and is based on fully searchable and standardized research profiles. Sign up today to find the science and the scientists you need.

Finally don't forget to search! The powerful search tool searches the entire site and will return web pages and PDFs containing your search term. The advanced search will allow you to narrow your search to the *CRS Newsletter*, webcasts, or meetings. Make the CRS website your primary tool to reach the top delivery science and technology. Be sure to log in to access it all! ■

CRS Bylaws Updated

In November 2012 the CRS Board decided to amend the bylaws and establish a Treasurer-Elect position, thereby reducing the number of Directors-At-Large by one person. In this way, candidates with skills tailor-made for the Treasurer position may be nominated and get Board training during the year as Treasurer-Elect before serving as Treasurer. Members were sent this information along with a copy of the bylaws showing tracked changes and were given the opportunity to ask questions and potentially file a petition. No petitions were received, and the bylaws are now in force as approved by the Board in December. You can find a copy of the bylaws online in the governance section of the CRS website. ■

Welcome New Members

Miriam Amiram
Hidetoshi Arima
Teresa Barata
Erica (Ying-Shan) Chen
Malay K. Das
Pilar De la Puente
Solmaz Dehghan
Jayant Venkatesh Deshpande
Per Djupesland
Yizhou Dong
Ryan Donnelly
Risako Fujita
Maneesh Gujrati
Eggehard Holler
Gregory L. Hunt
Jeong Eun Hye
Fatima Khaja
Aparajita Khatri
Gloria Kim
Arun Kumar Kotha
Kellin Krick
Tomoaki Kurosaki
Daniel Y. Lee
Ine Lentacker
Tonglei Li
Vladimir Malinin
Yu Mima
Katherine A. Moga
Simon E. Moulton
Kazuya Nagano
Miho Nishio
Shawn C. Owen
Apurva R. Patel
Andrew Phimister
Amalendu P. Ranjan
Gemma M. Ryan
Aliasger K. Salem
Richard Salzstein
Quazi T. H. Shubhra
Julie Wieland
Emma J. Wright
Xiaoyang Xu
Hong Zhang

CRS Leading Delivery Science and Technology

People in the News

Compiled by Steven Giannos, University of Maryland, Baltimore, MD, U.S.A.
Industrial Editor

CASIS Board Member Awarded National Medal of Science

January 14, 2013 – KENNEDY SPACE CENTER, FL, U.S.A. – Dr. Leroy Hood, a member of the Center for the Advancement of Science in Space (CASIS) board of directors, and president of the Institute for Systems Biology (ISB), will be one of 12 renowned researchers awarded the National Medal of Science by President Barack Obama in early 2013.

The National Medal of Science is one of the highest honors bestowed by the United States government upon scientists, engineers, and inventors. It was created by statute in 1959 and is administered for the White House by the National Science Foundation. Awarded annually, the medal recognizes individuals who have made outstanding contributions to science and engineering. A committee of presidential appointees selects nominees on the basis of their extraordinary knowledge in and contributions to chemistry, engineering, computing, mathematics, or the biological, behavioral/social, and physical sciences.

"We are honored to now have a National Medal of Science Award recipient as part of our team at CASIS," said CASIS Interim Executive Director Jim Royston. "Dr. Hood is extremely deserving of this recognition and is a true pioneer in biology and medicine."

In 2000, Dr. Hood cofounded ISB, a nonprofit research organization based in Seattle, Washington, that applies a cross-disciplinary approach to deciphering biological complexity. At ISB, scientists and engineers collaborate to discover the molecular basis of disease and pioneer analysis methods and technologies that are revolutionizing the field. Dr. Hood has cofounded more than 14 biotechnology companies, including Amgen, Applied Biosystems, Darwin, Accelerator Corp., and Integrated Diagnostics.

In addition to his most recent accolade, Dr. Hood has received numerous other professional awards throughout his career, including the Lasker Award for Studies of Immune Diversity, the Kyoto Prize in Advanced Technology, the Heinz Award for pioneering work in systems biology, and the coveted National Academy of Engineering Fritz J. and Delores H. Russ Prize in 2011 for automating DNA sequencing—an advancement that revolutionized genomics.

InVivo Therapeutics Cofounder Robert S. Langer to be Awarded National Medal of Technology and Innovation by President Barack Obama at the White House in Early 2013

Business Wire: January 3, 2013 – CAMBRIDGE, MA, U.S.A. – InVivo Therapeutics Holdings Corp. (NVIV), a developer of groundbreaking technologies for the treatment of spinal cord injuries (SCI) and other neurotrauma conditions, today congratulates Robert S. Langer, Sc.D., InVivo cofounder and member of the company's scientific advisory board, on receiving the National Medal of Technology and Innovation. President Barack Obama will present the award to Dr. Langer, who also won the National Medal of Science in 2006, at a White House ceremony in early 2013.

Dr. Langer, the David H. Koch Institute Professor at the Massachusetts Institute of Technology (MIT), is among 23 renowned researchers who have been awarded the nation's highest honors for scientists, engineers, and inventors this year. With this award, he joins the ranks of five engineers and inventors from MIT who have earned the same honor and becomes one of three Americans to have won both the National Medal of Science and the National Medal of Technology and Innovation.

"The impact of Bob's biomaterials research and drug/cell delivery innovations are enormous, and his discoveries have now led to over 55 products either currently in clinical trials or already approved by the FDA," said InVivo chief executive officer Frank Reynolds. "The range of Bob's humanitarian impact is only exceeded by his dedication to help people with 'tough to solve' unmet medical needs. InVivo is fortunate to benefit from many of his patents, and as we look forward to beginning clinical studies in early 2013, our team couldn't be happier to see Bob recognized by President Obama for his major contributions to the worlds of biomaterials, tissue engineering, tissue regeneration, and drug delivery."

For more on the National Medal of Technology and Innovation, please visit www.whitehouse.gov/the-press-office/2012/12/21/president-obama-honors-nation-s-top-scientists-and-innovators. ■

In the News

Compiled by Steven Giannos, University of Maryland, Baltimore, MD, U.S.A.
Industrial Editor

January

Pfizer Announces Availability of Quillivant XR™ (Methylphenidate Hydrochloride) CII for Extended-Release Oral Suspension in the United States

Business Wire: January 14, 2013 – NEW YORK, NY, U.S.A. – Pfizer Inc. (NYSE: PFE) today announced that Quillivant XR™ (methylphenidate hydrochloride) CII for extended-release oral suspension is now available in the United States for the treatment of attention deficit hyperactivity disorder (ADHD). Quillivant XR is the first once-daily, extended-release liquid methylphenidate for ADHD and is now available by prescription.

"In order to effectively treat patients with chronic conditions such as ADHD, it is important to consider individual patient needs, including options for medication administration," said Ann Childress, M.D., president of the Center for Psychiatry and Behavioral Medicine, Las Vegas, who was an investigator in the Quillivant XR laboratory classroom study. "As the first once-daily, extended-release liquid medication for patients with ADHD, Quillivant XR represents a new alternative to other ADHD treatments."

Quillivant XR was approved by the U.S. Food and Drug Administration (FDA) on September 27, 2012 for the treatment of ADHD in patients aged 6 years and above. The efficacy of Quillivant XR was evaluated in a randomized, double-blind, placebo-controlled, crossover, multicenter, laboratory classroom study of 45 children with ADHD. Quillivant XR significantly improved ADHD symptoms compared to placebo at the primary endpoint of four hours post-dose, and in a secondary analysis, showed significant improvement at every time point measured, from 45 minutes to 12 hours after dosing.

ADHD is one of the most common neurobehavioral disorders in the United States. According to the Centers for Disease Control and Prevention's 2007 data, about one in ten children aged 4 to 17 in the United States had at any time in their life received a diagnosis of ADHD. Patients with ADHD may suffer from symptoms such as difficulty paying attention, impulsivity, and being overly active in some cases. The condition can last into adulthood. Although there are many treatment options for ADHD, until Quillivant XR there was no once-daily, extended-release liquid option for the treatment of this condition.

"Pfizer is pleased to provide patients and their caregivers with a new option to help manage this challenging condition," said Sam Azoulay, M.D., senior vice president of medical and development for Pfizer's Emerging Markets and Established Products Business Units. "We also recognize that caring for and treating a child with ADHD goes beyond medication. We look forward to working with mothers and other caregivers of children with ADHD to provide meaningful resources to the ADHD community."

Pfizer acquired NextWave Pharmaceuticals on November 27, 2012. Quillivant XR was developed in conjunction with NextWave's manufacturing partner, Tris Pharma, using Tris Pharma's patent-protected drug delivery platform. For more information, please visit www.quillivantxr.com.

BIND Biosciences and Amgen Sign Agreement for the Worldwide Development and Commercialization of a Kinase Inhibitor Nanomedicine

Business Wire: January 8, 2013 – CAMBRIDGE, MA, U.S.A. – BIND Biosciences, a clinical-stage biopharmaceutical company developing a new class of highly selective targeted and programmable therapeutics called Accurins™, announced today that it has entered into a global collaboration agreement with Amgen Inc. to develop and commercialize a kinase inhibitor nanomedicine for treating a range of solid tumors. The collaboration will develop a novel Accurin based on BIND's platform for targeted and programmable nanomedicines and Amgen's undisclosed proprietary kinase inhibitor. The collaboration aims to create a kinase inhibitor nanomedicine with optimized therapeutic properties, applying for the first time tissue targeting to molecularly targeted drugs.

Under the terms of the agreement, Amgen will have the exclusive right to pursue development and commercialization of the Accurin kinase inhibitor against solid tumor targets to be selected by Amgen. Both companies will work together on preclinical development, and Amgen will assume responsibility for future development and commercialization. BIND could receive up-front and development milestone payments totaling $46.5 million, and BIND could receive up to an additional $134 million in regulatory and sales milestone payments for the first therapeutic indication and is eligible for additional payments. BIND will receive tiered royalties on potential future sales. "BIND's technology is well aligned with Amgen's focus on the development of highly targeted and selective oncology

therapeutics," said Joseph P. Miletich, M.D., Ph.D., senior vice president of research and development at Amgen. "We look forward to collaborating with the BIND scientific team to leverage this technology to address unmet medical needs of cancer patients."

"We are pleased to collaborate with Amgen, an industry leader with a proven track record of success in oncology, on extending our technology into molecularly targeted drugs, such as kinase inhibitors," said Scott Minick, CEO of BIND. "Through this collaboration, Amgen has recognized the unique potential of BIND's Medicinal Nanoengineering platform to create programmable oncology therapeutics that combine molecular and tissue targeting for unsurpassed selectivity and activity."

BIND Biosciences is a clinical-stage biopharmaceutical company developing a new class of highly selective targeted and programmable therapeutics called Accurins™. BIND's Medicinal Nanoengineering® platform enables the design, engineering and manufacturing of Accurins with unprecedented control over drug properties to maximize trafficking to disease sites, dramatically enhancing efficacy while minimizing toxicities.

BIND is developing a pipeline of novel Accurins that hold extraordinary potential to become best-in-class drugs and improve patient outcomes in the areas of oncology, inflammatory diseases, and cardiovascular disorders. BIND's lead product candidate, BIND-014, is currently in phase 1 clinical testing in cancer patients and is designed to selectively target a surface protein upregulated in a broad range of solid tumors. BIND also develops Accurins in collaboration with pharmaceutical and biotechnology partners to enable promising pipeline candidates to achieve their full potential and to utilize selective targeting to transform the performance of important existing drug products.

BIND is backed by leading investors, Polaris Venture Partners, Flagship Ventures, ARCH Venture Partners, NanoDimension, DHK Investments, EndeavourVision, and Rusnano. BIND was founded on proprietary technology from the laboratories of two leaders in the field of nanomedicine: Professors Robert Langer, David H. Koch Institute Professor of the Massachusetts Institute of Technology (MIT), and Omid Farokhzad, Associate Professor of Harvard Medical School. For more information, please visit the company's web site at www.bindbio.com.

Fuisz Announces a New Lozenge Product to Enhance E-cigarette Tobacco Satisfaction as well as THC Delivery from Medical Marijuana

PRNewswire: January 8, 2013 – MIAMI, FL, U.S.A. – Fuisz LLC today announced that it will launch a new oral pre-product in the form of a lozenge in early 2013 designed to enhance tobacco satisfaction from electronic cigarettes, as well as to enhance THC absorption from medical marijuana. The product is protected by a patent pending.

Joseph Fuisz, managing member of Fuisz, commented, "The extraordinary growth in electronic cigarette consumption at the expense of conventional cigarettes is perceived as large net positive for public health. However, the e-cigarette industry is still struggling to enhance tobacco satisfaction from what is essentially a buccal delivery product. That means that nicotine absorption is occurring across the oral mucosa in the mouth as opposed to the lung. As a result, the nicotine levels delivered by an e-cigarette are much lower (C_{max}) and slower to build (T_{max}) than the nicotine levels delivered by a traditional cigarette. Our new oral dosage unit contains a number of agents designed to enhance the speed and level of tobacco satisfaction from the electronic cigarette. Best of all, the product works dramatically."

Mr. Joseph Fuisz continued: "Our lozenge product itself contains no tobacco, nicotine, or other active drug ingredient. We intend to market our product under our own trade name—to be announced—through conventional retail channels."

Dr. Richard Fuisz, Fuisz founder, remarked: "We have invented and developed an oral pre-product which is easy and pleasant to use, and enhances delivery for medical marijuana users who vaporize their material. The user simply uses the pre-product while vaporizing the medical marijuana. Consistent with the macro trend in pharmaceutical drug delivery toward more effective smaller dosing, this advance allows for lower dosing with the same medicinal effect from a lesser amount of vaporized THC. The growth of medical marijuana, and in particular the growth of vaporization of medical marijuana, has been recognized by global authorities including Health Canada to result in a smaller toxicant profile than the conventional smoking of marijuana, and hence the need to maximize its efficiency."

Fuisz LLC is a private technology company originated by the Fuiszes. The Fuiszes have made substantial contributions in drug delivery including orally dissolving tablets and novel particle coating systems at Fuisz Technologies; inventing and developing thin film drug delivery technologies at Kosmos Pharma and MonoSol Rx; as well as independently developing extruded sheet technology and diagnostic applications. Fuisz has extensive experience working with big and specialty pharma, as well as large consumer products companies. Fuisz has its headquarters in Miami. www.fuisz.com

Dr. Robert S. Langer Joins HealthCare Royalty Partners Strategic Advisory Board

PRNewswire: January 4, 2013 – STAMFORD, CT, U.S.A. – HealthCare Royalty Partners ("HC Royalty"), a global healthcare investment firm, today announced that Dr. Robert S. Langer, Institute Professor and founder of the Langer Lab at the Massachusetts Institute of Technology, has joined its Strategic Advisory Board.

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"Dr. Langer's lab at MIT has been at the front lines of turning discoveries into a range of drugs and drug delivery systems. We are honored to have him serve as one of our advisors," commented Todd Davis, founding managing director at HC Royalty.

Dr. Langer served as a member of the U.S. Food and Drug Administration's SCIENCE Board, the FDA's highest advisory board, from 1995 to 2002 and as its chairman from 1999 to 2002. He has helped start 25 companies, and more than 250 pharmaceutical, chemical, biotechnology, and medical device companies have licensed or sublicensed Langer Lab patents. Over the course of his tenured career, Dr. Langer has received over 210 major awards including the 2013 Wolf Prize in Chemistry, which is considered Israel's Nobel Prize, and the U.S. National Medal of Technology and Innovation.

"HC Royalty has played a critical role to bring new and differentiated products to market, and I look forward to working with the senior team to evaluate many more promising discoveries," stated Dr. Langer.

HealthCare Royalty Partners is a global healthcare investment firm focused on providing financing solutions to healthcare companies and royalty owners with interests in approved pharmaceutical and medical device products. The firm's senior investment team has participated in 45 royalty financings valued at over $2 billion over the past decade. For more information, visit www.healthcareroyalty.com.

Impax Laboratories Launches Oxymorphone Hydrochloride Extended-Release Tablets

Business Wire: January 4, 2013 – Hayward, CA, U.S.A. – Impax Laboratories, Inc. (NASDAQ: IPXL) today announced that it is commencing shipment of oxymorphone hydrochloride extended-release tablets, through Global Pharmaceuticals, Impax's generics division.

In June 2010, Impax reached agreement with Endo Pharmaceuticals and Penwest Pharmaceuticals (collectively Endo) to settle U.S. patent litigation with regard to the production and sale of its oxymorphone hydrochloride extended-release tablets approved by the U.S. Food and Drug Administration (FDA) as therapeutically equivalent to the original formulation of OPANA® ER. Under the terms of the settlement, Endo agreed to grant Impax a license to sell Impax's approved product on January 1, 2013.

As a company whose mission is to provide high quality, lower-cost prescription drugs, Impax is actively participating in efforts to support prescriber and patient education of this product through the FDA-approved risk evaluation and mitigation strategy (REMS).

Oxymorphone hydrochloride extended-release tablets are indicated for the relief of moderate to severe pain in patients requiring continuous, around-the-clock opioid treatment for an extended period of time.

Icon's Melphalan Intraocular Injection Granted U.S. Orphan Drug Designation for the Treatment of Retinoblastoma

PRNewswire: January 3, 2013 – SUNNYVALE, CA, U.S.A. – Icon Bioscience, Inc. (IBI), a privately held biopharmaceutical company that specializes in the development and commercialization of novel ophthalmic pharmaceuticals, today announced that melphalan intraocular injection, the company's investigational product for the treatment of retinoblastoma, has been granted orphan drug designation by the U.S. Food & Drug Administration (FDA).

Orphan drug designation is generally granted to drugs or biologics intended for treatment of rare diseases and disorders, i.e., those affecting fewer than 200,000 people in the United States. This designation conveys special incentives to the sponsor, including tax credit for fifty percent of the cost of clinical trials, prescription drug user fee waiver, and seven years of U.S. market exclusivity for the drug or biologic upon FDA approval.

Icon's melphalan intraocular injection is formulated using its proprietary Verisome® drug delivery technology. It is designed to safely deliver therapeutic levels of the drug for an extended period of time using a single intravitreal injection.

The Verisome® drug delivery technology was invented by the founder of Icon Bioscience, Inc., Vernon G. Wong, M.D. The technology encompasses over 20 related, but distinct, novel and proprietary drug delivery systems. Highly versatile, it is capable of incorporating a broad range of active agents including small molecules, proteins, and monoclonal antibodies and can deliver drugs in a controlled release manner for up to a year with a single injection.

Icon Bioscience, Inc. (IBI), is a privately held biopharmaceutical company that specializes in the development and commercialization of novel ophthalmic pharmaceuticals based on its Verisome® drug delivery platform technology. IBI is developing a broad portfolio of clinically superior specialty pharmaceuticals targeting all major ophthalmic indications including macular edema, glaucoma, age-related macular degeneration, and cataract surgery. IBI has also entered into agreements with multiple international pharmaceutical companies interested in the use of the Verisome® technology for their own ophthalmic products. For more information, please refer to www.iconbioscience.com.

December

NovaDel Announces Preliminary Agreement to Sell Its NovaMist™ Technology

Business Wire: December 26, 2012 – BRIDGEWATER, NJ, U.S.A. – NovaDel Pharma Inc. (NVDL.PK) has signed a preliminary agreement to sell its NovaMist™ technology to Suda Ltd., an Australian publicly held pharmaceutical company.

The proposed transaction includes the sale of NovaDel's patents and trademarks relating to its NovaMist technology. The sale, as contemplated, does not include the NitroMist® or ZolpiMist™ intellectual property or licenses.

The commercial terms of the preliminary agreement are subject to confidentiality at this time and subject to satisfactory completion of due diligence by both parties, as well as the execution of a definitive agreement and subject to NovaDel board and stockholder approval, if required.

Suda Ltd. is listed on the Australian Securities Exchange (ASX) and is engaged in developing and marketing pharmaceutical products. Its principal activity is the development of a sublingual aerosol and pump formulation of artemisinin derivatives for the treatment of malaria. ArTiMist™, its artemisinin product, is administered sublingually and enters the bloodstream where the parasite lives, attacking at a far greater speed than conventional tablets and reducing the need for continued hospitalization while presenting significant cost savings to governments and relief organizations. ArTiMist is particularly effective in the treatment of children and young infants who are experiencing malaria-related and gastro-intestinal problems and cannot tolerate tablet treatments. The company has completed the required phase 3 trials for this product and is expected to release the final trial report within the next 30 days.

Halozyme Therapeutics and Pfizer Enter into a Collaboration to Develop and Commercialize Subcutaneous Biologics Using Recombinant Human Hyaluronidase

PRNewswire: December 21, 2012 – SAN DIEGO, CA, U.S.A. – Halozyme Therapeutics, Inc. (NASDAQ: HALO) announced today that it has entered into a worldwide collaboration and license agreement with Pfizer Inc. (NYSE: PFE) for the purpose of developing and commercializing products combining proprietary Pfizer biologics with Halozyme's Enhanze™ technology. Enhanze is Halozyme's proprietary drug delivery platform and is based on the company's patented recombinant human hyaluronidase enzyme (rHuPH20).

Under the terms of the agreement, Halozyme has granted to Pfizer a worldwide license to develop and commercialize products combining rHuPH20 with Pfizer proprietary biologics directed to up to six targets. Targets may be selected on an exclusive or nonexclusive basis. Halozyme will receive an initial payment of $8 million, which includes the upfront fee for exclusive licenses to two specified therapeutic targets in primary care and specialty care indications and the right for Pfizer to elect up to four additional targets upon payment of additional fees.

"I am delighted about this opportunity as it has the potential to enhance Pfizer's ability to optimize treatments for patients," said Jose Carlos Gutierrez-Ramos, Senior Vice President, Pfizer BioTherapeutics R&D.

Halozyme is eligible to receive additional payments upon Pfizer's achievement of specified development, regulatory, and sales-based milestones, totaling up to $507 million. Halozyme is also entitled to royalty payments based on net sales of any licensed products.

"We look forward to working with Pfizer to apply Enhanze to these exciting targets," said Gregory I. Frost, Ph.D., President and Chief Executive Officer, Halozyme. "Enhanze enables biologics to be delivered as a simple subcutaneous injection."

International Collaborative Funds Three Early-Stage Pediatric Medical Device Concepts

PRNewswire: December 20, 2012 – CINCINNATI, OH, U.S.A. – A recently launched collaborative led by Cincinnati Children's Hospital Medical Center (CCHMC) and Ben-Gurion University of the Negev (BGU) is funding the research and development of three pediatric-specific medical devices.

The collaboration, which pairs the medical expertise of CCHMC physicians with the technical and engineering capabilities of BGU, started with nearly 80 unaddressed problems facing surgeons and physicians. After reviewing these ideas and proposed solutions, 10 projects went through rigorous application cycles, thorough market analyses and review by internal and external stakeholders.

The initial three projects that will be funded have potential to not only improve patient care and outcomes but also reduce costs to the healthcare system.

"The pediatric market, especially with regard to medical devices, has historically been neglected primarily due to prohibitive development costs," said Niki Robinson, assistant vice president of CCHMC's Center for Technology Commercialization. "This

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initiative presents an unprecedented opportunity for early stage ideas to receive funding and move through a development plan backed by world-class physicians and engineers."

The three approved projects include a smart sensing catheter, a surfactant delivery device, and an image-guided needle insertion device. Each project is being led by a CCHMC clinician or surgeon and a BGU engineer.

The smart sensing catheter concept was developed by Richard Azizkhan, M.D., surgeon-in-chief at CCHMC and the Lester W. Martin Chair of Pediatric Surgery, and Ibrahim Abdulhalim, professor of electro-optical engineering at BGU. The device provides immediate and continuous assessment of the metabolic and physiological profile of critically ill infants and small children. "Secondarily, this technology will reduce the need for repeated tests, thus reducing costs for the health system and society," said Azizkhan. Because catheter utilization is so widespread, this technology has the potential for broader application in the adult market.

The surfactant delivery device concept was developed by Jeffrey Whitsett, M.D., codirector, Perinatal Institute and chief, Section of Neonatology, Perinatal and Pulmonary Biology at Cincinnati Children's, and Joseph Kost, Dean of the Faculty of Engineering Sciences and professor of biomedical engineering at BGU. It consists of a delivery system for prolonged administration of surfactants to the lungs of premature babies using nanoparticles. Current procedures do not allow for the sustained release of proteins or other complex particles in the alveoli of infants or adults. This technology would do that with the potential to deliver numerous therapies to the lower airway through a noninflammatory delivery system.

Daniel von Allmen, M.D., director, Division of General and Thoracic Surgery at CCHMC, and Hugo Guterman, professor of electrical and computer engineering at BGU, are collaborating on the image-guided needle insertion device concept. It combines sophisticated new imaging techniques with the precision of robotics to improve the accuracy of many procedures currently done in medicine. "The device substantially improves the accuracy for a number of invasive procedures while decreasing the level of necessary expertise and therefore costs associated with current practice," von Allmen said. While initially targeting the pediatric market, this technology represents potential for the adult market as well.

Each project will receive up to $100,000 in the first round, with all funding contingent upon achieving project-specific developmental milestones.

Speaking to the value of early stage investment in research, von Allmen said, "One of the enormous struggles for physicians, many of whom are very experienced in their fields and knowledgeable about challenges to care, is the ability to get an idea from the back of a napkin in the cafeteria to a coordinated development effort. Cincinnati Children's has put a lot of resources into creating the infrastructure to make the translation of good ideas to products a reality."

The CCHMC-BGU collaborative will seek new ideas and solutions for pediatric-specific medical devices from experts at both institutions for its next round of funding starting in January 2013.

The initiative is managed by CCHMC's Center for Technology Commercialization and BGU's technology commercialization company, BGN Technologies, Ltd. This collaboration is one of several that CCHMC has in Israel through its Israel Exchange Program. Cincinnati-based seed-stage investor CincyTech and Israel-based Ridgeback Business Development, Ltd., helped evaluate the projects.

Radius, 3M Drug Delivery Systems Announce Exclusive Agreement for Development, Commercialization of Transdermal Delivery of BA058 for Osteoporosis

Business Wire: December 20, 2012 – CAMBRIDGE, MA, U.S.A. – Radius Health, Inc. ("Radius") and 3M Drug Delivery Systems are pleased to announce an exclusive partnership agreement for development and commercialization of BA058-transdermal (TD). BA058 is a novel, synthetic proprietary peptide analog of human parathyroid hormone related protein or "hPTHrP," a bone building anabolic compound with the potential to treat patients with osteoporosis at high risk of fracture. This agreement updates the general development agreement announced in May 2011 by the two companies for BA058-TD.

"With this exclusive agreement, 3M and Radius demonstrate our commitment to this innovative therapeutic treatment and this unique drug delivery mechanism. We believe this new drug potentially will improve the health of patients with severe osteoporosis and that 3M's microneedle patch technology may improve medication compliance among patients."

BA058-transdermal (TD) is being studied in a phase 2 clinical trial in healthy postmenopausal women with osteoporosis at 10 clinical centers. BA058-TD is a short-wear time patch based on 3M's patented Microstructured Transdermal System technology. The transdermal patch is expected to combine ease of use, convenience, and self-administration attributes of a patch with the bone building efficacy of the BA058 compound.

"We are excited that 3M Drug Delivery Systems, which has long demonstrated a commitment to quality, safety, and innovation, is partnering with us to bring a novel approach of drug delivery to the underserved osteoporosis patient population," said Michael Wyzga, Radius president and chief executive officer. "Our study data for BA058-TD showed that a five-minute wear time of the patch delivers peak drug levels consistent with subcutaneous injection, and we hope to see increased patient compliance with 3M's innovative technology."

"We are pleased to be part of Radius' mission of advancing therapeutics for healthy aging with its deep expertise in osteoporosis," said Ingrid Blair, MTS/TDD business vice president of 3M Drug Delivery Systems. "With this exclusive agreement, 3M and Radius demonstrate our commitment to this innovative therapeutic treatment and this unique drug delivery mechanism. We believe this new drug potentially will improve the health of patients with severe osteoporosis and that 3M's microneedle patch technology may improve medication compliance among patients."

BA058 is also being studied as a daily subcutaneous injection (BA058-SC) in a phase 3 study with 2,400 patients for fracture prevention in women with postmenopausal osteoporosis at high risk of fracture. Phase 2 human testing of the injectable BA058-SC showed that BA058 significantly increased bone mineral density (BMD) at the lumbar spine and femoral neck (a common osteoporotic fracture site located in the hip joint) after six months of therapy.

Atlantic Pharmaceuticals, Inc., Announces Two Patent Issuances for Its Tamper-Resistant Pharmaceutical Platform

PRNewswire: December 20, 2012 – ATLANTA, GA, U.S.A. – Atlantic Pharmaceuticals, Inc., a specialty pharmaceutical company, today announced that new patents have been issued by the U.S. Patent and Trademark Office (USPTO) relating to its tamper-resistant SMART/Script™ drug delivery platform. U.S. Patent Nos. 8,187,636 and 8,349,362 contain claims that cover Atlantic's proprietary tamper-resistant platform, which is designed to resist dose dumping of orally delivered opioids and may sequester and reduce drug release of a drug that has been subjected to a variety of physical methods of tampering. The technology can be applied to immediate as well as sustained release drug candidates.

"We believe SMART/Script™ is a unique technology that may have a significant effect on prescription drug abuse and misuse," said Anthony Soscia, president of Atlantic Pharmaceuticals. "These patents further add to our intellectual property portfolio and provide us with extensive coverage until 2028 for our novel, tamper-resistant technology."

SMART/Script™ (SMART, simple, controllable, resistant, insoluble, physical trap), a novel, patented drug delivery platform, was designed to prevent easy drug extraction and to deter the abuse of medications via known routes of abuse, including chewing, snorting, and injecting. Orally delivered tamper-prone pharmaceuticals are frequently subjected to abuse and misuse via chewing and swallowing or crushing and either snorting or injecting the resultant powdered drug. A product formulated with SMART/Script™, however, resists dose dumping in water or alcohol and can be used with a broad range of opioids and nonopioids in immediate or extended release forms. SMART/Script™ is also unique among competitive technologies in that physical tampering of the dosage form may reduce the release rate of the drug from the dosage when subject to certain forms of physical tampering as opposed to increasing it.

Atlantic Pharmaceuticals is a specialty pharmaceutical company using its patented technology to produce novel therapeutics that resist attempts at tampering and may be useful to reduce abuse of certain prescription drugs. Based on the company's proprietary technology, SMART/Script™, Atlantic is developing a pipeline of tamper-resistant opioids that are nearing pivotal testing.

The company's lead SMART/Script™ candidate, ATLP-02, is an immediate release formulation of oxycodone that is in development and will be covered by the issued patents. In addition, these patents will also cover other product candidates being formulated using the SMART/Script™ technology. The company finalized a Pre-Investigational New Drug Meeting with the FDA in March of 2011 for ATLP-02. SMART/Script™ has also been recognized as a leading technology that may potentially decrease tampering with medication by the Center for Lawful Access and Abuse Deterrence. Please visit atlanticpharma.com for more information.

Fuisz Pharma Completes Sale of New Buccal Film Patent to MonoSol Rx

PRNewswire: December 20, 2012 – MIAMI, FL, U.S.A. – Fuisz Pharma announced today that it has closed a transaction with MonoSol Rx whereby MonoSol Rx has acquired all rights for U.S. Patent 8,241,661 and its foreign counterparts. The terms of the sale were not disclosed.

Joseph Fuisz Esq., managing member for Fuisz Pharma, explained, "We are pleased to have quickly completed this transaction after a closed bidding process. We are particularly

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excited that the '661 patent has been acquired by MonoSol Rx. The '661 patent will complement our earlier patent filings for drug containing films, made together with other inventors for Kosmos Pharma, that were similarly acquired by MonoSol Rx and subsequently matured into a robust set of issuances."

Mr. Fuisz continued, "The MonoSol Rx patent estate has achieved a dominant position over an entire dosage form class—orally soluble films. In contrast, the patent estates in orally dissolvable tablets only protected product approaches that were ultimately substitutable in large part. As a result, we believe that MonoSol Rx is the best steward for the '661."

Richard C. Fuisz, M.D., founding member for Fuisz Pharma, commented, "We are pleased to close this transaction with MonoSol Rx and look forward to announcing additional completed transactions this coming year."

Antares Pharma Announces Submission of New Drug Application for OTREXUP™

Business Wire: December 17, 2012 – EWING, NJ, U.S.A. – Antares Pharma, Inc. (NASDAQ: ATRS) today announced the submission of a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) for OTREXUP™, a combination product for the delivery of methotrexate (MTX) using Medi-Jet™ technology. OTREXUP was developed for easy subcutaneous administration of MTX to enhance the treatment of rheumatoid arthritis (RA), poly-articular-course juvenile RA, and moderate to severe psoriasis.

"The NDA submission of OTREXUP represents yet another significant accomplishment in the company's history," said Paul K. Wotton, Ph.D., president and chief executive officer. "It is the first product designed for convenient subcutaneous delivery of methotrexate in patients with rheumatoid arthritis or psoriasis. We believe OTREXUP will benefit most patients that have not reached a satisfactory response to oral methotrexate alone or in combination with a biologic or another disease-modifying anti-rheumatic drug."

OTREXUP was developed to optimize the clinical benefit of MTX, leading to cost effective treatment outcomes. Historically, parenteral MTX use has been limited in clinical practice for several reasons including the inconvenience of weekly intramuscular injections by a healthcare professional and/or the challenges associated with teaching patients with impaired hand function safe and sterile self-injection techniques. Studies conducted to date indicate OTREXUP is safe, easy, and comfortable for RA patients to self-administer precise subcutaneous doses of MTX with improved systemic availability compared to oral doses.

The NDA submission, subject to acceptance and approval by the FDA, was supported by data generated from a clinical development program completed in accordance with the FDA's guidance and recommendations. Antares executed and completed all of the clinical studies agreed with the agency and described in the clinical development program.

"The dedicated efforts of the entire Antares team have allowed us to submit a New Drug Application to the FDA ahead of schedule," said Kaushik J. Dave R.Ph., Ph.D., Executive Vice President Product Development. "The results from the clinical development program have shown that OTREXUP can provide greater systemic exposure to methotrexate compared to oral doses. We believe OTREXUP is easy to use and comfortable for RA patients with moderate to severe hand function impairment, thereby enhancing self-administration and patient compliance."

Aphios Granted U.S. Patent for Oral Delivery of Insulin

Business Wire: December 17, 2012 – WOBURN, MA, U.S.A. – Aphios Corporation today announced that it received notification of allowance for a U.S. Patent entitled "Polymer Microspheres/Nanospheres and Encapsulating Therapeutic Proteins Therein" for the oral delivery of insulin.

With completion of the human genome sequence, the growth of the biotechnology marketplace is expanding rapidly. One of the major factors limiting the marketability and industrialization of biotechnology drugs is the method of delivery. These macromolecules are usually very effective when they can get to the disease site. They are also, for the most part, nontoxic since they mostly mimic human proteins. Unfortunately, these molecules, like insulin, are quite large and are most readily delivered by daily injections or intravenously in a hospital setting. These macromolecules are all candidates for improved oral, patch, and pulmonary drug delivery.

"Aphios is enhancing the oral bioavailability of therapeutic proteins by encapsulating protein macromolecules and nanoparticles in biodegradable polymer nanospheres," says Dr. Trevor P. Castor, President & CEO, Aphios Corporation. Nanoencapsulation is being used to protect the protein macromolecules/nanoparticles during the stomach passage; the residence time in the stomach will be short compared to the protein release rate from the polymer nanospheres. Animal data demonstrates that insulin, a labile peptide, being nanoencapsulated was protected in the stomach and then transported to the blood. When protein nanoparticles reach the gut, they are transported across the lining, which may be mediated by M cells in the lymphatic tissue of the gut. Alternatively, the protein can be mobilized from nanospheres and rapidly transported to systemic circulation by the epithelial cells. Both the polymer "shell" and the protein macromolecules/nanoparticles are intended to enable and regulate this stage of

drug transport. With the optimal combination of the biodegradable polymer nanospheres shell properties and protein characteristics, we anticipate a significant improvement in oral bioavailability of protein therapeutics. We believe that our oral delivery nanotechnology will be applicable to large as well small protein molecules since we have demonstrated that our protein nanoparticles technology is independent of size and molecular weight (MW).

Aphios® Corporation (www.aphios.com), Woburn, Massachusetts, is a clinical stage biotechnology company developing green, enabling technology platforms for improved drug discovery and manufacturing, nanotechnology drug delivery and pathogenic drug safety. Based on these platforms, Aphios is developing enhanced therapeutic products for health maintenance, disease prevention, and the treatment of certain cancers, infectious diseases, and central nervous system disorders, such as Alzheimer's disease.

November

NanoSmart® Pharmaceuticals to Present as Top Innovator Company at New England Venture Summit, December 5

NanoSmart® Pharmaceuticals: November 30, 2012 – LAGUNA HILLS, CA, U.S.A. – Dr. James Smith, President of NanoSmart Pharmaceuticals, has been selected as a Top Innovator to present at the New England Venture Summit on Wednesday, December 5, in Boston, Massachusetts. Dr. Smith will discuss NanoSmart Pharmaceuticals' novel drug-delivery platform utilizing a human-derived antinuclear antibody that targets areas of necrosis present in all solid tumors. The presentation will include current status and planned development milestones, while explaining the benefits of reformulating existing drugs using NanoSmart's tumor targeting platform.

"There is a need for new and more-effective therapeutic products across all types of cancers, but particularly for those rare cancers that are often overlooked and/or underserved," said Dr. Smith. "We are pleased with the progress we are making in developing our pipeline and the success of our initial preclinical studies. Our ability to nonspecifically target cancer tumors affords us the opportunity to rapidly commercialize new treatments for a wide range of pediatric/orphan indications."

IntelliCell BioSciences Announces Research Agreement with the New Jersey Center for Biomaterials at Rutgers–The State University of New Jersey

PRNewswire: November 28, 2012 – NEW YORK, NY, U.S.A. – IntelliCell BioSciences, Inc. ("company") (OTCQB: SVFC) announced today that it has entered a sponsored research agreement with the New Jersey Center for Biomaterials at Rutgers–The State University of New Jersey.

Under terms of the agreement, the New Jersey Center for Biomaterials will be conducting a series of research projects that will further define the unique characteristics and properties of IntelliCell's proprietary cellular population. The work will be conducted on behalf of IntelliCell under the direction of Professor Joachim Kohn, the noted researcher and inventor who directs the New Jersey Center for Biomaterials.

Initial research will focus on documenting any differences between IntelliCell's proprietary cellular population and similar cell populations isolated from human adipose tissue using conventional methods of cell isolation. After successful completion of the initial phases of the clinical research, the company hopes to engage the New Jersey Center for Biomaterials in development projects that may lead to bioengineered products containing the proprietary IntelliCell cellular population and products under development at the New Jersey Center for Biomaterials.

Dr. Steven Victor, chairman and CEO of IntelliCell, stated, "We are very pleased to be working with Professor Kohn and the New Jersey Center for Biomaterials. Our vision for the future includes a number of bio-applications whereby we can apply our technology to exciting new areas in regenerative medicine and work with top tier research institutions in the United States."

Professor Joachim Kohn, Director of the New Jersey Center for Biomaterials at Rutgers–The State University of New Jersey, added, "This is a truly exciting opportunity for us. We have a number of highly advanced scaffolds for regenerative therapies (e.g., regrowing bone, nerve, and skin), and we expect that IntelliCell's cell populations will significantly enhance the effectiveness of our biomaterials-based scaffolds. In this collaborative research project, we are combining the outstanding cell biology expertise of IntelliCell with the expertise of our chemists and materials scientists. We believe that through this collaboration, we will be able to demonstrate the merits of interdisciplinary research efforts between industry and academia. In addition, emerging companies like IntelliCell are the main driving force for health care innovation, and we are delighted to assist such companies with technologies under development."

Added Robert Sexauer, EVP of clinical development at IntelliCell, "We are looking forward to working with Professor Kohn and his team in our primary focus of translating IntelliCell technology into clinical opportunities."

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Discovery Labs Presents New SURFAXIN® and AFECTAIR® Data at 2012 Hot Topics in Neonatology Annual Meeting

PRNewswire: November 28, 2012 – WARRINGTON, PA, U.S.A. – Discovery Laboratories, Inc. (NASDAQ: DSCO) today announced it will present both SURFAXIN® and AFECTAIR® data at the 2012 Hot Topics in Neonatology annual meeting being held December 3–4 in Washington, D.C. Hot Topics in Neonatology is an internationally recognized medical meeting dedicated to advancing the practice of neonatology.

Earlier this year, SURFAXIN became the first Food and Drug Administration (FDA)-approved synthetic, peptide-containing surfactant for the prevention of respiratory distress syndrome (RDS) in premature infants at high risk of developing RDS. Also, in February 2012, the company's AFECTAIR device was registered with the FDA and cleared for marketing in the United States. AFECTAIR is a proprietary disposable airway connector that simplifies the delivery of aerosolized medications to critical-care patients requiring ventilatory support from either intermittent mechanical ventilation or continuous positive airway pressure.

Discovery Labs presentations at Hot Topics in Neonatology include:

- Pharmacoeconomic Impact of Bronchopulmonary Dysplasia in Reintubated Infants—Simmons PD and Clayton RG
- *In Vitro* Comparison of Albuterol Delivery Using a Novel Neonatal Ventilator Circuit Connector with Three Different Neonatal Ventilators—Gregory TJ, Henderson C, Mazela J, Boppana V, and Clayton RG

Additionally, a late-breaker platform presentation entitled "New Insights into Effective Aerosol Therapy in Premature Infants—Are We Ready to Inhale Surfactants?" will provide a comprehensive review of aerosolized treatment options for RDS today and into the future. This topic, which is relevant to Discovery Labs' aerosolized KL4 surfactant development candidate, AEROSURF®, will be presented at 11:45 a.m. on December 4th.

For over 30 years, Hot Topics has been the premier neonatal conference, with more than 1,000 neonatologists and perinatologists attending each year. For more information about Discovery Labs and its products, attendees can visit Discovery Labs in the Hot Topics in Neonatology Internet Café or visit www.discoverylabs.com.

Unigene and Tarix Pharmaceuticals Enter Definitive Licensing Agreement for "Peptelligence-Engineered" TXA127

PRNewswire: November 27 – BOONTON, NJ, and CAMBRIDGE, MA, U.S.A. – Unigene Laboratories, Inc. (OTCBB: UGNE) and Tarix Pharmaceuticals today announced that the companies have entered into a definitive licensing agreement to develop an oral formulation of TXA127, Tarix's lead peptide drug candidate. The oral formulation of TXA127 is being developed jointly by Unigene and Tarix under a previously agreed upon feasibility program whereby the companies leveraged Unigene's Peptelligence™ technology platform to enable enhanced oral delivery of TXA127.

According to terms of the licensing agreement, Tarix will have an exclusive worldwide license to Unigene's Peptelligence™ technology covering the use of that technology with angiotensin (1–7), the pharmaceutical ingredient in TXA127, as well as its functional equivalents, analogues, or derivatives. In return for the license, Tarix will pay Unigene a percentage of revenues, if any, derived from the direct sales of any oral dose form of an approved angiotensin (1–7) product by Tarix or from any upfront, milestone, or royalties received by Tarix from a third-party sublicensee of Unigene's Peptelligence™ technology with respect to any angiotensin (1–7) product. There is no upfront payment being made by Tarix to Unigene in connection with the execution of the license.

Ashleigh Palmer, Unigene's chief executive officer, commented, "Our licensing agreement with Tarix is further validation of the strength of Unigene's Peptelligence™ platform and the tremendous value that our feasibility program offers to innovators in the therapeutic peptide field. We are very excited to extend our feasibility partnership with Tarix into a fully-fledged licensing agreement and to work with Dr. Franklin and his company's scientific team to advance the development of what we all agree is a potentially groundbreaking drug."

Rick Franklin, M.D., Ph.D., Chief Executive Officer of Tarix, commented, "TXA127 has always been a high-value opportunity, given its potential to treat multiple therapeutic conditions. However, our ability to potentially deliver TXA127 orally will significantly enhance its transactability with prospective advanced-stage development partners and serves to greatly differentiate it from other peptide-based drugs. Based on our experience, Unigene's Peptelligence™ technology and feasibility program offer the potential to truly transform the therapeutic peptide market."

In September, data from a feasibility study of TXA127 demonstrated that the oral formulation produced extremely high exposure in the blood that resulted in a several-fold increase in bioavailability as compared to the oral delivery of the unformulated drug and was equal to or greater than that achieved by the current subcutaneous formulation.

Ranbaxy Launches Absorica™ (Isotretinoin) Capsules in the U.S. Healthcare Market

PRNewswire: November 26, 2012 – PRINCETON, NJ, U.S.A. – Ranbaxy Laboratories, Inc. (RLI), a wholly owned subsidiary of Ranbaxy Laboratories Limited (RLL), today announced the sales and promotion launch of Absorica (isotretinoin) capsules, a product that is licensed from Cipher Pharmaceuticals Inc. of Mississauga, Ontario. Absorica is indicated for the treatment of severe recalcitrant nodular acne in patients 12 years of age and older.

Due to its high lipophilicity, oral absorption of isotretinoin is enhanced when given with a high-fat meal; however, Absorica, which is formulated using patented Lidose® technology, can be given without regards to meals. The fasted AUC0-t of Absorica is approximately 83% greater than that of Accutane, while both products are bioequivalent under fed conditions. Absorica is therefore not interchangeable and not substitutable with generic products of Accutane®. Absorica, NDA, was approved based on a large pivotal clinical trial enrolling 925 patients.

Senior Director, Ranbaxy Laboratories Inc., Dr. Ashish Anvekar said, "We are most pleased to make Absorica available as a valuable option for dermatologists and a subset of patients who suffer from severe recalcitrant nodular acne. Absorica will be the flagship brand of the Ranbaxy dermatology product portfolio in the United States."

Alliqua to Explore Business Development Efforts for Hydrogel Transdermal Delivery Platform in the Cosmeceutical Industry

PRNewswie: November 19, 2012 – NEW YORK, NY, U.S.A. – Alliqua, Inc. (OTCQB: ALQA) ("Alliqua" or the "company"), a biopharmaceutical company focused on the development, manufacturing, and distribution of proprietary transdermal wound care and drug delivery technologies, today announced the company's exploration of business development efforts for its proprietary transdermal delivery platform in the cosmeceutical industry.

According to market research data from the Freedonia Group, the cosmeceutical market reached $6.4 billion in 2010 and is projected to grow to $8.5 billion by 2015, largely fueled by consumers searching to stave off the physical signs of aging. While this market has traditionally been focused on consumers aged 45 and older, recent trends show younger consumers are seeking out anti-aging products designed to prevent or treat even early signs of aging including fine lines and wrinkles. Alliqua believes its transdermal platform is ideal for administering the key ingredients of these anti-aging products more effectively to targeted areas of the body. In doing so, the Alliqua technology has the potential to greatly enhance the performance of a variety of cosmeceutical products across a broad spectrum of areas. Additionally, the time to market for cosmeceutical products is typically much shorter than for traditional drug delivery, making it a very attractive business opportunity for Alliqua.

James Sapirstein, CEO of Alliqua, stated, "The cosmeceutical industry represents a vast market opportunity for our proprietary transdermal platform. What is equally as exciting for Alliqua is that with our hydrogel technology, we can reach the market in a relatively short time frame when compared to traditional drug delivery platforms. We intend to aggressively pursue partnerships with various manufacturers to help them increase the effectiveness of their products and achieve more optimal results for the consumer. By doing this we have the potential to build a highly profitable business segment for Alliqua in the cosmeceutical marketplace."

Sanovas, Inc., Receives Patent Allowance for Nested Balloon Catheter for Localized Drug Delivery

PRNewswire: November 19, 2012 – SAUSALITO, CA, U.S.A. – Sanovas, Inc., a life science technology company focused on developing and commercializing the next generation of micro-invasive diagnostics, devices, and drug delivery technologies, announced today that the U.S. Patent and Trademark Office (USPTO) has issued a Notice of Allowance for the company's nested balloon catheter for localized drug delivery, a component of Sanovas's Vas Zeppelin™ Smart Catheter technology portfolio. The patent covers a unique minimally invasive system and method for delivering diagnostic and therapeutic agents to small diameter anatomy in the lungs and throughout the body.

"This patent is an important milestone in the protection of the company's proprietary drug delivery technologies," said Erhan Gunday, chief technology officer and cofounder of Sanovas.

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"With more than 45 patents and patents pending, Sanovas has built a strong IP portfolio for our micro-invasive diagnostics, devices, and drug delivery technologies that are poised to significantly advance the way pulmonary diseases, such as lung cancer, are detected and treated."

The nested balloon catheter patent, written by Sanovas founders Erhan Gunday and Larry Gerrans, will protect an integral part of the company's NanoVas™ drug delivery technology. The ability of new drug delivery systems, such as the nested balloon catheter for localized drug delivery, to deliver targeted, tumor-specific treatments holds the potential for overcoming one of the greatest hurdles to chemotherapy—systemic toxicity.

"As we advance the science of personalized medicine, the ability to deliver customized immune and gene therapy will transform the way cancer and chronic disease are treated. Sanovas is proud to be at the forefront of these significant advances," Gerrans said.

Sanovas' Vas Zeppelin™ Smart Catheter technology portfolio is designed to access, image, measure, and diagnose anatomy in small airways and vessels residing at, or below, three millimeters in diameter. Featuring the world's smallest surgical camera, the Vas Zeppelin™ allows the removal of tumors and other obstructions and enables the local delivery of drug and immune therapies to patients suffering from lung cancer and related pulmonary and vascular diseases.

OptiNose Receives Grant to Fund Nose-to-Brain Research in Autism Spectrum Disorders

PRNewswire: November 8, 2012 – YARDLEY, PA, U.S.A. – OptiNose US Inc. today announced that its Norwegian affiliate was awarded NOK 12.3 million (US$2.1 million) by the Research Council of Norway to study its unique nasal drug delivery technology in the treatment of autism spectrum disorders (ASDs). The OptiNose project was one of 59 company projects selected among the nearly 200 applications submitted to the Research Council's program for user-driven, research-based innovation research. OptiNose will use this research grant to investigate "nose-to-brain" transport of oxytocin via the patented OptiNose Bi-Directional™ delivery technology for the treatment of ASDs. Partners who have agreed to collaborate with OptiNose in the project include the Department of Psychiatry at Oslo University Hospital, SINTEF, Smerud Medical Research, and Norwegian academic institutions. It is anticipated that the Department of Psychiatry at the University of Minnesota will also participate in the program.

"The opportunity to investigate nose-to-brain drug transport with the OptiNose technology in an effort to develop a new treatment for autism spectrum disorders is very exciting," said Per G. Djupesland, M.D., Ph.D, chief scientific officer (CSO) of OptiNose. "Autism spectrum disorders are growing in prevalence, and there are no drugs approved to treat the core symptoms which burden children, adults, and families with these conditions. We hope to see significant benefits from delivering treatment with our innovative nasal technology."

Micell Technologies Announces Issuance of Core Technology Patent

PRNewswire: November 6, 2012 – DURHAM, NC, U.S.A. – Micell Technologies, Inc., today announced that the U.S. Patent and Trademark Office (USPTO) has issued a patent covering the company's surface and polymer modification technology. This intellectual property protection is related to Micell's investigational MiStent® sirolimus eluting absorbable polymer coronary stent system (MiStent SES™), as well as potential additional biomedical products. The patent rights are assigned to and wholly owned by Micell.

The patent, "Polymer Coatings Containing Drug Powder of Controlled Morphology" (U.S. Patent Number 8,298,565), covers:

- Coating methods enabling medical devices with unique and potentially advantageous clinical properties.
- Coating methods that are key to Micell's proprietary manufacturing technology.
- Formulations for implantable device/drug combination products, which are intended to confer enhanced stability and delivery by controlling the morphology of the drug(s) in the coating.

James B. McClain, Ph.D., senior vice president and cofounder of Micell, said, "This marks an important milestone in the execution of Micell's international intellectual property strategy. This patent issuance is the beginning of the realization of over 6,000 filed patent claims and supports our belief that Micell's coating technology and methods are novel, differentiated, scalable, and transferable."

Micell currently is using its proprietary technology in products under development including the MiStent SES—a thin-strut sirolimus-eluting stent distinguished by a rapid-absorbing drug/polymer coating designed to control drug release. The MiStent SES clinical development program recently completed the 12-month patient follow-up in the DESSOLVE II study and 18-month patient follow-up in the DESSOLVE I study. In addition, Micell also has a drug-coated balloon under development for vascular interventions. These products are not currently approved or available for sale in any market. ■

Controlled Release Society
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United States of America

Calendar of Events

2013

Controlled Release
March 18–19
London, United Kingdom
www.smi-online.co.uk

5th Ocular Diseases and Drug Development Conference
March 21–22
San Francisco, CA, U.S.A.
www.gtcbio.com

European Molecular Imaging Meeting (EMIM 2013)
May 26–28
Torino, Italy
www.emim.eu

15th International Workshop on Physical Characterization of Pharmaceutical Solids (IWPCPS-15)
June 24–27
Philadelphia, PA, U.S.A.
www.assainternational.com

40th Annual Meeting & Exposition of the Controlled Release Society
July 21–24
Hawaii Convention Center
Honolulu, Hawaii, U.S.A.
www.controlledreleasesociety.org

5th BBBB International Conference
September 26–28
Athens, Greece
www.bbbb-eufeps.org