CRS Leading Delivery Science and Technology

Newsletter

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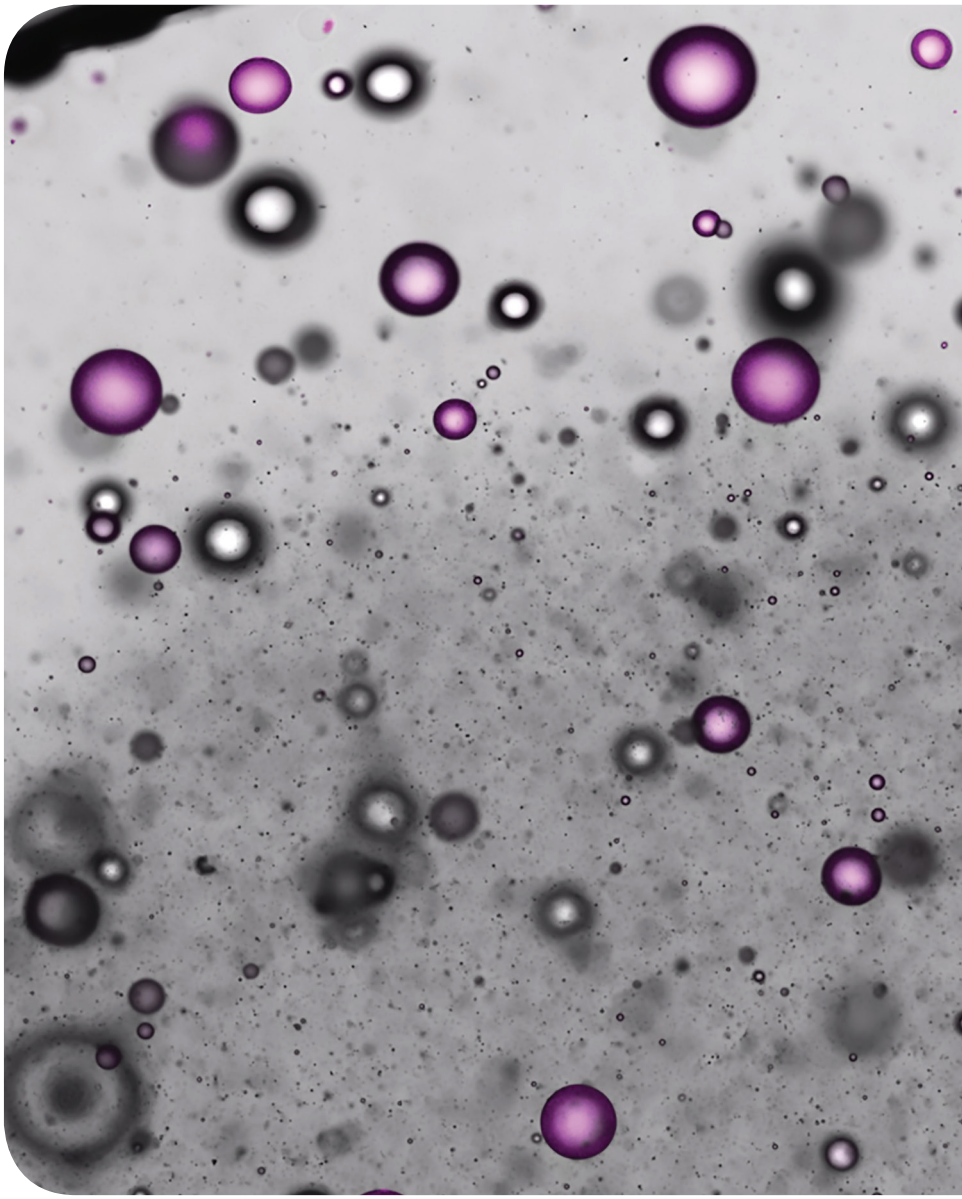
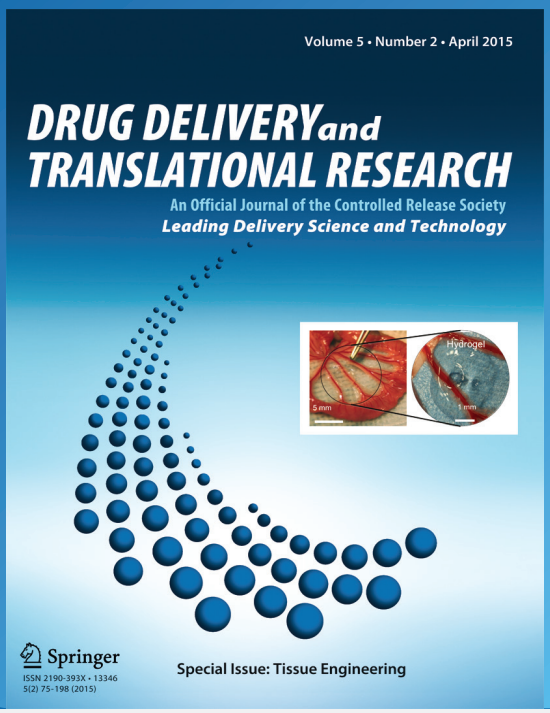
What's Inside





Drug Delivery and Translational Research

An Official Journal of the Controlled Release Society

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CRS Newsletter

Leading Delivery Science and Technology

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Cover image: Confocal microscopy image with bright-field overlay depicting fragrance droplets, stained with Nile Red embedded in κ-carrageenan hydrogel simulating an air freshener. Courtesy of Firmenich.

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 controlledreleasesociety.org.

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Roderick B. Walker
Rhodes University
South Africa

Exciting Science in Edinburgh

The 42nd CRS Annual Meeting has come and gone but not before ensuring that approximately 1,400 delegates were exposed to the latest cutting-edge science of controlled release with a little history, culture, and networking thrown in.

The theme "Creating Value Through Customised Delivery" pertained not only to the science of controlled release but to the innovative programming approach taken by the programme committee led by Justin Hanes and Kinam Park, resulting in a new format that provided a much needed facelift to the annual meeting.

The excellent conference centre with friendly staff hosted several preconference workshops, Innovation Sunday, and the Soapbox Sessions, followed by the opening reception, which set the scene for a memorable meeting. Rumour has it that several delegates started the social events before the meeting, having discovered the ambience of Lubowski's bar a few minutes' walk from the conference centre.

The opening session with the first of four plenary lectures, this one delivered by Vincent Lee, was humbling. Audience members were exposed to challenges and achievements of those acknowledged in the session, in which five new fellows were inducted into the College of Fellows. No doubt those who could not attend the meeting were able to follow on Twitter, as Nicholas Peppas kept us up to speed with proceedings. The other plenary lectures at different sessions were delivered by Cameron Alexander, Maria José Alonso, and Renata Pasqualini, who eloquently provided vision for the future of drug delivery. A highlight for me was the special session in which Nicholas Peppas described his journey in controlled release and the history and future of hydrogels as a delivery technology.

Two and a half days of five parallel scientific sessions, roundtable discussions, Lunch with Luminaries, evening events, and approximately 850 posters ensured there was much to keep us occupied. The programme committee, the volunteers, and the headquarters team are to be congratulated on this successful meeting. One challenge I experienced with the new format was that I had to stick with the session I initially selected, as there was no chance to move between venues due to the research highlight presentations being short. Perhaps this is something Kinam Park and his committee can look to address in 2016.

A further highlight for me was the closing reception in which delegates were able to observe the address to the haggis, sample whisky and beer, and savour traditional Scottish fare in the ambience of the Assembly Rooms, a UNESCO heritage site.

The other editors of the *CRS Newsletter* join me in thanking Art Tipton for his leadership of the society and for listening to the need to embrace change. I am sure that Debra Bingham will continue the hard work, make her mark as incoming president, and ensure that the society continues to create value for its members.

All in all a great meeting—and judging by the innovations introduced in Edinburgh, we are all bound to be "Sleepless in Seattle" in 2016. ■

Art Tipton
Southern Research Institute
Birmingham, Alabama, U.S.A.

Thanks for the Memories

Well, that went by quickly! The year from our 2014 annual meeting in Chicago to this year's meeting in Edinburgh likely seemed brief to most of you. For me, that year interval from when I took the president's gavel from Ian Tucker to when I passed it to Debra Bingham flew by!

I tremendously enjoyed our signature annual meeting this year. Some highlights for me from Edinburgh include additional time spent with a committed Board, other volunteer leadership, and staff. At a series of Board discussions in Edinburgh prior to the annual meeting we focused on plans for the balance of 2015 and beyond. Going forward you will often hear the themes "education" and "industry engagement," two areas we spent time focused on together in Edinburgh.

For me, there were many, many memories once the annual meeting started. I snuck in for the last session at Saturday's workshop on ocular delivery and was thrilled to listen in on an active exchange of data and ideas from delivery scientists and clinicians. On Sunday I enjoyed meeting with several first-time attendees, being touched by our opening plenary from Vincent Lee, and interacting with many of our attendees on the exhibit floor during our opening reception. As the full meeting started on Monday, a highlight was Nicholas Peppas's passionate talk that touched on so much of the history of our field and CRS. As Board members, we spend time in a number of meetings parallel to the scientific sessions. I enjoyed meeting with the chairs of most of our committees and sitting in on some of our volunteer committees, including our Annual Meeting Program, Young Scientist, and International Committees. I enjoyed a new meeting with a group of our industry members, spearheaded by Debra, in which we jointly explored how to make our meeting even more interactive.

It was great to see our luminaries including Nicholas and Vincent interact so much with many members, particularly many of our young scientists. By my count we had 12 past presidents at the meeting (I became number 13 as my term ended). I don't know if that is a record, but it is a clear indication of a strong combination of science and site selection for our annual meeting.

I hope you enjoyed the new structure of most of our sessions, where there was more opportunity to hear from both academic and industry perspectives and to have a more open discussion after the talks. And I hope you enjoyed the return of a larger closing reception. Please give us feedback on these and any other parts of the annual meeting either via the survey you have already received or directly to the Board or staff.

In my previous update I included several items we will focus on as we develop a revised strategic plan: a refocus on our annual meeting, better roles for our engaged volunteers, enhanced early outreach in communities prior to our annual meetings, further capitalizing on our significant publication and science content, and a stronger focus on sales and marketing.

I want to again thank a strong Annual Meeting Program Committee led by Justin Hanes and deputy chair Kinam Park. Kinam will lead that group as we look forward to Seattle, assisted by deputy chair Christine Allen.

I was delighted to transfer the gavel to Debra Bingham as president. Debra brings more than 20 years of drug delivery industry expertise to the role, coupled with years of volunteer service to CRS, including Board roles as treasurer and secretary. CRS will prosper with her committed leadership over the next year.

I close with a quote from the anthropologist Margaret Mead that is relevant for our field and for CRS:

> "Never doubt that a small group of thoughtful, committed citizens can change the world; indeed, it's the only thing that ever has."

Thank you for the opportunity to serve as president! ■

Rendezvous with Silicon Valley Serial Entrepreneur and Guru Gary Cleary on Commercializing Drug Delivery Systems

Vishwas Rai[1] and Bozena B. Michniak-Kohn[2]

Gary Cleary cofounded Corium.

"Never let anyone hold you from pursuing your goals in life" and "Keep learning every day" have been the life philosophy of Gary W. Cleary, a successful, award-winning serial entrepreneur and an astute professional with exceptional scientific acumen who is internationally recognized in the field of small molecules and large biomolecules and their delivery systems. He is the founder of Cygnus, Inc., and cofounder of Corium International. He currently is starting a new company, Cape Therapeutics, which is in the early stage and is focused on regenerative medicine using gene-based therapy. He has held research and management positions in the pharmaceutical and biotechnology industries at Bayer AG, Genentech, Alza, Key Pharmaceuticals, Cygnus, and Corium. He served as an officer in the U.S. Public Health Service (PHS) and the U.S. Food and Drug Administration (FDA) after graduating from the University of California, San Francisco (UCSF). At this year's CRS Annual Meeting, Gary Cleary received the Founders Award for outstanding contributions in the science and technology of controlled release.

He has been an inventor and contributor to projects with first-of-their-kind delivery systems such as passive transdermal patch products to treat motion sickness (scopolamine), hypertension (clonidine), diabetes (GlucoWatch), and hormone deficiencies (human growth hormone), provide contraception (norelgestromin/ethinyl estradiol), and aid in smoking cessation (nicotine), along with other areas including teeth whitening strips (hydrophilic adhesion). At Genentech, he was the one of the first to investigate development of drug delivery systems for large-molecular-weight bioengineered molecules (human growth hormone, interferon). At Bayer, he formulated vaccines and parenteral lipids. He has received the Entrepreneur of the Year Award in Life Sciences for Northern California, the Biomaterials Entrepreneur Award of the New Jersey Center for Biomaterials, the American Association of Pharmaceutical Sciences (AAPS) Rainer Hoffman Award for Products through Science, and the Distinguished Alumnus of the Year Award from UCSF.

He has worked with and developed products for companies in Europe, Japan, and the United States, including Johnson & Johnson, Leo Pharma, Merck Darmstadt, Pharmacia, Sanofi, Parke-Davis, McNeil Pharmaceuticals, Procter & Gamble, Yamanouchi, Sankyo, and Nichiban. At Cygnus, he explored active delivery systems such as ultrasound, iontophoresis, electroporation, and active transdermal technologies throughout the 1980s and 1990s. Cygnus received FDA approval of the GlucoWatch, which was the first active programmable transdermal-like product to reach the market; it used microprocessors, microchips, LCD, biosensors, and an enzyme with iontophoresis technology. At Corium, Gary Cleary headed the research arm based in Menlo Park, California, while Adrian Fossee headed the manufacturing arm based in Grand Rapids, Michigan. Cleary's work at Corium included hydrophilic adhesive polymers for teeth whitening products sold by Proctor & Gamble and microneedle technology for delivering large biomolecules (vaccines and large-molecular-weight proteins) through the skin. Corium received the Edison Award for their micro-jet technology and the Procter & Gamble Partner of the Year Award in 2010. In a recent press release, Peter S. Staple, current president and CEO of Corium, mentioned, "Gary's visionary leadership in the field of drug delivery systems and materials laid the groundwork for many innovations in the field."

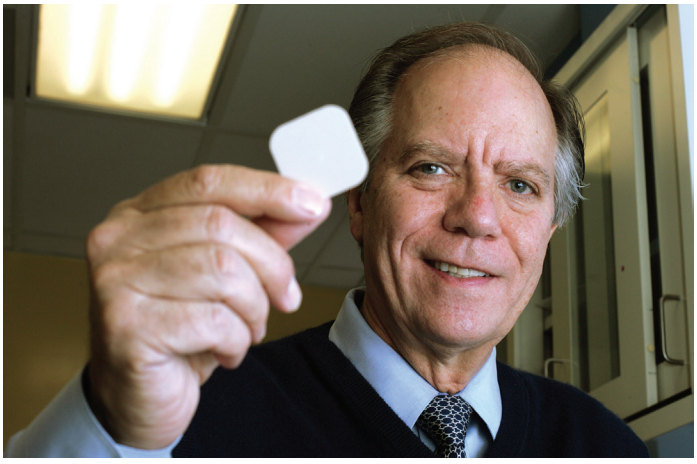
Gary Cleary earned a Pharm.D. from UCSF, a Ph.D. in pharmaceutical sciences from Rutgers University, and an M.B.A. in health sciences from the University of Miami. He holds more than 50 issued U.S. patents and has a few other U.S. patents pending related to transdermal delivery, mucosal delivery, bioerodible polymer adhesives, and other drug delivery technologies. He is a member of the International Society of Stem Cell Research and a fellow of CRS, AAPS, and the American Institute for Medical and Biological Engineering. He is a past president of CRS and served as the first chair of the CRS College of Fellows. He served on the boards of Corium and Cyterion and on the scientific advisory board of Appian Labs. His past corporate board affiliations have included Angiogenix, Cygnus (chairman), New Jersey Center for Biomaterials, Center for Military Biomaterials Research, and the scientific advisory boards of Purdue University Bioengineering, Rutgers Biomedical Engineering, University of the Pacific, and UCSF. His community service affiliations have been as a board member of the Community School of Music and Arts and as the benefit chair of the Glaucoma Research Foundation for several years.

[1] Chrono Therapeutics Inc., Hayward, CA, U.S.A.
[2] Ernest Mario School of Pharmacy, Rutgers–The State University of New Jersey, U.S.A.

Q *Please tell us about your journey from being a pharmacist to pursuing a research-oriented Ph.D. and finally securing an M.B.A. Which part did you enjoy the most and why?*

A While at UCSF, I worked part time as a student pharmacist at Bowerman's Pharmacy in San Francisco. Bowerman's was established about a hundred years before I joined. They had a basement where we made drugs into capsules, tablets, eye drops … you name it. Because I was a student, I did most of the small production of off-brand prescription and over-the-counter tablets, ointments, powders, and so on. This is where I really got started making medicine, in a pharmacy lab. This was probably as small a production and research company as one could find in the 1960s. After graduating from UCSF, I joined the PHS and was sent to New York for a two-year stint with the FDA to help implement the Harris-Kefauver Act in the New York–New Jersey area. The U.S. Congress approved this federal act. There were 12 of us young pharmacists from across the United States to make this particular act happen in real time. As an officer in the PHS (prior to getting my Ph.D.), we had to close down these small pharmacy labs (and even large ones too) for lack of manufacturing controls. While in the PHS in the late 1960s I visited and performed inspections along with FDA inspectors in tiny companies like Bowerman's and in large ones like Bristol Myers, Squibb, Johnson & Johnson, Ciba-Geigy, and other giant pharmaceutical companies located in the New York–New Jersey area. They now have merged with others to become even larger. It was a very memorable event in my life.

After my two years at PHS were up, I was introduced to the Rutgers dean of pharmacy, Roy A. Bowers, who convinced me to take advantage of the GI Bill to get a Ph.D. at Rutgers. There must have been over 100 giant pharma companies during that period in the New York–New Jersey area. Rutgers, at that time, was surrounded by these companies and was a very popular place to get educated in pharmacy and pharmaceutical companies. I thought that I would have a better chance to join a large top-notch pharmaceutical company there than I would in California, especially in the San Francisco Bay Area. Again, I was lucky to get a position at Cutter Labs (later bought by Bayer AG) in Berkeley, California. I worked in a large company that was located near the University of California at Berkeley and near the home where I grew up.



Cleary holding a transdermal patch, one of Corium's products.

I look at my experiences at new and small pharma companies when I moved back to the San Francisco Bay Area. Not long after I started working at Bayer in Berkeley, I was recruited by a new startup drug delivery company—Alza Pharmaceuticals. Alza was in Palo Alto in the Silicon Valley, and that is where I primarily invented and developed new transdermal drug delivery products called patches. After seven or so years at Alza I was recruited to join Key Pharmaceuticals in Miami, Florida. That was where I learned more about founding a company and how to run a company that was a startup a few years before. Mike Jaharis and Phil Frost, who founded many other biotech companies and are billionaires, founded Key Pharmaceuticals. Mike ran the company as president, and Phil was the chairman. One day, Mike called me into his office and offered me the opportunity to get an M.B.A. at the University of Miami. Key would pay for my M.B.A. entirely only if I was a straight A student. I asked what if I got a B or two, and he agreed to be flexible. So I was going back to school but still working at Key full time. I didn't realize the amount of reading and homework that I would have to do for each class in a short period of time. However, I did pass all the courses over a couple of years and got my executive M.B.A. I will never forget how much I learned at Key. With my M.B.A., Pharm.D., and Ph.D., Mike would send me up to New York to meet with the advertising agencies to teach them about Key's technology and about the unique products we were developing for Key's oral and skin products, including transdermals, lotions, and so on. I really got trained in advertising and the business side of Key's products.

Q *You completed part of your studies at Rutgers University in New Jersey. Can you tell us some of your memories of that time?*

A I was initially worried that I might not pass the advanced physical chemistry class. It had been about six years since I took this class at UCSF. I was told this physical chemistry class was required and was used to eliminate those who were not so good in chemistry. This scared me. In any event I got exceptionally good grades and was not eliminated after all. I surprised myself and finished out the next three years with good grades while also spending the summers working at Johnson & Johnson's exploratory research lab in New Brunswick, not far from the Rutgers campus. There I was able to see what it was like to do applied research and learn the importance of an advanced degree—and, yes, I did graduate. I filled in on various projects while the scientists were on vacation. I got to be the first one at Johnson & Johnson to work on vitamin A for skin products. I got to meet physicians and dermatologists who were giants in this field, such as Al Kligman (the inventor of Retin-A) from the University of Pennsylvania and Howard Maibach from UCSF. With this exposure, I found that I really liked R&D, especially regarding skin, skin biology, and basic research.

Interview with Gary Cleary continued on page 6

Interview with Gary Cleary continued from page 5

Q *What was your first position after gaining your Ph.D.? What was your reaction to moving from academia to the corporate world?*

A I was lucky that I was recruited to work at Cutter Labs in Berkeley, California, after graduating from Rutgers, thus returning home to California. While I was there, Bayer AG bought Cutter Labs. I was then exposed to the biological side of pharmaceutics such as vaccines, injectables, extremely large scale-ups of new biological products, and learning how to develop a biotechnological products company. I learned a lot about formulation R&D and developed Cutter's mosquito lotions R&D, while I continued to learn more about the skin, the production of Cutter's mosquito lotions, and what it is like working in a large company like Bayer. I also have had the opportunity to work not only in scientific labs but also in manufacturing scale-up, quality control, production, product design, and advertising. I've worked in both very large (thousands of employees) and very small companies (startups starting with one person). I've enjoyed both experiences. They both have their differences, advantages, and disadvantages. I really like to start up new companies and watch them grow over time. It is very important for me that the people working for the company can work together cohesively and help each other to make the company successful.

Q *What do you think should be the current focus of biotech and medical device sectors, in terms of pathological states?*

A I think it's important that we advance technology in drug, gene, and cellular delivery to continue R&D in regenerative medicine, improving lives, and enabling us to treat diseases that we have never been able to treat before. We should advance treatments early enough to cure all diseases including rare diseases, as much as we can afford to do.

Q *What drove you to become an entrepreneur?*

A It was a combination of a number of headhunters wanting me to join other companies in high-level positions and many discussions with Bob Swanson, president of Genentech, about my next steps at Genentech. He encouraged me to start a company because of my background in startup companies or to stay with Genentech. At that time, Bob had me working in the gene manufacturing and production group, as well as other assignments in business development. While I had a bunch of ideas that I always wanted to develop in previous companies where I worked, they were not always interested in my ideas, or they didn't fit the larger companies' focus. Bob really was helpful in encouraging me to start my own first company and to develop my own ideas into products. I left Genentech and started a new company in 1985, which I named Cygnus, the Latin word for swan, and the name was related to Bob Swanson's friendship. I had never met a person—particularly the president of a company like Bob Swanson—who encouraged someone like me to follow my dreams, thoughts, and ideas. I ultimately left Genentech. Later at a local banquet, Bob proudly introduced me to those at the banquet and to two other former Genentechians who had also left to start up new companies. My experiences at other successful startups along with Bob Swanson's encouragement drove me to become an entrepreneur too. I literally started in my two-car garage.

Cleary standing next to an aseptic hood during the early stages of Corium Pharmaceuticals.

Q *Since the first company is always special for an entrepreneur, please share your experience with building your first company and making it a success.*

A At a CRS Annual Meeting in Europe, I was fortunate to encounter a French company that was interested in my work at Cygnus and my history with transdermal technology. A few weeks later, Elf Technology came to the Cygnus lab in my garage, where I had a few HPLCs and film coating capacity. Elf decided to put in $1 million and have me develop some products for them. At the time, Elf owned Sanofi. With that money I started Cygnus and began to spend most of my time in Europe and Japan. At that time most of the U.S. pharmas were not interested in startups and transdermal. Ultimately, I had projects from the United States and Europe, along with a joint venture, in Japan, with Nichiban and Taiho Pharmaceutical.

Q *Out of so many companies you cofounded and contributed to, where did you experience the most ups and downs in terms of science and raising capital? What led to such circumstances? Looking back, what would you have done differently?*

A Out of Key Pharmaceutical, Alza, and Genentech (companies started by others), only Alza had some financial problems in its early stages, about six or seven years after founding the company. They were saved by Ciba-Geigy (precursor to Novartis), which helped Alza with finances by putting a few million dollars into the company. Alza thereafter was able to pay off their loan from Ciba-Geigy and ultimately sold the company to Johnson & Johnson for about $8 billion around early 2003.

Cygnus and Corium (cofounded by me) had some ups and downs. Cygnus's early stage went well with financing its initial public offering, but we soon after hit some bumps. When Cygnus launched a nicotine patch, we experienced ups and downs when some of our customers kept having problems with their sales forecasts, which dropped our share price, but it helped us when our customers ran big promotions. Johnson & Johnson paid Cygnus $8 million a year before they bought

Alza Pharmaceuticals. Corium had to raise some more funds when it was about six years out. I recall talking to 71 venture capitalists trying to get some funding without anyone having an interest in putting funds in Corium. On my 72nd presentation a venture company was excited to help us with a sufficient amount of money (around $40 million). Corium has since been able to raise funds and went public in April 2014, and it is doing quite well as a public company.

When a company has been in business for nine or ten years, has developed a product or process, or has gone public, the ups and downs of the market become more difficult. Customers changing their product forecasts for the worse can really impact your financials.

Q *What do you find is the hardest part of starting a company and making it successful?*

A The hardest parts early on are developing a team, finding a need or reason to start a company, raising enough capital to support the team and the office/lab, licensing or having one's own technology, and finding a suitable lab, particularly for biotechnology R&D. Once you have started the company, a lot of time is needed to keep the investors up to date at board meetings and between meetings. Once you have a suitable team with good teamwork, there are always issues that come up that need to be resolved, which often takes a lot time that conflicts with day-to-day work advancement. Having a good team and financial overview is extremely important these days.

Q *You are one of the founders of CRS. Can you tell us how you got involved? Please also tell us more about those first years.*

A In the early 1970s I got involved with CRS when I met Bob Langer, then a student from Massachusetts Institute of Technology (MIT), who came to Alza to give presentations on his work with delivery systems. I worked for Alan Michaels at Alza, who formerly was the head of chemical engineering at MIT. Richard Baker and Jorge Heller, who also were early members of CRS in the early 1970s, also worked at Alza when I first joined the company. With Bob, Richard, and Jorge around from time to time I attended some CRS events, where I met people from other parts of the country such as Danny Lewis, Frank Harris, Nicholas Peppas, and Allan Hoffman. When Bob Langer started a summer course at MIT and brought in a number of CRS members to lecture, I was in his first class. Later, in the late 1970s, we began to meet during the hot summers in Fort Lauderdale, Florida, because the prices for hotels there were much lower during the summer, quite inexpensive compared with what we pay today. We probably had 50 or 60 people attending these Fort Lauderdale annual meetings in the late 1970s.

I had joined Key Pharmaceuticals in the late 1970s and lived near Fort Lauderdale, so it was easy for me to get to the CRS meetings. I recall many of the members at the meeting would run out to the beach to swim, only to burn their bare feet on the extremely hot sand as they ran across the shore.

Q *In the midst of such a busy schedule, how did you manage to keep up with your professional and personal life and maintain your health?*

A Somehow my wife, Nobuko, and I have learned to find time to travel to meetings, the symphony, and parties up in San Francisco and near our home in Silicon Valley. We somehow can always squeeze in some time to be with friends or go to lectures around the San Francisco Bay Area (at museums, UCSF, Silicon Valley, Stanford, and Celebrity Forum, which is a forum of well-known international speakers at a local college in Cupertino). I try not to overeat, and I get eight hours of sleep most nights. From time to time I enjoy a little holiday, and I take some time to exercise by playing golf or walking in the hills where we live.

Both of us are involved with local charities that we believe in supporting: the Community School of Music and Arts, the Glaucoma Research Foundation, Hidden Villa (an organic farm that once hosted Japanese-American families returning from internment camps), Angel Island Immigration Station (a national historic landmark), and the Japan Society of Northern California.

Cleary after receiving the Founders Award at the 2015 CRS Annual Meeting.

Q *What are your favorite vacation spots? What do you like to do in your leisure time?*

A My favorite vacations are hiking in the mountains: both Switzerland and Yosemite National Park, near where I grew up in Merced, California. I also like to visit Hawaii and Japan from Kyushu to Hokkaido. I really enjoy drawing and oil painting, especially outdoors, and engineering and research. I find that this experience in art has helped me greatly to develop ideas, designs, and engineering, including bioengineering. Drawing helps me envision what our products might look like. ■

The CRS Annual Meeting brings renowned researchers, industry experts, and young scientists together from around the globe to discover customized approaches and high-value solutions in delivery science and technology. Over 1,400 attendees joined us in Edinburgh, Scotland, to experience a dynamic exposition, targeted networking events, and a compelling and interactive scientific program. The 2015 Annual Meeting was redesigned to give you more:

- Industry participation within the scientific program
- Posters – over 850 were available for viewing
- Time for Q&A among speakers and session attendees
- Brief research updates with further opportunity to discuss a scientific poster presentation
- Speakers with a fourth plenary speaker, as well as a special address by Nicholas Peppas
- Value-added moderation by esteemed CRS Fellows and society leaders
- Networking opportunities such as Lunch with the Luminaries and the Closing Reception

2015 CRS Awards

The Controlled Release Society is proud to honor this year's awardees for their dedication and contributions to delivery science and CRS.

Distinguished Service Award

Established in 1994, the Distinguished Service Award is presented to a CRS member who has exhibited exceptional commitment and service to the society and is selected by the Board of Directors.

Kinam Park received his Ph.D. in pharmaceutics from the University of Wisconsin in 1983. After postdoctoral training in the Department of Chemical Engineering at the same university, he joined the faculty of Purdue University in 1986. Since 1998, he has held a joint appointment in the Department of Biomedical Engineering, and he became the Showalter Distinguished Professor of Biomedical Engineering in 2006. His research focuses on oral delivery, drug-device combination products, and long-term microparticle formulations. He is the founder of Akina, Inc., specializing in polymers for drug delivery. He is currently the editor-in-chief of the *Journal of Controlled Release*. He is a past CRS president (2001–2002) and is the 2016 CRS Annual Meeting Program Committee chair. Moreover, as a CRS Foundation board member since 2007, he has raised significant donations to fund postdoctoral fellowships and student travel grants.

College of Fellows

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

Hamid Ghandehari is a professor of pharmaceutics and bioengineering at the University of Utah, U.S.A.

Edith Mathiowitz is a full professor of medical science and engineering at Brown University, U.S.A.

Samir Mitragotri is a professor of chemical engineering at the University of California, Santa Barbara, U.S.A.

Yvonne Perrie is the head of pharmacy and chair in drug delivery within Aston Pharmacy School, Aston University, United Kingdom.

Thomas Rades is the research chair in pharmaceutical design and drug delivery in the Department of Pharmacy, University of Copenhagen, Denmark.

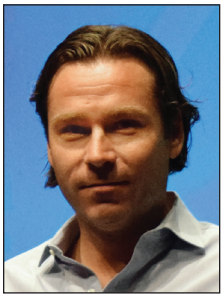
Founders Award

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

Gary W. Cleary is an internationally recognized scientist in the field of drug delivery systems and polymer technologies, as well as founder and cofounder, respectively, of Cygnus and Corium, Inc., both drug delivery companies where he has served as chairman, president, and chief technology officer. He holds 50 patents in this area. He has received several entrepreneur of the year awards from Life Sciences for Northern California, New Jersey Center for Biomaterials, AAPS Rainer Hoffman Award, and the UCSF Distinguished Alumnus Award. During his career he has held research and management positions at the U.S. Public Health Service, FDA, Alza, Key Pharmaceuticals, Genentech, Cygnus, and Corium. Cleary has a Pharm.D. (University of California, San Francisco), Ph.D. (Rutgers), and M.B.A. (University of Miami).

Young Investigator Award

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



Twan Lammers obtained a D.Sc. in radiation oncology from Heidelberg University in 2008 and a Ph.D. in pharmaceutics from Utrecht University in 2009. In the same year, he started the Nanomedicine and Theranostics Group at the Institute for Experimental Molecular Imaging at RWTH Aachen University Clinic, where he was promoted to full professor in 2014. His work focuses on image-guided drug delivery and on materials and methods to longitudinally monitor tumor growth, angiogenesis, inflammation, and metastasis.

CRS/T. Nagai Postdoctoral Research Achievement Award

Cosponsored by The Nagai Foundation Tokyo

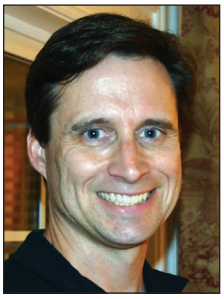
This award recognizes an individual postdoc who has recently completed postdoctoral research in controlled release science and technology and the postdoc's advisor, who played an integral role in the achievements.

Gaurav Sahay is an assistant professor in the College of Pharmacy at Oregon State/ Oregon Health Science University. Profs. Robert Langer and Daniel Anderson served as his mentors for postdoctoral training at the Massachusetts Institute of Technology. Dr. Sahay received his Ph.D. under Prof. Alexander Kabanov at the University of Nebraska. Currently, Sahay Lab is dissecting the molecular mechanisms involved in intracellular trafficking of nanomedicines and engineering methods to trigger their endosomal escape for cytosolic delivery of RNA therapeutics.

Jorge Heller *Journal of Controlled Release* Outstanding Paper Award

Cosponsored by Elsevier

This award recognizes an outstanding regular paper related to the science of controlled release (not an invited, review, or special meeting paper) that was published during 2014 in the Journal of Controlled Release.



Richard J. Price, Ph.D., is a professor of biomedical engineering at the University of Virginia (UVA). Early in his career, he performed seminal studies demonstrating that microbubble activation with ultrasound could be used to deliver nanoparticles across endothelial barriers. His current research centers on the use of MRI-guided focused ultrasound for targeting the delivery of drugs and genes across the blood–brain barrier for the treatment of brain tumors and the prevention of Parkinson's neurodegeneration. He is also the research director of the UVA Focused Ultrasound Center. In this capacity, he leads an institution-wide effort to identify, investigate, and translate new focused ultrasound applications.

Non-invasive Delivery of Stealth, Brain-Penetrating Nanoparticles Across the Blood–Brain Barrier Using MRI-Guided Focused Ultrasound
Journal of Controlled Release 189: 123-132 (2014)
Richard J. Price, Elizabeth Nance, Kelsie Timbie, G. Wilson Miller, Ji Song, Cameron Louttit, Alexander L. Klibanov, Ting-Yu Shih, Ganesh Swaminathan, Rafael J. Tamargo, Graeme F. Woodworth, Justin Hanes, and Richard J. Price

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Drug Delivery and Translational Research Outstanding Paper Award

Cosponsored by Springer

This award recognizes outstanding research in the field of drug delivery and translational research that was published during 2014 in Drug Delivery and Translational Research.

Kanjiro Miyata received his Ph.D. under the supervision of Kazunori Kataoka in the Department of Materials Engineering, University of Tokyo, in 2006. From 2006 to 2009, he worked as an assistant professor in the Department of Bioengineering. In 2009, he moved to the Center for Disease Biology and Integrative Medicine, University of Tokyo. Since 2013, he has been an associate professor in the center. His main research interest is smart polymeric nanocarriers for nucleic acid delivery.

Kazunori Kataoka, Ph.D., is a professor of biomaterials at the Graduate School of Engineering, University of Tokyo, Japan. He has been appointed to a joint position since 2004 at the Graduate School of Medicine, University of Tokyo, as a professor of clinical biotechnology at the Center for Disease Biology and Integrative Medicine. He served as a president of the Society of Polymer Science, Japan (2010–2012) and as a president of the Controlled Release Society (2012–2013). He is a founding fellow of the CRS College of Fellows (2010). He is on the editorial and advisory boards of 14 international journals, and he has been the editor of *Journal of Biomaterials Science, Polymer Edition* since 2004. His current major research interest is supramolecular materials for nanobiotechnology, particularly focusing on drug and gene targeting, and he has published more than 500 papers with an *h*-index of 113 (Google Scholar).

Multifunctional Polyion Complex Micelle Featuring Enhanced Stability, Targetability, and Endosome Escapability for Systemic siRNA Delivery to Subcutaneous Model of Lung Cancer
Drug Delivery and Translational Research 4: 50-60 (2014)
Hyun Jin Kim, Takehiko Ishii, Meng Zheng, Sumiyo Watanabe, Kazuko Toh, Yu Matsumoto, Nobuhiro Nishiyama, Kanjiro Miyata, and Kazunori Kataoka

Outstanding Pharmaceutical Paper Award

Cosponsored by PharmaCircle

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

Jason Li received a master's degree in mechanical and biomedical engineering in 2011 from the University of Toronto, Canada, and is currently a Ph.D. candidate in the Department of Pharmaceutical Sciences at the University of Toronto. His research experience spans the development of nanomaterials-based diagnostic biosensors, implantable closed-loop drug delivery systems, nanomedicines for drug delivery and imaging applications, and the application of these technologies to both *in vitro* and whole animal models of bone remodeling, diabetes, and cancer.

New Structural Design of a Closed-Loop Insulin Delivery Implant Extends the Duration of Insulin Efficacy in a Type 1 Diabetic Rat Model by Impeding Immune Cell Infiltration

CRS Foundation

Nicholas A. Peppas has been an icon in the field of controlled release through his innovative research, leadership of the Controlled Release Society, and exceptional support of students. One of his many legacies is the formation of local CRS chapters to enhance globalization and student development. Therefore, CRS honored Nicholas Peppas via funding student travel awards so promising young scientists could attend the 2015 CRS annual meeting. Following is a list of recipients of the 2015 Nicholas A. Peppas Travel Award:

- Vivek Agrahari, University of Missouri, Kansas City, U.S.A.
- Jaclyn Obermeyer, University of Toronto, Canada
- Ryan Pearson, University of Michigan, U.S.A.
- Mary Tang, University of Illinois, U.S.A.
- Jennifer Wong, University of Sydney, Australia
- Mimi Yang, University of Auckland, New Zealand ■

Reflections on the Alexander "Sandy" Florence Postdoctoral Fellowship, 2014–2015

Christopher E. Nelson
Postdoctoral Fellow, Gersbach Laboratory, Duke University, U.S.A.

I completed my Ph.D. in biomedical engineering in Craig Duvall's laboratory at Vanderbilt University. During my dissertation research, I designed local and systemic nonviral delivery strategies for small interfering RNA that would mediate the potent and specific silencing of specific genes of interest. The major application of this work was controlling gene expression to improve regenerative medicine. Two major research interests were fostered, including the ability to use biology to our advantage (e.g., synthetic and molecular biology) and the prospect of using nonpathogenic viral vectors to assist with efficient gene delivery. I wanted to apply my skills from my dissertation work and gain a new set of skills in gene therapy. Therefore, I sought out mentors for my postdoctoral training who have a proven track record in these fields.

With the support of the Alexander "Sandy" Florence Postdoctoral Fellowship from the CRS Foundation, I joined the laboratory of Charles Gersbach at Duke University. His laboratory focused on using genome engineering techniques to better understand disease states and improve human health. I was excited to join a highly translational project in gene therapy. In the Gersbach lab, I have been able to foster my interest in applying new genome engineering tools for regenerative medicine and for the treatment of genetic disorders.

Significance of the Research

Monogenic genetic diseases have a large impact on human health and are often debilitating and fatal. Specifically, Duchenne muscular dystrophy (DMD) impacts around one in 5,000 males and leads to significant muscle wasting and loss of ambulation through the teen years, leading to pulmonary and cardiac failure in the twenties. DMD is the result of genetic mutations that result in absence of dystrophin, an essential musculoskeletal protein. Dystrophin is an X-linked (locus Xp21.2) gene that spans 2.5 million base pairs and is composed of 79 exons; it is transcribed into a final mRNA product of 14 thousand base pairs and translated into a 427 kDa protein. Dystrophin is the largest known protein-encoding gene in the genome, which partially explains the high relative prevalence of mutations. In fact, it is estimated that ~30% of cases are noninherited spontaneous mutations. Because DMD is monogenic, prevalent, and fatal, a large body of work has been dedicated to applying gene therapy to this illness for which no clinically approved treatment exists. Gene therapy has recently made preclinical strides in the treatment of DMD by providing exogenous dystrophin DNA to patients.

Genome engineering tools including zinc finger nucleases, transcription activator-like effector nucleases, meganucleaes, and the newer clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPR-associated protein-9 nuclease (Cas9) system allow investigators to target specific regions of DNA to make precise modifications. The CRISPR/Cas9 system was discovered as a bacterial cell's acquired immunity for fighting invading viruses. The system was then adapted for use in human cells. The Cas9 nuclease uses a single guide RNA (gRNA), which directs the nuclease to the genomic location to make the desired modification. This targeting mechanism makes the CRISPR platform more easily adaptable than the previous engineered nucleases. As a result, the CRISPR platform has found a wide variety of uses from correcting genetic disease to modifying the epigenome.

Using genome engineering tools, we set out to develop a gene therapy that can correct genetic mutations associated with DMD—a potentially curative approach. Previous work in the Gersbach lab adapted the CRISPR system for correcting DMD mutations in patient-derived cells *in vitro*. The next big challenge was correcting mutations associated with DMD in a relevant animal model.

Efficient Delivery of Genome Engineering Tools

Genome engineering has made it possible to make specific targeted modifications to the host genome. This has been demonstrated for a number of conditions *in vitro*; however, gene delivery barriers are a large obstacle to clinical translation of this new technology. Adeno-associated virus (AAV) has been adapted for the delivery of exogenous genes. Recently, a few groups including our own have adapted AAV for the delivery of the components of the CRISPR/Cas9 system including the Cas9 nuclease and the gRNAs. We built AAVs containing the components of the CRISPR/Cas9 system targeting the dystrophin gene in mice. This approach would use Cas9 to excise a nonessential exon containing the mutation from the *mdx* mouse, the most common mouse model of DMD. We hypothesized that removing this exon from the genomic DNA would improve the phenotype. We have been able to demonstrate DNA editing activity in mouse muscle *in vivo*. We have found that genomic deletions of exon 23 restore dystrophin protein expression. In the future, we hope to demonstrate recovery of muscle function and reversal of the dystrophic phenotype in mice.

Professional Development

As a Sandy Florence fellow, I have had the opportunity to present my research, collaborate outside of my own work, and

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develop my future career. I had the opportunity to present my work at the Society for Biomaterials sponsored "Biomaterials Day" in Nashville, Tennessee. Also, I had the opportunity to present my work at the annual meeting of the American Society for Gene & Cell Therapy (ASGCT) in New Orleans, Louisiana. At ASGCT, I was able to interact with experts in gene therapy including leading researchers in DMD. In July, I attended the annual CRS meeting in Edinburgh, Scotland, to present an update on my current research. At Duke University, I have also had the opportunity to take part in interdisciplinary and collaborative projects that extend my own research interests. In the future, I plan to remain an active member of CRS because delivery science helps to improve the translation of gene therapies.

I am grateful to the CRS Foundation and those who contributed to the Sandy Florence Fellowship. I would also like to thank Sandy Florence for his work and leadership in CRS. Finally, I would like to thank my Ph.D. advisor, Craig Duvall, and my postdoctoral advisor, Charles Gersbach, for their mentorship and encouraging my continued career development. ■

2015 Nicholas Peppas Student Travel Awards

As a past CRS president, Nicholas A. Peppas encouraged the development of local CRS chapters to enhance globalization and provide opportunities for student development. To honor this icon in our field, this year the CRS Foundation presented student travel awards to six promising young scientists. The students were nominated by their respective chapters.

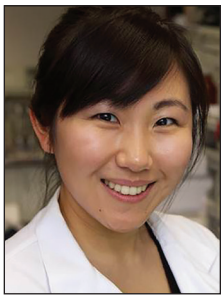
Vivek Agrahari (University of Missouri, Kansas City, U.S.A.) is a Ph.D. candidate in pharmaceutical sciences. In 2011, he attended and presented his research at the CRS Annual Meeting in Maryland. His experiences at that meeting prompted him to start a CRS Student Chapter at his institution. Vivek is a member of the Preclinical Sciences & Animal Health division.

Jaclyn Obermeyer (University of Toronto, Canada) is a Ph.D. student in the Shoichet Lab. She presented a poster at this year's meeting, "Local Delivery of Brain-Derived Neurotrophic Factor for Functional Recovery Following Stroke." She was a member of the student organizing committee for the Canadian Biomaterials Society (CBS) 2015 Conference in Toronto; the annual meeting of the CRS Canadian Local Chapter was held to coincide with it, and Jaclyn seized the opportunity to encourage all CBS participants to join CRS.

Ryan Pearson (University of Michigan, U.S.A.) is a postdoctoral research fellow with a degree in biopharmaceutical sciences. For four years, he was an active member of the CRS Illinois Student Chapter and held multiple leadership positions. He played a critical role in organizing two research symposia that the chapter sponsored. Ryan was selected to give a podium presentation at the 2014 CRS Annual Meeting in Chicago.

Mary Tang (University of Illinois, U.S.A.) is a Ph.D. candidate in biopharmaceutical sciences with a focus in controlled drug delivery for cancer treatment. Mary has held multiple leadership positions in the CRS Illinois Student Chapter, including two terms as president. She presented posters at the 2013 CRS Annual Meeting in Honolulu, Hawaii, and the 2014 CRS Annual Meeting in Chicago, Illinois. She is scheduled to graduate this summer.

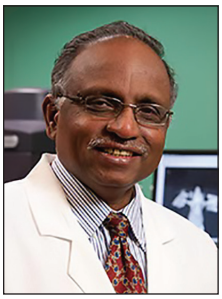
Jennifer Wong (University of Sydney, Australia) is a Ph.D. candidate in pharmaceutical sciences and an active CRS volunteer. As a member of the Young Scientist Committee, she helped organize and lead the YSCs two full-day workshops at the annual meeting. She is a member of the 2016 Annual Meeting Program Committee and of the Volunteer Recruitment Committee.



Mimi Yang (University of Auckland, New Zealand) is in her final year of Ph.D. study. Her research focuses on pH-sensitive liposomal delivery of a novel hypoxia-activated prodrug to target solid tumors. She presented a poster at this year's annual meeting. Mimi has volunteered for the CRS New Zealand Local Chapter for the past two years. Last year, she attended the CRS Annual Meeting in Chicago, where she presented a poster.

Drug Delivery and Translational Research Update

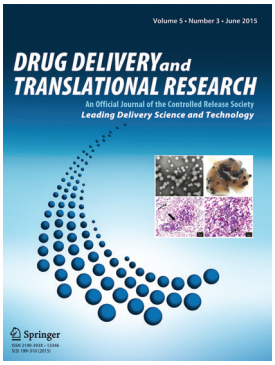
Vinod Labhasetwar, Editor-in-Chief, Cleveland Clinic, Cleveland, Ohio, U.S.A.



Vinod Labhasetwar

DDTR in PubMed, ISI, BIOSIS Previews, and Biological Abstracts

With recent indexing in PubMed, 11 theme issues, and over 250 articles published covering preclinical/clinical research to clinical trials, *DDTR* is poised to become a leading journal for publication of high-impact translational drug delivery science and technology research. Contributing authors to *DDTR* come from both academia and industry. With indexing in PubMed, all the articles published in *DDTR* appear in PubMed immediately. Because PubMed is a widely searched database, we hope that it will further increase citations of articles published in *DDTR*. Recently, Springer added a new feature that allows authors to check citations of their publications. In addition to PubMed, *DDTR* is now indexed by the Institute for Scientific Information (ISI), BIOSIS Previews, and Biological Abstracts, which are managed by Thomson Reuters. This all means we are closer to getting our first Impact Factor. Consider submitting your best cutting-edge scientific paper to compete for the 2015 outstanding *DDTR* research/clinical trial paper award (information at www.controlledreleasesociety.org/about/Awards/Pages/DDTROustandingPaper.aspx).



Ben J. Boyd Joins _DDTR_ as an Associate Editor

We are pleased to announce that Ben J. Boyd has joined *DDTR* as an associate editor. Prof. Boyd is a colloid and physical chemist with a Ph.D. from the University of Melbourne, Australia (1999). After industry experience in the explosives and pharmaceutical industries, in 2004 he commenced an academic position at Monash University, in what was then the Victorian College of Pharmacy, now Monash Institute of Pharmaceutical Sciences. He currently holds an Australian Research Council Future Fellowship. He leads a research group focused on colloidal and structural aspects of lipids, lipid self-assembly, and pharmaceutical systems, focused on controlling materials at the colloidal scale for delivery in pharma and other fields. He has published over 130 peer-reviewed publications on nanotechnology and nanomaterials for drug delivery, controlled release, colloidal drug delivery, and new techniques for the study of self-assembly systems. He is also an inventor on 13 patents and international patent applications. He was awarded the 2008 Grimwade Prize in Industrial Chemistry and the 2011 AAPS Outstanding Research in Lipid-Based Drug Delivery Award.

He is currently president of the Australian Local Chapter of CRS, past chair of the CRS Board of Scientific Advisors, a CRS Board member, and past secretary of the Colloid and Surface Science Division of the Royal Australian Chemical Society. He serves on the editorial boards *Journal of Pharmaceutical Sciences*, *Journal of Colloid and Interface Science*, *Journal of Pharmacy and Pharmacology*, *Journal of Liposome Research,* and *Current Drug Delivery*. He has coedited a special issue of *DDTR* based on the Drug Delivery Australia meeting in 2012 and has published three research papers in the journal.

Upcoming _DDTR_ Special Issue

The next *DDTR* special issue will be "Microneedles for Drug and Vaccine Delivery and Patient Monitoring," which will showcase emerging pharmaceutical, engineering, and formulation approaches to manufacture of microneedles while also looking at their applications in drug and vaccine delivery and minimally invasive patient monitoring and diagnosis. Topics include gene/drug delivery systems, vaccine delivery systems, and material design and production, with a strong focus on clinical translation and commercialization. Guest editors are Ryan Donnelly (r.donnelly@qub.ac.uk) and Dennis Douroumis (D.Douroumis@greenwich.ac.uk). ■

Moisture and Fragrance Release from Hydrogel Air Fresheners

Rutger M. T. van Sleeuwen,[a] Anaïck Nicolae, and Brian MacDougall
Firmenich, Inc., Plainsboro, NJ, U.S.A.

Introduction

Hydrogel air fresheners are often based on a gellant (e.g., carrageenan), water, and a fragrance. These devices typically have a mass of 200–300 g and are generally effective for about 30 days.[1] The hydrogel is usually held in a sealed container that is opened by twisting or pulling to expose the gel.[2] Under typical ambient conditions these gels dry, shrink, and release the fragrance contained within, albeit with decreasing intensity over time.[1,3]

In this study, the release of a fragrance from model κ-carrageenan hydrogel beads (Figure 1) simulating a typical air freshener is measured. The learnings from this study will aid in designing improved fragrance formulations for hydrogel air fresheners.

It is well-known that a typical liquid fragrance or perfume consisting of several ingredients will change in character as it evaporates. The evaporation of individual compounds is linked to the relative vapor pressure or volatility of each compound; the higher the vapor pressure, the more rapid the weight loss. This forms the basis for perfumery design: ranking chemicals as base, middle, and top notes. Additionally, as compounds deplete from the liquid, the headspace composition is altered, leading to nonlinear fragrances.[2] In this study, the mass transfer of a four-component model fragrance is studied from a spherical hydrogel and is compared with a simple liquid system using thermogravimetric analysis (TGA) in combination with gas chromatography–mass spectrometry (GC-MS).

Experimental Methods

A solution of κ-carrageenan (Ticaloid® 710 H, TIC Gums) at 2.85 wt%, 1% model fragrance (equal weight-parts of linalool, hexyl acetate, benzyl acetate, and isoamyl acetate), and 0.1% microbicide was prepared in deionized water at ~85°C using a high-speed agitation mixer. Hydrogel beads were prepared by prilling this solution into cold NEOBEE® medium-chain triglycerides. The beads were rinsed and then dried using TGA (TG209 F1 Libra®, Netzsch Instruments) connected to a GC-MS (Agilent 7820/5975) under defined settings (helium flow 80 mL/min, temperature 40°C). The instrument was used in bypass mode, in which released fragrance enters directly into the MS. The MS instrument was calibrated using a Payne diffusion cell (SMS, Allentown, PA) filled with a single liquid (chosen from the four components) and covering it with a polyethylene film. The rate of mass loss (mg/min) from this diffusion cell in the TGA was correlated to the MS abundance of the selected major ion in single-ion monitoring (SIM) mode.

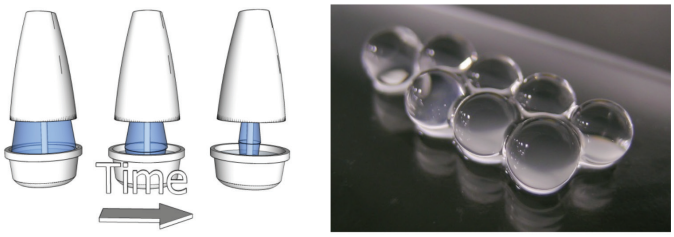


Figure 1. *Example of a typical commercial hydrogel air freshener (left), κ-carrageenan hydrogel beads (right, radius of several millimeters).*

Results and Discussion

Figure 2 shows cumulative release kinetics of fragrance compounds from a liquid mixture. The pie charts represent approximate headspace compositions (in wt% of the total fragrance) at different time points.

The evaporation profile of the liquid fragrance is initially dominated by isoamyl acetate, then hexyl acetate, followed by linalool and benzyl acetate, approximately following the order of decreasing vapor pressure (5.7, 1.4, 0.1, and 0.2 mm Hg at 25°C, respectively).[4] Isoamyl acetate is depleted after ~30 min, whereas benzyl acetate and linalool continue to evaporate for more than 2 h. The pie charts clearly show that the headspace composition is changing dramatically over time.

Moisture loss from the hydrogels loaded with the model fragrance mixture is summarized in Figure 3. These data are converted to moisture content (% wet basis), neglecting the 1% fragrance. The shape of the mass-loss curve is typical for a biological material that is drying, showing a constant-rate drying period followed by a falling-rate drying period.

Figure 4 shows that the overall fragrance (purple line) release from the hydrogel decreases dramatically as the sample dries. Analogous to the moisture loss, initial fragrance release is steep and rapid, followed by a decline as the mobility in the gel is reduced.

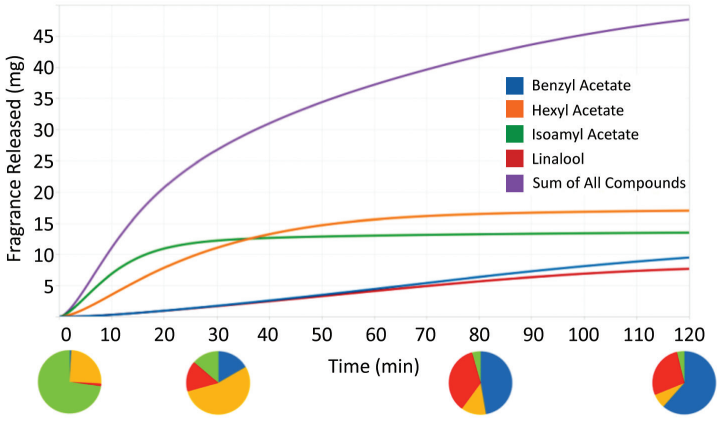


Figure 2. *Cumulative mass release of liquid mixture at 40°C analyzed by TGA–MS. Pie charts show approximate headspace compositions at time ~1, 30, 80, and 120 min.*

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The fragrance release profile of the hydrogel system showed a more linear character over time compared with the neat liquid mixture (compare pie charts). Although the amount of fragrance released diminished considerably over time, the fragrance retained its characteristic balance more or less. This probably underscores the utility of hydrogels in air freshener systems in their ability to linearize certain fragrance compositions.

Hydrogel beads containing the model fragrance stained with Nile Red were sectioned into flat, circular disks (radius of several millimeters) and observed while drying at room temperature using confocal microscopy. Time-lapse images were taken, and selected frames are shown in Figure 5.

Figure 5 shows that droplets close to the surface disappear relatively rapidly and completely. We acknowledge that this is the result a of complex mass transfer process in which various physical/chemical properties of the compounds will play a role (e.g., logP and Henry's Law constants). Another contributing factor is the receding front of drying hydrogel beads reducing the permeation distance for fragrance compounds to reach the bead surface.

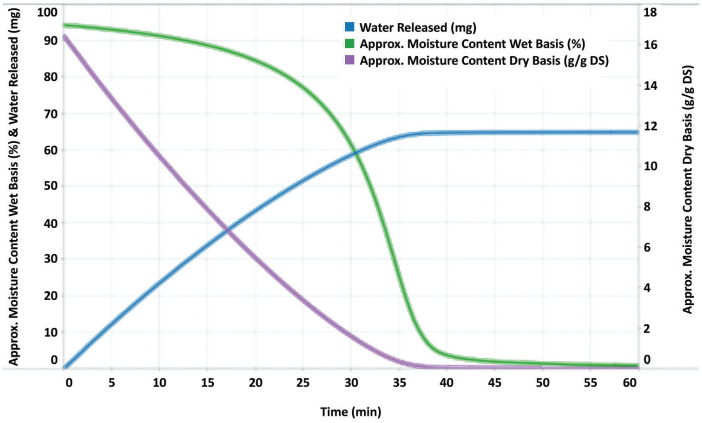

Figure 3. *Approximate moisture content of a hydrogel bead (% wet basis in green and dry basis in purple) and cumulative weight of water released versus time (blue).*

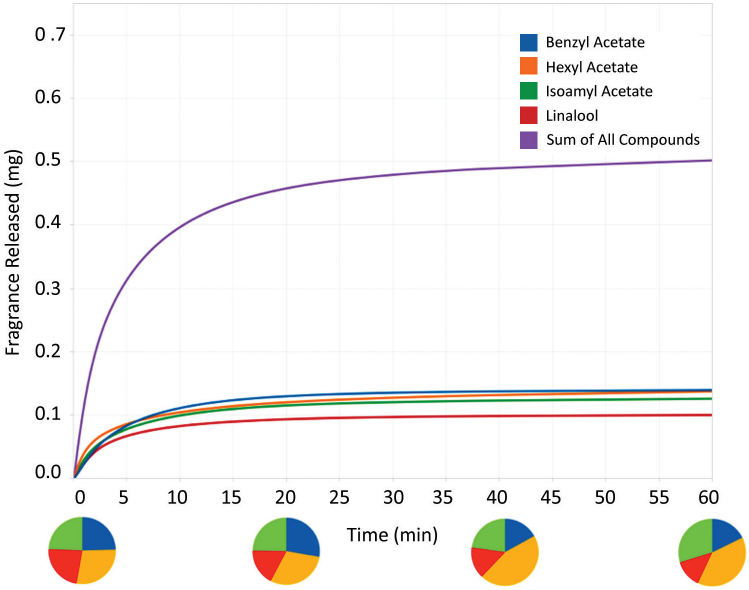

Figure 4. *Release at 40°C of four-compound mixture in hydrogel spheres analyzed by TGA-MS. Pie charts show approximate headspace compositions at time ~1, 20, 40, and 60 min.*

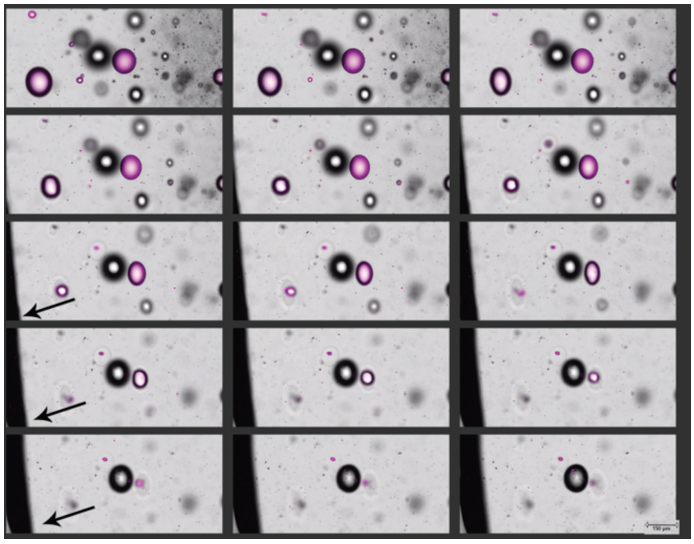

Figure 5. *Time-lapse images of confocal microscopy images (with bright-field overlay) showing depletion of fragrance droplets stained with Nile Red over the course of around 240 min. The arrow indicates the receding front of the hydrogel.*

Conclusions

Headspace composition of the model fragrance released from hydrogels was more linear with time compared with evaporating pure liquid fragrance. In other words, the hydrogel delivery system had a linearizing effect on this fragrance headspace composition. Microscopy observations showed that droplets near the receding surface released their fragrance relatively quickly and completely, as the distance over which they had to permeate was reduced. It is conceivable that if a fragrance composition is selected with more diverse chemicals, the physical/chemical properties of individual fragrance components and their mixture properties may play a more important role.

Acknowledgements

The contents of this manuscript were presented as an abstract and poster during the 2014 CRS Annual Meeting in Chicago, IL, U.S.A. We thank Gerald Allison and Nicholas O'Leary for their valuable insight and Huda Jerri for help on confocal imaging.

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3. Allison, G, O'Leary, N. Carrageenan gel air freshener, PCT patent application, WO 2013/030153 A1 (2013).
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Nanohydroxyapatite-Based MicroRNA Delivery on Collagen-Nanohydroxyapatite Scaffolds for Bone Tissue Engineering

Irene Mencía Castaño,[a,b,c] Caroline M. Curtin,[a,b,c] Garry P. Duffy,[a,b,c] and Fergal J. O'Brien[a,b,c]

Introduction

Critical-size bone defects impact life, health, and economy worldwide,[1] resulting in a clinical need for improved repair alternatives that can mimic the native bone structure (Figure 1A) and deliver factors to stimulate quick tissue repair. Tissue engineering approaches aim to regenerate the defect void by combining progenitor cells, tissue repair stimuli, and biomaterials (scaffolds). Collagen-nanohydroxyapatite (coll-nHA) scaffolds are composite biodegradable materials specifically designed in-house for bone repair and are capable of supporting plasmid DNA delivery[2] owing to the ability of nHA to complex with plasmid DNA,[3] resulting in reduced cell cytotoxicity in comparison to lipids and other synthetic vectors. MicroRNAs (miRNAs) are small noncoding nucleic acid molecules (Figure 1B) involved in posttranscriptional gene regulation, causing silencing effects over proteins, which have a critical role in stem cell osteodifferentiation[4] and are currently in need of efficient delivery systems. This study hypothesised that the bioactivation of coll-nHA scaffolds using nHA-based miRNA delivery is a promising and innovative bone regeneration approach (Figure 1C). The results of this study, published in the *Journal of Controlled Release*,[5] demonstrated that nHA particles serve as nonviral miRNA delivery vectors (nanomiR, Figure 1D), and coll-nHA scaffolds serve as supportive platforms for nanomiR delivery (miRNA-activated scaffolds, Figure 1E). Importantly, the platform has potential for enhancing stem cell–mediated tissue repair in a myriad of applications when combined with different therapeutic microRNA activators (miR-mimics) or inhibitors (antagomiRs).

Methods

nHA particles were synthesised by the precipitation method previously developed in the lab.[2] For nanomiR synthesis, nHA particles were combined *in situ* with an aqueous preparation of miRNAs. Scrambled, target-lacking miRNA molecules were used for transmission electron microscopy (TEM) analysis. coll-nHA scaffolds were manufactured using a freeze-drying technique.[3] miRNA activation was carried out by drop-wise addition of nanomiRs and assessed by scanning electron microscopy (SEM). Cytotoxicity of human mesenchymal stem cells (hMSCs) treated with scrambled (scr.) nanomiRs, in monolayer and coll-nHA scaffolds, was assessed using a PicoGreen assay. To determine uptake efficiency, hMSCs treated with fluorescently tagged nanomiRs (Dy547), in monolayer and coll-nHA scaffolds, were analysed by fluorescence microscopy. To determine nanomiR functionality, treatment with nanomiRs for silencing basally expressed targets in monolayer and coll-nHA scaffolds was followed by mRNA and miRNA quantitative polymerase chain reaction (qPCR). Glyceraldehyde phosphate dehydrogenase (GAPDH) and miR-16 were targeted by the reporter miR-mimic and antagomiR, respectively. Two-way ANOVA with the Tukey posthoc test was performed, and statistical significance was determined at $P < 0.05$ (*) and $P < 0.001$ (**).

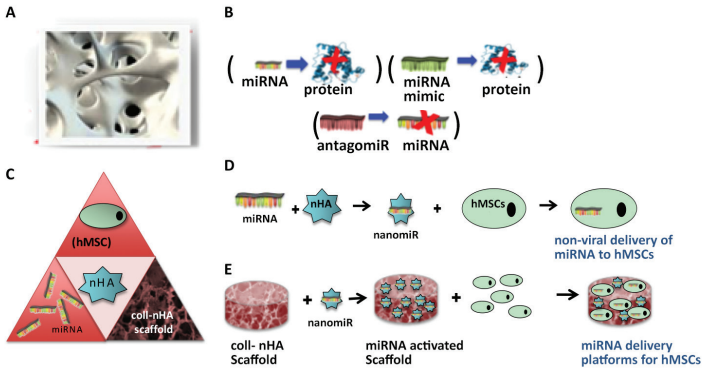

Figure 1. *Bone tissue engineering approach of miRNA delivery from bioactive scaffolds. (A) Native bone structure. (B) Types of miRNAs and final outcome of their silencing effects. (C) Elements combined in this project. (D) nHA-based miRNA delivery (nanomiR) to hMSCs. (E) nanomiR-activated scaffolds for three-dimensional culture of hMSCs.*

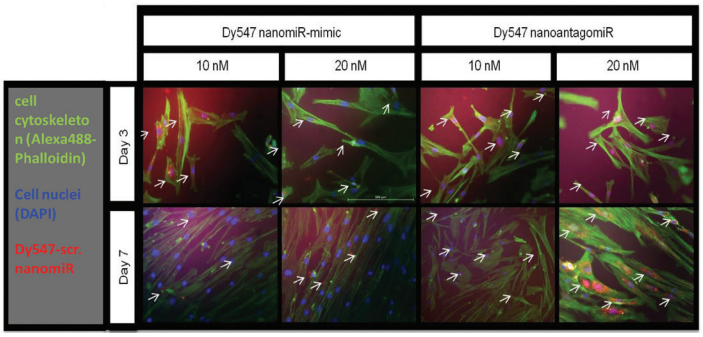

Figure 2. *Fluorescence microscopy showed varying degrees of uptake of nanomiRs by hMSCs, depending on the time and dose (n = 3, scale bar = 200 µm). © Elsevier; used by permission.*[5]

[a] Tissue Engineering Research Group, Department of Anatomy, Royal College of Surgeons in Ireland (RCSI), Dublin, Ireland.
[b] Trinity Centre for Bioengineering, Trinity College Dublin (TCD), Dublin, Ireland.
[c] Advanced Materials and Bioengineering Research Centre, RCSI and TCD, Dublin, Ireland.

Results

nHA Particles as Delivery Vectors for Reporter miRNAs. Uptake efficiency of red fluorescently labelled scrambled miR-mimics and antagomiRs was observed across all groups using fluorescence microscopy (Figure 2) and quantified by flow cytometry in 18–40% of hMSCs for the miRNA-mimic and antagomiR, respectively. Uptake efficiency was two- to threefold higher than that previously reported for nHA-plasmid DNA (pDNA) complexes.[2] More importantly, over 90% functionality in silencing the respective targets, GAPDH for miR-mimic reporters (Figure 3) and miR-16 for antagomiR reporters (Figure 4), was obtained using single administration of low-miRNA doses as compared with the literature. The level of silencing functionality detected was comparable to that reported for viral and lipid-based carriers, and the extent of this effect was maintained over a 7 day period.

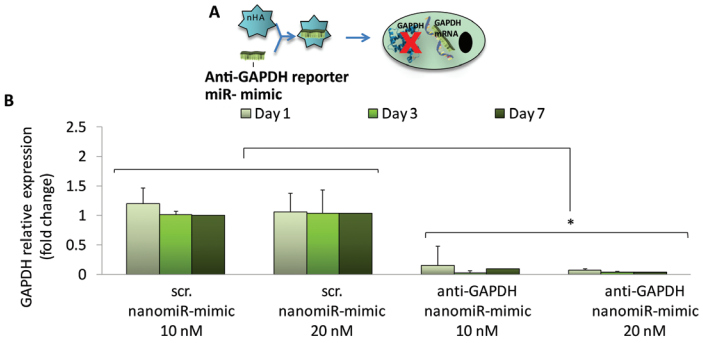

Figure 3. *Reporter nanomiR-mimic delivery achieved high silencing. (A) Schematic of the treatment with reporter miR-mimic, designed to decrease GAPDH expression. (B) Treatment significantly silenced the target GAPDH (n = 4,* indicates P < 0.05).*

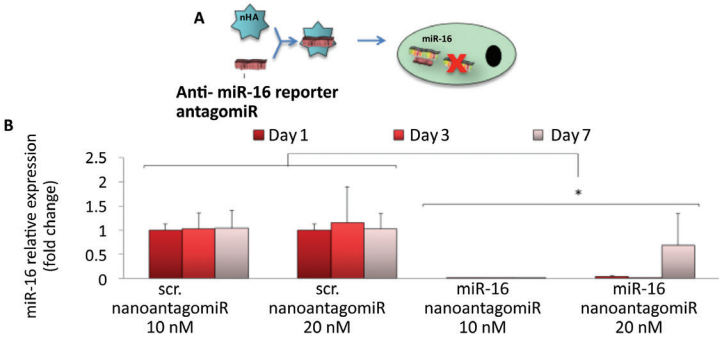

Figure 4. *Reporter nanoantagomiR delivery was highly functional. (A) Schematic of the treatment with reporter antagomiR, designed to decrease miR-16 expression. (B) Treatment significantly decreased miR-16 expression (n = 4,* indicates P < 0.05).*

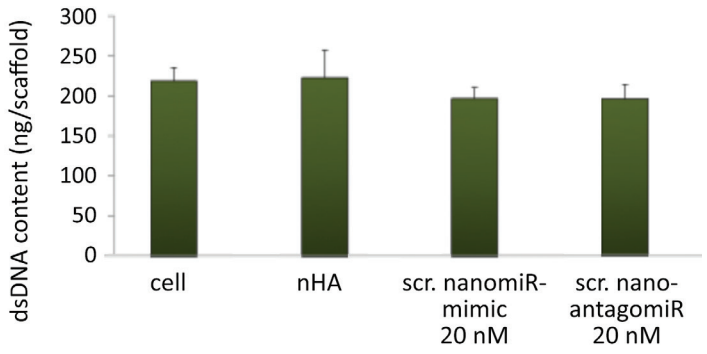

Figure 5. *Cell number (dsDNA content) was not affected after 7 days of culture on scrambled miRNA-activated scaffolds, demonstrating no association of cytotoxic effects with the treatment (n = 3, no statistical differences).*

Coll-nHA Scaffolds as nanomiR Delivery Platforms. The 20 nM nanomiR dose was selected following assessment of nanomiR loaded coll-nHA scaffolds in the second part of this work, utilising scrambled and reporter miR-mimics and antagomiRs. miRNA-activated scaffolds were seeded with hMSCs to assess delivery characteristics. The lack of cytotoxicity was demonstrated by means of a PicoGreen assay (Figure 5). Uptake assessment by fluorescence microscopy (Figure 6) showed a marked increase in calcein-AM green-labelled live cells between the two time points studied and confirmed the intracellular location of red fluorescently labelled miRNAs, resulting in yellow points in the overlaid images. Lastly, significant silencing functionality was demonstrated with the reported miR-mimics and antagomiRs, confirming successful posttranscriptional gene manipulation in these cells using the coll-nHA platform (Figure 7).

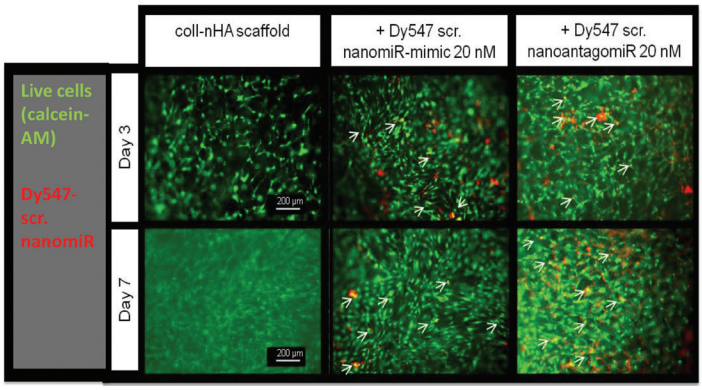

Figure 6. *Fluorescence microscopy showed successful uptake of nanomiR complexes within the miRNA-activated scaffolds (n = 3, scale bar = 200 µm). © Elsevier; used by permission.[5]*

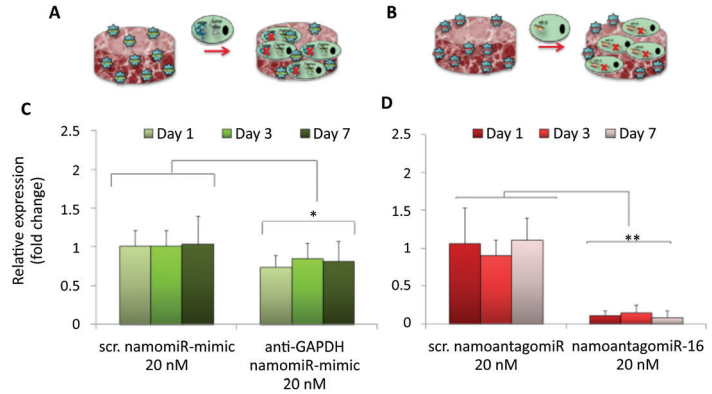

Figure 7. *Reporter mimic and antagomiR activated scaffolds retained significant silencing. Schematic of the treatment designed to decrease (A) GAPDH and (B) miR-16 expression. qPCR showed (C) significant GAPDH silencing and (D) significantly decreased miR-16 expression (n = 4,* indicates P < 0.05, and ** indicates P < 0.001).*

Scientifically Speaking Castano continued on page 18

Scientifically Speaking Castaño continued from page 17

Conclusion

The nHA particles delivered miRNAs to hMSCs safely and efficiently in monolayer and on coll-nHA scaffolds with effects of a single low dose of 20 nM miRNA maintained over 7 days. The functionality levels surpassed other lipid and synthetic vectors for this particular cell type, known to be difficult to transfect. Furthermore, miRNA delivery from coll-nHA scaffolds achieved efficient posttranscriptional gene manipulation in hMSCs, thus providing an exciting approach to enhance the therapeutic potential of these promising bioactive biomaterials for bone tissue engineering. This novel method of miRNA activation of scaffolds can be translated to numerous other tissue engineering applications. Future work will focus on the selection and assessment of candidate therapeutic (pro-osteogenic) miRNAs for incorporation into the bioactive coll-nHA scaffolds for bone regeneration both *in vitro* and *in vivo*.

Acknowledgements

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Raha Ahmad Khanbeigi
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Suha Zwayen

UKICRS Symposium

Maria Marlow and Laura Mason
University of Nottingham, United Kingdom

This year's annual UKICRS Symposium was hosted by the University of Nottingham on April 16–17 with a specially extended programme. The symposium opened with two parallel workshops: one called the "Early Researcher Forum" for our postgraduate students and an academic workshop focussing on U.K. and European research grants.

The Early Researcher Forum had over 70 attendees with Clare Jones (University of Nottingham Careers Service), Antony Williams (Royal Society of Chemistry), Arpan Desai (AstraZeneca), and Claire Madden-Smith (Molecular Profiles) speaking about how their careers have progressed and how postgraduates can best maximise their future prospects. At the academic workshop, Mark Gilbert and Christina Mellor (University of Nottingham) led a session promoting research collaborations and highlighting funding opportunities. Attendees had the chance to present research interests including elevator pitches and collaborative requests.

In the afternoon, we welcomed our industrial exhibitors, including Stable Micro Systems, Surface Measurement Systems, SOTAX, Biopharma Systems, AstraZeneca, and ISAC, who showcased their products and technologies through a series of short talks and exhibitions.

The scientific programme for the second day included two keynote speakers, 11 talks from postgraduate students and postdoctoral researchers, and 81 poster presentations, with a record 151 delegates in total. Francesca Greco (University of Reading) kicked off the morning session with a keynote lecture about polymer-drug conjugates and how recent developments are offering potential for combination therapies and antiangiogenic therapy.

The keynote lecture was followed by two short presentations: Laura Martinez-Marcos (University of Strathclyde) speaking about the use of hot-melt extrusion to enhance drug dissolution properties and Nichola Starr (University of Nottingham) describing the use of time-of-flight secondary ion mass spectrometry (TOF-SIMS) to monitor compound permeation through human stratum corneum. After the coffee break, three further short presentations were delivered. Francesca Citossi (University of Nottingham) discussed the use of low-molecular-weight gelators for targeted cancer therapy; Sameer Joshi (Aston University) talked about the use of a liposomal drug delivery system enabling coencapsulation of two antidiabetic drugs; and Mariarosa Mazza (University of Manchester) described the treatment of glioblastoma using peptide nanofiber vectors of siRNA.

This year's symposium drew a record number of delegates.

CRS president Art Tipton listens intently to a poster presenter.

Following a busy poster session and lunch, the afternoon session was opened by Ben Boyd (Monash University, Australia), who spoke about the digestion of lipid-based formulations. He highlighted how little we know about the digestion of everyday food products such as milk, and he discussed the implications and opportunities of the nanostructure formed during digestion. He was followed by Caroline Herron (Royal College of Surgeons in Ireland), who spoke about the development of a triggerable drug delivery system for use in critical limb ischaemia. Farah Arikat (Cardiff University) described the steps behind developing a microneedle delivery system for delivering antigen-specific immunotherapy. Riham El-Gogary (Ain Shams University, Egypt) spoke about using surfactants to coat poly(lactic-*co*-glycolic acid) (PLGA) nanoparticles, enabling brain targeting of antioxidants.

After more coffee and posters, three talks closed out the final session of the meeting. Fraser Crofts (Aston University) gave a presentation on producing cationic liposomes by microfluidics. Ana Cadete (University of Santiago de Compostela, Spain) described the development of antibody-loaded hyaluronic acid nanocapsules for anticancer drug therapy. Daniel Margetson (Diurnal Ltd.) discussed the development and manufacture of Infacort as a taste-masked hydrocortisone product for the paediatric population.

The meeting was concluded by UKICRS chair Gavin Andrews (Queen's University Belfast), who announced the winners of the best talk and poster awards. After a bumper year, we decided two prizes in each category! The prizes for best oral presentation were awarded to Caroline Herron and Ana Cadete, while the awards for best posters were awarded to Emma Leire (University of Nottingham) and Zahraa Al-Ahmady (University of Manchester).

Thank you to all delegates, sponsors, and speakers, and we look forward to welcoming you to Cardiff in 2016. ■

In the News

Compiled by Steven Giannos, Independent Consultant

July

Expanded Use for IntelliCap with Further CE Mark for Aspiration of Fluids

July 20, 2015 – EINDHOVEN, the Netherlands – The small, pill-shaped IntelliCap wireless medical device is opening up research opportunities into the impact of the small intestine microbiota on health and disease. For the first time, scientists have been able to obtain and analyse samples of the small intestine's microbiome in a noninvasive way.

This is likely to lead to a greater understanding of the significant role the gut microbiome plays in health and disease, and with it, opportunities for new therapeutics.

The IntelliCap CR system, which already had CE Marking for drug delivery and the real-time measurement of temperature and pH on the gastrointestinal tract, has recently been further approved for the aspiration of fluids. Measuring just 11 × 26 mm, IntelliCap was developed by Medimetrics, a company pioneered by Philips, with offices in Germany, the Netherlands, and the United States. The IntelliCap system is already being successfully used by the pharmaceutical industry for the targeted and controlled delivery of drugs into the gut.

"Understanding the environment of the small bowel is very difficult. For the first time, this device presents scientists with a convenient and noninvasive method of exploration," said Jeff Shimizu, chief technical officer, Medimetrics. "By extending its use, the IntelliCap technology has the potential to play an even more powerful role in the development of therapeutic products."

To demonstrate the capabilities of the IntelliCap fluid sampling technology, Medimetrics joined forces with NIZO food research and Wageningen University, also in the Netherlands. They carried out a pioneering research study that used the IntelliCap system to take samples from the small intestine. These were then sequenced and analyzed by scientists both at NIZO and the university. Preliminary results are encouraging, and their detailed findings are expected to be published in a prestigious journal later in 2015.

Dr. Michiel Kleerebezem, from the university's Host Microbe Interactomics Group, is one of the leaders in this study. He commented: "The role of the small intestine in human health is potentially of greater importance than that of the large bowel. However, using traditional methods, it has been very complicated to take samples, and this has held back research.

"We wanted to evaluate the IntelliCap performance in being able to gather gut samples and retain sample integrity so that we could study bacterial communities in the small intestine—which had previously been hard to access. While we cannot yet discuss our findings in detail, early indications are that the capsule presents a breakthrough for scientific research in the small intestine." Dr. Kleerebezem added: "Sampling using the IntelliCap enabled us to obtain reliable and well preserved small intestinal samples that more clearly and with higher resolution reflected the impact of treatment, as compared to faecal samples."

The small intestine is critical to health. It is where the absorption of approximately 90% of nutrients takes place and where important signals are generated to control our metabolism and immune function. Mounting scientific evidence shows that an imbalance in the "microbiota" in our gut is linked to a variety of diseases, including metabolic and immune disorders such as obesity, diabetes, and inflammatory diseases. However, most studies have targeted the microbial communities in faecal material and have not adequately addressed the possible role of the small intestine microbiota.

The project has been financially supported by the European Regional Development Fund as part of the OP-Zuid programme, and by the Dutch Ministry of Economic Affairs, Agriculture, and Innovation.

OptiNose Announces Positive Early Phase Clinical Trial with OPN-300, an Investigational Product in Development for Treatment of Autism Spectrum Disorders

Business Wire: July 15, 2015 – YARDLEY, PA, U.S.A. – OptiNose today announced positive results from an early phase trial of OPN-300, an investigational product in development for the treatment of autism spectrum disorders (ASD or autism), have been published in the peer-reviewed journal *Translational Psychiatry*. The publication reports the primary results from a randomized, placebo-controlled, double-blind, double-dummy, four-arm cross-over study comparing intravenous (IV) administration of the hormone oxytocin with two doses of OPN-300 (8 IU or 24 IU) delivered intranasally with a device incorporating the patented OptiNose Bi-Directional™ Breath Powered™ drug delivery system technology. OPN-300 is an investigational drug-device combination product that uses a unique new technology to deliver the hormone oxytocin deeply into the nose to target sites in the upper part of the nose. Target sites high in the nose are believed to have potential to enable or enhance direct-to-brain activity of drugs, particularly drugs that do not otherwise cross easily into the brain. The study evaluated social cognition and other effects of OPN-300 in 16 healthy adult volunteers. The results provided encouraging early phase evidence supporting direct nose-to-brain effects of oxytocin when delivered using the OptiNose technology, and have solidified OptiNose enthusiasm for further development of OPN-300. Currently there are no drugs approved anywhere in the world for the treatment of the core social deficiency of autism.

In this study low-dose OPN-300, despite producing similar blood levels as the control administration of IV oxytocin, resulted in statistically significantly greater brain (social-cognitive) effect, as measured using emotional ratings of facial images (the primary outcome). The findings of this study support the possibility of direct nose-to-brain effect, independent of blood absorption, with low dose OPN-300 using OptiNose Bi-Directional Breath Powered delivery technology. There is tremendous need for better therapies in many neurological, neurodegenerative, and psychiatric disorders.

"Researchers have been searching for a way to get improved and more reliable brain activity with many medications. These include oxytocin to treat diseases like ASD and schizophrenia, and a variety of other drugs for treatment of Alzheimer's and other brain diseases", said Ole A. Andreassen, M.D., Ph.D., professor, NORMENT – KG Jebsen Centre for Psychosis Research, Institute of Clinical Medicine, University of Oslo, and Division of Mental Health and Addiction, Oslo University Hospital, Oslo, Norway. "The OptiNose technology significantly changes the way drug is delivered high up in the nose, and may be the drug delivery solution we've been looking for. If we can improve social cognition in healthy people with OPN-300 low-dose oxytocin, then we may be able to address a core symptom suffered by millions of patients worldwide with autism."

"Nose-to-brain activity in humans has been sought after for years. It's important because getting medicine from a pill, or even an injection, into the brain to treat brain diseases is difficult due to a natural barrier that blocks most drugs in the blood from entering the brain. Nose-to-brain drug delivery could be an important way of solving the problem of getting drugs into the brain so they can do their job," said Per Djupesland, M.D., Ph.D., CSO, inventor of the technology, and one of the founders of OptiNose. "Although animal data has been encouraging, many would argue that medication transport from the nasal cavity directly to the brain has not been previously proven in humans. Today's results are quite promising and bolster our belief that we can enable and enhance the treatment of common brain disorders with OptiNose delivery technology." Work to initiate a phase II trial of OPN-300 in patients with autism has begun in Norway.

"Our pipeline is producing extremely encouraging results," said Peter Miller, chief executive officer of OptiNose. "AVP-825, the investigational product for migraine that we developed and out-licensed, is under review by the U.S. Food and Drug Administration, and we look forward to a positive decision in the second half of this year. Recently, we were pleased to report that our investigational product OPN-375, a potentially important new treatment for chronic nasal inflammatory diseases, met both of its primary endpoints in its first double-blind phase III trial: reduction in congestion/obstruction and in nasal polyp size. And now in this trial, OPN-300 produced promising results that suggest nose-to-brain activity that supports a development program on the path to a treatment for social-cognitive symptoms of autism. We plan to continue to develop these and other important products for people with needs that are not being met by today's therapies."

To access the online publication, please go to www.nature.com/tp/journal/v5/n7/full/tp201593a.html.

BD Opens Advance Diabetes Care Headquarters in Andover, Massachusetts

PRNewswire: July 15, 2015 – ANDOVER, MA, U.S.A. – BD (Becton, Dickinson and Company) (NYSE: BDX), a leading global medical technology company, officially opened its Advanced Diabetes Care facility in Andover, Massachusetts, which will house R&D and manufacturing of novel solutions for type 1 and type 2 diabetes.

"The opening of this facility represents an exciting opportunity for BD to accelerate the development of next-generation technologies to help simplify the management of type 1 and type 2 diabetes," said Dr. Ellen Strahlman, chief medical officer and executive vice president of research and development at BD. "This new model will help increase the rate of innovation and enable us to provide therapeutic advances in the diabetes care sector."

The Andover facility, which will serve as the new headquarters for BD's Advanced Diabetes Care platform, incorporates a "center of excellence" model, bringing R&D and manufacturing of solutions for type 1 and type 2 diabetes patients under one roof. The joining of multiple disciplines in one, central location allows for improved synergies in diabetes advancements. Approximately 100 associates will be located in the 75,000 square foot facility.

BD would like to recognize and thank the Massachusetts government officials and representatives of local organizations who participated in the ceremonial ribbon cutting.

BD is a leading medical technology company that partners with customers and stakeholders to address many of the world's most pressing and evolving health needs. Our innovative solutions are focused on improving medication management and patient safety; supporting infection prevention practices; equipping surgical and interventional procedures; improving drug delivery; aiding anesthesiology and respiratory care; advancing cellular research and applications; enhancing the diagnosis of infectious diseases and cancers; and supporting the management of diabetes. We are more than 45,000 associates in 50 countries who strive to fulfill our purpose of "helping all people live healthy lives" by advancing the quality, accessibility, safety, and affordability of healthcare around the world. In 2015, BD welcomed CareFusion and its products into the BD family of solutions. For more information on BD, please visit www.bd.com.

Enteris BioPharma Oral Formulation Progresses into Phase 2 Study with Cara Therapeutics's CR845

PRNewswire: July 14, 2015 – BOONTON, NJ, U.S.A. – Enteris BioPharma, Inc., an industry leader in innovative oral dosage formulations, today announced that it has entered into a new agreement for continued clinical testing with development partner Cara Therapeutics (Nasdaq: CARA) involving Cara's

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peripherally selective kappa opioid agonist, CR845, for the treatment of acute and chronic pain.

Cara's formulation of oral CR845 will continue to utilize Enteris's proprietary oral delivery technology under a renewed and revised manufacturing and clinical supply agreement. The new agreement includes technology access payments to Enteris and is representative of Enteris's broader "feasibility-to-licensing" strategy involving its peptide and small molecule oral drug delivery platform.

Brian Zietsman, president and CFO of Enteris BioPharma, commented: "We are pleased to be continuing our collaboration with Cara and with the progress of oral CR845. This collaboration and this new agreement showcase the value of Enteris's proprietary oral delivery technology to our strategic partners. The continuing clinical testing of oral CR845 is yet another validation of our oral drug delivery platform, which has been shown to be safe and well tolerated and has demonstrated clinically meaningful efficacy and enhanced bioavailability in phase 2 and phase 3 studies conducted by other partners."

Derek Chalmers, Ph.D., D.Sc., president and chief executive officer of Cara Therapeutics, remarked, "We continue to be very impressed with the bioavailability and bioactivity exhibited by the oral formulation of CR845 utilizing Enteris's proprietary technology, and we look forward to initiating our phase 2 study in osteoarthritis in Q3 of this year. In our estimation, oral CR845 has the potential to address a significant market opportunity in the treatment of acute and chronic pain for which there continues to be a very large unmet need for safer, nonabusable alternatives to narcotic opioids and NSAIDs."

Cara Therapeutics is a clinical-stage biopharmaceutical company focused on developing and commercializing new chemical entities designed to alleviate pain and pruritus by selectively targeting kappa opioid receptors. Cara is developing a novel and proprietary class of product candidates that target the body's peripheral nervous system and have demonstrated efficacy in patients with moderate-to-severe pain without inducing many of the undesirable side effects typically associated with currently available pain therapeutics.

Enteris BioPharma, Inc., is a privately held, New Jersey-based biotechnology company offering innovative formulation solutions built around its proprietary drug delivery technologies. Enteris's proprietary oral delivery technology has demonstrated a track record of success across a range of compounds and therapeutic indications and has also been the subject of numerous feasibility studies and active development programs, of which several are in clinical development. For more information on Enteris BioPharma and its proprietary oral delivery technology, please visit www.EnterisBioPharma.com.

Sinopharm Capital-Hefei Signs Letter of Intent with Oramed for $50,000,000 Investment and Licensing Deal in China

PRNewswire: July 7, 2015 – JERUSALEM, Israel – Oramed Pharmaceuticals Inc. (NASDAQ: ORMP) (www.oramed.com), a clinical-stage pharmaceutical company focused on the development of oral drug delivery systems, announced today that it has signed a nonbinding letter of intent for an investment and license agreement in China with Sinopharm Capital Management Co. Ltd. and Hefei Life Science & Technology Park Investments and Development Co., Ltd. (Sinopharm/Hefei) potentially valued at $50,000,000 plus royalty payments. Oramed will receive $500,000 in exchange for exclusively negotiating with Sinopharm/Hefei for 60 days, while the final terms of the agreement are negotiated and finalized.

The transaction, which additionally includes 10% royalties on sales, will allow Sinopharm/Hefei to purchase a roughly 10% stake in Oramed Pharmaceuticals and acquire rights for oral insulin in China. The terms are to be broken down as follows: Oramed will sell Sinopharm/Hefei 1,155,367 shares of common stock for approximately $12,000,000. In addition, Oramed's wholly owned subsidiary, Oramed Ltd., will license to Sinopharm/Hefei the exclusive rights to ORMD-0801, oral insulin capsule in China, for a total amount of $38,000,000, of which $18,000,000 will be paid upon the signing of the license agreement and the remaining $20,000,000 will be paid following the completion, and release of results, of Oramed's current phase IIb trial in the United States.

China National Pharmaceutical Group Corporation (Sinopharm) is the largest medical and healthcare group in China, which is directly managed by the State-owned Assets Supervision and Administration Commission of the State Council (SASAC), with the core businesses of distribution, logistics, retail, scientific research, and manufacture of healthcare related products. Sinopharm owns 11 wholly owned or holding subsidiaries and six listed companies. The sales revenue of Sinopharm exceeded $39 billion in 2014. Sinopharm Capital Management Co. Ltd. is a professional asset management company within Sinopharm.

Hefei Life Science & Technology Park Investments and Development Co., Ltd.'s (HLST's) business focus includes industrial investment and incubation services, high-tech product R&D, technology transfer, and related consulting services. HLST has state-of-the-art insulin production facilities in Hefei, China.

Oramed Pharmaceuticals is a technology pioneer in the field of oral delivery solutions for drugs currently delivered via injection. Established in 2006, Oramed's Protein Oral Delivery (POD™) technology is based on over 30 years of research by top scientists at Jerusalem's Hadassah Medical Center. Oramed is seeking to revolutionize the treatment of diabetes through its proprietary flagship product, an orally ingestible insulin capsule (ORMD-0801). Having completed multiple phase IIa clinical trials, the company has started its phase IIb on type 2 diabetes under an

Investigational New Drug application with the U.S. Food and Drug Administration. In addition, the company is developing an oral GLP-1 analog capsule (ORMD-0901).

For more information, please visit www.oramed.com.

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Tris Pharma and Pfizer Consumer Healthcare Enter into Agreement to Commercialize 12-Hour Extended Release Dextromethorphan Cough Syrup Under the Robitussin® Brand

PRNewswire: June 29, 2015 – MONMOUTH JUNCTION, NJ, U.S.A. – Tris Pharma, Inc. ("Tris") today announced that it has entered into a license, supply, and distribution agreement with Pfizer Consumer Healthcare.

Under the terms of the agreement, Pfizer Consumer Healthcare will commercialize Tris's extended release dextromethorphan cough syrup under the Robitussin® Brand. In exchange for providing Pfizer Consumer Healthcare U.S. branded rights to its protected intellectual property for an extended release dextromethorphan formulation, Tris will receive an upfront payment, milestone payments, and sales-based royalties. Tris will be responsible for manufacturing and regulatory activities while Pfizer Consumer Healthcare will manage sales, marketing, and distribution.

Pfizer Consumer Healthcare plans to launch extended-release Robitussin in July, prior to the 2015–2016 cough/cold season.

Dextromethorphan is indicated for the treatment of cough due to minor throat and bronchial irritation. According to the National Institute of Health (NIH), each year there are millions of cough/cold suffers, and for many of these patients self-medicating with long-acting dextromethorphan will be the preferred option.

Ketan Mehta, CEO of Tris commented, "The U.S. cough and cold market has been ripe for innovation, and when you consider that market research shows most patients prefer long-lasting relief in the form of a liquid, rather than a solid pill, our technology is well positioned to address this market. We are delighted to partner with Pfizer Consumer Healthcare and have our product marketed under the Robitussin® brand, the #1 pharmacist recommended for cough, cold, and flu combinations."

Tris Pharma is a specialty pharmaceutical company focused on drug delivery technologies based products including difficult-to-formulate or complex generic products. Through its OralXR+ platform, Tris has pioneered the delivery of sustained release in the liquid, chewable/ODT, and strip dosage forms so patients do not have to swallow a pill. Tris's Nobuse platform provides abuse-deterrence for opioids and other abuse-prone drugs. Tris's R&D and manufacturing facilities are located in Monmouth Junction, New Jersey. For more information, visit www.trispharma.com.

DURECT Announces Plans for a New POSIDUR™ (SABER®-Bupivacaine) Clinical Trial

PRNewswire: June 23, 2015 – CUPERTINO, CA, U.S.A. – DURECT Corporation (Nasdaq: DRRX) announced that, based on feedback from the FDA, it plans to conduct a new POSIDUR™ (SABER®-Bupivacaine) phase 3 clinical trial consisting of approximately 300 patients undergoing laparoscopic cholecystectomy (gallbladder removal) surgery. DURECT anticipates beginning the trial in the fall of 2015 and expects that it will take approximately one year to complete enrollment.

"With the FDA's guidance in hand, we now have a clear path forward for POSIDUR," stated James E. Brown, president and CEO of DURECT. "We believe that the data from this additional clinical trial will be supportive of the data we have seen in our other pivotal trials in hernia repair and shoulder surgery, and that these three pivotal trials will support a robust NDA resubmission, for which there would be a 6 month review per PDUFA guidelines. We have previous clinical trial experience with laparoscopic cholecystectomy, which is one of the most common general surgeries performed in the United States each year. We believe this is an excellent surgical model and that our overall clinical program for POSIDUR will support a broad label."

The study will be a randomized, parallel-group, double-blind, placebo-controlled, multicenter trial of POSIDUR in patients undergoing laparoscopic cholecystectomy. The objective of the study will be to evaluate the safety and efficacy of POSIDUR for the management of postoperative pain. Approximately 300 patients will be randomized on a one-to-one basis to receive either POSIDUR or placebo as a one-time intra-incisional instillation at the close of surgery. The primary efficacy endpoint will be pain intensity on movement over 0–72 hours after surgery.

Cholecystectomy is a surgical procedure for removal of the gallbladder. Laparoscopic cholecystectomy, which is done using a camera and instruments inserted through a set of small incisions in the abdomen, has largely supplanted the traditional open approach, which requires an abdominal incision several inches in length. Approximately 800,000 such procedures are performed in the United States each year, most of them on an outpatient basis.

In a previous clinical trial consisting of 50 patients, when using the statistical analysis that will be employed in the upcoming trial, POSIDUR demonstrated an approximately 25% reduction in pain intensity on movement for the first 3 days after surgery ($p = 0.0235$) when compared with the active control bupivacaine hydrochloride.

POSIDUR is an investigational postoperative pain relief depot that utilizes our patented SABER technology and is intended to deliver bupivacaine to the surgical site to provide up to three

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days of pain relief after surgery. We are in discussions with potential partners regarding licensing development and commercialization rights to POSIDUR, for which we hold worldwide rights, while at the same time we are evaluating whether to commercialize POSIDUR on our own in the United States in the event that we determine that is the preferred route of commercialization.

Teva and Microchips Biotech Announce Partnership to Enhance Patient Outcomes Through Digital Drug Delivery Technology

Business Wire: June 18, 2015 – JERUSALEM, Israel, and LEXINGTON, MA, U.S.A. – Teva Pharmaceutical Industries Ltd. (NYSE: TEVA) and Microchips Biotech, Inc., today announced that they have entered into a partnership under which the companies will explore innovative ways to apply Microchips Biotech's implantable drug delivery device to Teva's portfolio of products with the goal of enhancing clinical outcomes for patients on chronic drug therapies. Microchips Biotech's electronic device is made up of microchip arrays that can store hundreds of therapeutic doses of drug for periods ranging from months to years and releases each dose at precise times. The device can be programmed to release drug on a predetermined schedule and will have wireless control features.

"The microchip-based implant is truly at the intersection of digital technology and medicine and the future of drug delivery for patients who cannot tolerate needles, require regular self-administered injections or where compliance is critical to outcomes," stated Michael Hayden, M.D., Ph.D., Teva's president of global R&D and chief scientific officer. "At Teva we are leading innovation in medicine with promising new drugs and solutions for drug adherence to improve patient outcomes and reduce unnecessary healthcare complications."

Under the terms of the agreement Teva will make a $35 million upfront payment to Microchips Biotech in the form of an equity investment and technology access fee. The partnership has an initial focus on one selected disease area but will provide Teva with the option to later expand the program into several additional therapeutic areas and sensing applications that are proprietary to Teva. As programs advance, Microchips Biotech will receive development and commercial milestone payments and royalties on future product sales. Microchips Biotech will also receive funding to develop products for any future additional indications Teva may develop, and Teva will be responsible for phase II and phase III clinical development and regulatory filings. "We are thrilled to be aligned with an organization that sees the potential of our technology to transform the way medications are delivered to patients, providing the potential to increase compliance and significantly improve outcomes," stated Cheryl R. Blanchard, Ph.D., chief executive officer of Microchips Biotech. "This is the first of what we hope to be many partnerships with industry to leverage our technology across a broad array of therapeutic applications and disease states."

Mission Pharmacal's Innovative Partnerships Fuel Rapid Growth

PRNewswire: June 18, 2015 – SAN ANTONIO, TX, U.S.A. – Mission Pharmacal Company has implemented a diversification strategy utilizing partnerships and acquisitions to continue to build on the company's nearly seven decades of success and excellence. President Neill "Gobie" Walsdorf, Jr., announced earlier this month that the Mission family of companies has expanded its specialty manufacturing capabilities with the acquisition of the assets of ProSolus Pharmaceuticals, LP, headquartered in Miami, Florida.

"The acquisition of ProSolus gives Mission exceptional expertise in the development and manufacturing of sophisticated and convenient transdermal (through the skin) drug delivery products to treat a variety of health conditions," says Walsdorf. "We're excited that we now have the opportunity to bring the convenience of well-designed and effective transdermal patches to healthcare providers and patients across the country."

The acquisition of ProSolus and its complete transdermal manufacturing operation further adds to Mission's already broad and progressive manufacturing vision. The company's state-of-the-art manufacturing campus in Boerne, Texas, features the latest high-capacity equipment for production of tablets, gels, liquids, creams, and semi-solids. Mission's expertise in solid dose tablet manufacturing has earned it international manufacturing agreements, including manufacturing Citracal® for Bayer Consumer Care and its affiliate companies.

By creating select forward-looking national and international partnerships, the company continues to grow and improve its portfolio with leading prescription and over-the-counter healthcare solutions in its core therapeutic areas of focus including women's health, urology, pediatrics, and dermatology with newly expanded reach into primary care and long-term care markets. The company formed wholly owned subsidiaries Alamo Pharma Services, a specialized turnkey contract sales organization founded in 2011, and BioComp Pharma, a generic drug marketer started in 2009.

Through Alamo Pharma Services, Mission offers full commercial support to its own sales teams as well as several partner pharmaceutical companies. Alamo also offers an exceptional customized prescription drug sampling solution for direct-to-physician promotion for turnkey management systems with electronic data interchange (EDI) capabilities and for national and international distribution services to clients' warehouses or directly to end users.

Mission's most rapidly growing area is its dermatology division founded in 2012 to help healthcare providers address chronic and one-time dermatological conditions affecting quality of life. The company's specially trained dermatology sales force already spans across the United States. These field representatives work closely with the healthcare community to provide product support and education to patients. Mission dermatology

offerings effectively treat acne, atopic dermatitis, secondary bacterial infections, and skin inflammation. Mission anticipates further expansion in the dermatology arena later this year.

Mission took another significant step in 2014 with the launch of a new primary care sales force to help reach more physicians and patients with select innovative dermatology, women's health, and pediatric products. The primary care sales team's strategic focus complements the work of Mission's specialty sales forces. Current product development, additional commercial partnerships, and acquisitions are expected to maximize the impact of this team as well as expand their reach.

On the international front, Mission has established consumer and prescription partnerships with the U.K. in two separate ventures to provide greater access for Mission's products in Europe. "These recent expansions are taking the company to a whole new level of national and global reach," says Walsdorf. "The years ahead promise to be exciting as Mission Pharmacal looks forward to the future to continue our history of meeting healthcare needs with the most innovative and effective products through both organic growth and our unique ability to partner with other companies."

To learn more about Mission Pharmacal Company and their business model or to discuss business opportunities, please visit missionpharmacal.com.

Bayer HealthCare and Johns Hopkins University Collaborate to Develop New Ophthalmic Therapies

PRNewswire: June16, 2015 – LEVERKUSEN, Germany – Bayer HealthCare and Johns Hopkins University in Baltimore have entered into a five-year collaboration agreement to jointly develop new ophthalmic therapies targeting retinal diseases. The partners will jointly work on the discovery and development of innovative drugs for the treatment of serious back-of-the-eye diseases that affect many people worldwide, including age-related macular degeneration (AMD), diabetic macular edema (DME), geographic atrophy, Stargardt's disease, and retinal vein occlusion (RVO).

"Bayer is strongly committed to further expanding its research efforts in the area of retinal diseases," said Prof. Andreas Busch, head of global drug discovery and member of the executive committee of Bayer HealthCare. "The Wilmer Eye Institute's deep understanding of eye disease biology and patient care and Bayer's expertise in drug discovery and development in ophthalmology complement each other perfectly. We are pleased to partner with this renowned institute, which is among the leading scientific and clinical institutions in ophthalmology worldwide."

The goal of the strategic research alliance is to accelerate the translation of innovative approaches from the laboratory to the clinic, ultimately offering patients new treatment options for several retinal diseases.

"There is a critical need for new therapies that treat a variety of serious diseases of the eye," said Peter J. McDonnell, director of the Wilmer Eye Institute and professor of ophthalmology at the Johns Hopkins University School of Medicine. "Additional research will allow us the opportunity to make significant advances in this area."

Under the agreement, Bayer and the Wilmer Eye Institute of Johns Hopkins will jointly conduct research activities evaluating new targets and disease mechanisms, drug delivery technologies, and biomarkers for back-of-the-eye diseases with high unmet medical need. Both parties will contribute personnel and infrastructure to address important scientific questions. Bayer will have an option for the exclusive use of the collaboration results. Financial terms of the agreement were not disclosed.

FDA Approves ZOMIG® (Zolmitriptan) Nasal Spray for Migraine in Pediatric Patients (Ages 12–17)

PRNewswire: June 16, 2015 – HAYWARD, CA, U.S.A. – Impax Specialty Pharma, a division of Impax Laboratories, Inc. (NASDAQ: IPXL), announced today that the U.S. Food and Drug Administration (FDA) has approved ZOMIG nasal spray for use in pediatric patients 12 years of age and older for the acute treatment of migraine with or without aura.

ZOMIG nasal spray is the first nasal-delivered prescription medicine approved for the treatment of acute migraine attacks in pediatric patients. Nasal sprays may offer an alternative method of administration when patients experience migraine-associated nausea, have difficulty taking oral formulations, or do not have liquids available.

ZOMIG nasal spray's approval came after the FDA's review of safety and efficacy data from pivotal clinical trials demonstrating that ZOMIG nasal spray 5 mg is significantly more effective than placebo in providing no headache pain, relief of headache, and other associated symptoms of migraine when treating migraine in pediatric patients. In clinical trials, the medication also had a safety profile similar to that demonstrated in adults. For full safety and efficacy information, please see the prescribing information.

The American Migraine Prevalence and Prevention (AMPP) Study estimated the one-year prevalence of migraine among U.S. children ages 12 to 19 at 6.3%, with prevalence among boys at 5.0% and among girls 7.7%. "Until now, there have been few medications to treat pediatric patients with painful, debilitating attacks of migraine," said Dr. Alan M. Rapoport, past president of the International Headache Society and clinical professor of neurology at the David Geffen School of Medicine. "We are pleased that ZOMIG nasal spray has been approved by the FDA for use in patients ages 12 to 17."

"Treatment options have been limited for pediatric patients, and we are pleased with FDA's decision and look forward to bringing migraine relief to pediatric patients by making ZOMIG nasal

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spray available to this 'school age' patient population," said Fred Wilkinson, president and chief executive officer of Impax Laboratories. "This expanded indication exemplifies our strategy to broaden the reach of our current product portfolio to address unmet needs in underserved therapeutic areas, thereby adding value for patients and shareholders alike."

The recommended starting dose for ZOMIG nasal sprays in pediatric patients 12 years of age and older is 2.5 mg. As the individual response to ZOMIG nasal spray may vary, the dose should be adjusted on an individual basis. The maximum recommended single dose of ZOMIG is 5 mg. The maximum daily dose should not exceed 10 mg in any 24-hour period.

ZOMIG nasal spray was first approved by the U.S. Food and Drug Administration (FDA) in September 2003 for the acute treatment of migraine attacks, with or without aura, in adults. In clinical trials, ZOMIG nasal spray provided relief in as soon as 15 minutes for some patients, and the maximum effect was reached within 2–4 hours for most adult patients. At 2 hours, 69% of patients taking the 5 mg dose had headache response (taking the patient from moderate to severe pain to mild or no pain) and 36% were pain free.

ZOMIG nasal spray is a serotonin (5-HT)1B/1D receptor agonist (triptan) indicated for the acute treatment of migraine with or without aura in adults and pediatric patients 12 years and older.

Smoke – Less: Nicofi™ Unveils New Alternative to Smoking with a Fast-Acting Pure Nicotine Tablet

Business Wire: June 15, 2015 – MIAMI, FL, U.S.A. – Nicofi™ announced the launch of a revolutionary patented, fast-acting dissolvable nicotine tablet intended for use as an alternative to smoking. Nicofi is a small sublingual tablet made from pure nicotine and other high-quality ingredients that allows smokers to quickly enjoy nicotine in any situation, especially when they are unable to smoke a cigarette or e-cigarette. This will be welcomed news to the estimated 42 million Americans who do smoke.

Nicofi, which is made in the United States, uses the finest pharmaceutical-grade materials and includes only eight ingredients. There is no tar, tobacco, formaldehyde, or any harmful ingredients. By comparison, cigarettes contain approximately 600 ingredients and, when burned, create more than 7,000 chemicals, 69 of which are known to cause cancer, according to the American Lung Association.

Available in packs of 20 tablets, Nicofi is meant for adults who are looking to substitute the use of cigarettes and e-cigarettes. It is recommended to take one tablet at a time without exceeding 20 tablets per day.

With its breakthrough, patented IntraTab™ drug delivery technology, Nicofi was studied in controlled trials and clinically proven to deliver nicotine quickly, similar to smoking a cigarette, but without the harmful dangers of tar, tobacco, carcinogens, vapors, or odors found in cigarettes or e-cigarettes. Nicofi's proprietary speed of action is two to three times faster than nicotine gum and lozenges. This gives smokers permission to enjoy nicotine quickly and conveniently in places where they are prohibited from smoking and vaping such as airplanes, trains, museums, public buildings, offices, schools, hotels, bars, restaurants, stadiums, arenas, and other locations or situations.

Nicofi is a sublingual tablet, which gets placed under the bottom of the tongue and dissolves without chewing or swallowing, to deliver a strong, fast rush of nicotine. The IntraTab drug delivery technology allows Nicofi to disintegrate and release a solution of nicotine directly into the bloodstream through the lining of the mouth. Nicofi works about as quickly as smoking a cigarette or e-cigarette, unlike nicotine polacrilex gum or lozenges, which take longer to deliver nicotine. One Nicofi tablet is equivalent to the approximate amount of nicotine received from one cigarette.

Nicofi is now available at select retailers and on www.nicofi.com. For additional information about Nicofi, visit www.nicofi.com.

Ruthigen and Pulmatrix Stockholders Approve Merger

PRNewswire: June 12, 2015 – SANTA ROSA, CA, and LEXINGTON, MA, U.S.A. – Ruthigen, Inc. ("Ruthigen") (NASDAQ: RTGN) and Pulmatrix Inc. ("Pulmatrix") today announced that at Ruthigen's special meeting of stockholders held on June 12, 2015, Ruthigen obtained sufficient votes for each proposal required to consummate the previously announced proposed merger between Ruthigen and Pulmatrix. Pulmatrix previously obtained a sufficient number of written consents from its stockholders to consummate the merger.

Ruthigen did not obtain sufficient votes to approve the proposal to declassify its board of directors; however, such approval was not required to consummate the merger.

Pursuant to the agreement and plan of merger, dated as of March 13, 2015, by and among Ruthigen, Pulmatrix, and Ruthigen Merger Corp., a wholly owned subsidiary of Ruthigen ("Merger Sub"), Merger Sub will merge with and into Pulmatrix (the "merger"), with Pulmatrix surviving the merger as a direct wholly owned subsidiary of Ruthigen. Immediately prior to the merger, Pulmatrix will change its name to "Pulmatrix Operating Company, Inc." (the "Pulmatrix name change"), and Ruthigen will change its name to "Pulmatrix, Inc." (the "Ruthigen name change"). Immediately following the merger, the combined company will effect a 1-for-2.5 reverse stock split of its common stock (the "reverse stock split"). Ruthigen and Pulmatrix made filings with the office of the Delaware Secretary of State (the "Secretary of State") today in order to give effect to the Ruthigen name change, the Pulmatrix name change, the reverse stock split, and the merger. Subject to the acceptance of these filings by the Secretary of State, Ruthigen and Pulmatrix expect the Ruthigen name change, the Pulmatrix name change, the reverse stock split, and the merger to become effective after market hours on Monday, June 15, 2015.

Subject to the aforementioned acceptance by the Secretary of State of the filings made by Ruthigen and Pulmatrix, the combined company will be named "Pulmatrix, Inc." and expects to begin trading on NASDAQ under the symbol "PULM" at the opening of trading on June 16, 2015.

Ruthigen is a biopharmaceutical company focused on the discovery, development, and commercialization of novel therapeutics designed to prevent and treat infection in invasive applications. The company's lead drug candidate, RUT58-60, is a broad-spectrum anti-infective that Ruthigen is developing for the prevention and treatment of infection in surgical and trauma procedures. For more information, visit www.ruthigen.com.

Pulmatrix is a clinical stage biotechnology company advancing a new generation of inhaled therapeutics in a novel dry powder delivery platform. The platform, called iSPERSE (inhaled small particles easily respirable and emitted), represents a new paradigm in inhaled drug delivery using particle engineering to create dry powders with unique properties: aerodynamically small, dense particles with highly efficient dispersibility and delivery to the airways. The iSPERSE powders can be used with an array of dry powder inhaler technologies and can be formulated with virtually any drug substance. Pulmatrix is advancing a pipeline of products including PUR0200, a once-daily inhaled bronchodilator for chronic obstructive pulmonary disease, and PUR1900, an inhaled anti-infective for the treatment of cystic fibrosis. Both PUR0200 and PUR1900 are developed using Pulmatrix's iSPERSE technology.

Mission Pharmacal Acquires ProSolus Pharmaceuticals

PRNewswire: June 9, 2015 – SAN ANTONIO, TX, U.S.A. – Effective May 29, 2015, Mission Pharmacal Company ("Mission") has acquired the assets of ProSolus Pharmaceuticals LP headquartered in Miami, Florida. Mission's wholly owned subsidiary, ProSolus Inc., offers unrivaled expertise in the development and manufacturing of sophisticated and convenient transdermal (through the skin) drug delivery products to treat a variety of health conditions.

"ProSolus is the new jewel in Mission's crown as a manufacturing supplier," says Pete Valko, chief operating officer of ProSolus Inc., who is adding this to his responsibilities as chief operating officer of BioComp Pharma. "To expand Mission's offerings, ProSolus brings high-barrier-to-entry transdermal solutions and a top-notch manufacturing facility with its own research and development arms. Mission's goal is to deliver this exceptional science and skill into customers' hands through innovative and convenient products."

ProSolus will operate with former ProSolus CEO Juan Mantelle continuing in executive leadership to oversee research and development as chief scientific officer. ProSolus enables Mission to offer the latest highly effective transdermal patches in a wide variety of therapeutic categories.

ProSolus will complement and work in tandem with the Mission family of companies. This includes wholly owned subsidiaries BioComp Pharma, a generic drug company formed in 2009, and Alamo Pharma Services, a specialized contract sales company founded in 2011.

This acquisition fits with Mission's mantra to improve patient access to products that significantly improve quality and enjoyment of life. Few therapies on the market today are as effective or easy to use as noninvasive, comfortable transdermal patches.

"Juan Mantelle and the ProSolus team excel in the design aspects of transdermal products. It's really an art more than a science," says Terry Herring, president of commercial operations, Mission Pharmacal. "They have significantly improved the wearability of transdermal patches, creating more desirable, smaller sizes that stay in place while working effectively. This design strength combined with state-of-the-art manufacturing capabilities gives us vast potential to quickly deliver patient-friendly transdermal solutions."

In fact, about five years ago, Mission began a successful partnership with ProSolus and Richmar Corporation to produce the LidoFlex™ pain relief patch. This patch conveniently delivers a 4% concentration of lidocaine, the highest available without a prescription, to provide targeted pain relief. The LidoFlex line includes assorted, extremity-specific sizes and shapes to provide localized pain relief without systemic or habit-forming medications. The long-lasting patches can be worn while exercising, bathing, or swimming for consistent relief. The LidoFlex trademark designated herein is proprietary to Naimco, Inc., its affiliates and licensors.

Aggressive development of unique partnerships such as this one has led to Mission's significant and substantial growth and rapid diversification in recent years. The expansion into transdermal delivery through the ProSolus acquisition continues to build on Mission's founding principle of finding ways to solve unmet healthcare needs with novel solutions.

The Mission Pharmacal family of companies offers complete pharmaceutical manufacturing, printing, packaging, distribution, and sales services to other biotech and pharmaceutical companies tailored as required for partner company needs. For more information or to contact a Mission team member, please visit missionpharmacal.com, prosoluspharma.com, biocomppharma.com, or alamopharma.com.

FDA Grants IND Approval for Phase IIa Clinical Trial Using Stemedica's itMSC Therapy to Treat Alzheimer's Disease

PRNewswire: June 9, 2015 – SAN DIEGO, CA, U.S.A., and EPALINGES, Switzerland – Stemedica Cell Technologies, Inc., received the FDA's investigational new drug (IND) approval for a U.S.-based, phase IIa clinical study using its allogeneic stem-cell

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therapy to treat subjects with mild to moderate dementia due to Alzheimer's disease (AD), the sixth leading cause of death in the United States. The study is sponsored by Stemedica International, S.A., and will start at the University of California, San Diego (UCSD) under principal investigator Douglas Galasko, M.D., and expand to other sites. Stemedica International will provide management and financial support for this clinical trial. The clinical trial is titled "A Phase IIa Multicenter, Randomized, Single-Blind, Placebo-Controlled, Crossover Study to Assess the Safety, Tolerability, and Preliminary Efficacy of a Single Intravenous Dose of Allogeneic Human Mesenchymal Stem Cells in Subjects with Mild to Moderate Dementia Due to Alzheimer's Disease."

"This study was approved based on the excellent safety profile of Stemedica's cGMP-manufactured, hypoxically grown stem cells and on solid preclinical data obtained by Stemedica International in cooperation with the École Polytechnique Fédérale de Lausanne of Switzerland and with a grant from the Swiss government," said Lev Verkh, Ph.D., Stemedica's chief regulatory and clinical development officer. He continued, "We are very proud of Stemedica's clinical program under U.S. INDs for several indications including ischemic stroke, acute myocardial infarction, chronic heart failure, cutaneous photoaging, and Alzheimer's disease. At the study's conclusion we will understand if our approach is efficacious versus placebo in subjects with Alzheimer's-related dementia, as evidenced by neurologic, functional, and psychiatric endpoints."

Stemedica's bone marrow–derived, allogeneic itMSCs are unique because they are grown under hypoxic conditions that more closely resemble the environment in which they live in the body. Compared to other MSCs, itMSCs secrete higher levels of growth factors usually associated with angiogenesis and healing. Stemedica International's AD stem cell therapies feature itMSCs, neural stem cells (NSCs), and stem cell factors, which are described in Stemedica International's U.S. patent application #20140286910.

Promising results were achieved during a three-year, intensive, preclinical research project supported by a grant from the Swiss Commission for Technology and Innovation (CTI). The research was conducted at the Laboratoire d'Optique Biomedicale headed by Prof. Theo Lasser at École Polytechnique Fédérale de Lausanne (EPFL) in Switzerland.

Stemedica International's preclinical research was led by chief scientist Tristan Bolmont, Ph.D. To evaluate the impact of an intravenous delivery of human mesenchymal stem cells on amyloid pathology, the well-established APPPS1 transgenic mouse model of Alzheimer's disease was used. Intravenous delivery of itMSC safely reduced cerebral Abeta pathology in APPPS1 animals analyzed one week after the last injection. Both aged and young APPPS1 mice exhibited significantly decreased Abeta amyloidosis following the itMSC treatments. Concomitantly, microglial activation was diminished in aged and young itMSC-treated APPPS1 mice. No increase of vascular amyloid or manifestation of microhemorrhages was observed following the repeated intravenous itMSC delivery. Biodistribution analysis revealed that intravenously delivered itMSC migrate to the brain and could be detected in this organ with the highest value at one hour postdelivery, decreasing after one day and subsequently dropping below detection level at one week after the injection.

According to Alzheimer's Disease International, nearly 44 million people have Alzheimer's or a related dementia. Alzheimer's and dementia are most common in Western Europe, followed closely by North America. The global cost of Alzheimer's and dementia is estimated to be US$605 billion, which is close to 1% of the world's gross domestic product.

"We are very excited to take this next step in developing a treatment for this devastating disease," says Nikolai Tankovich, M.D., Ph.D., president and chief medical officer of Stemedica Cell Technologies and executive chairman for Stemedica International. "Our upcoming phase IIa clinical trial will enable us to make progress toward determining if our stem cell treatment may be able to halt or slow down the progression of Alzheimer's disease and other forms of dementia."

Stemedica Cell Technologies, Inc., is a global biopharmaceutical company that manufactures best-in-class allogeneic adult stem cells and stem cell factors. The company is a government-licensed manufacturer of cGMP, clinical-grade stem cells currently used in U.S.-based clinical trials for acute myocardial infarction, chronic heart failure, cutaneous photoaging, ischemic stroke, and Alzheimer's disease. Stemedica's products are also used on a worldwide basis by research institutions and hospitals for preclinical and clinical (human) trials. Stemedica is currently developing additional clinical trials for other medical indications using adult, allogeneic stems cell under the auspices of the FDA and other international regulatory institutions. The company is headquartered in San Diego, California, and can be found online at www.stemedica.com.

Founded in Epalinges, Switzerland, in 2008, Stemedica International S.A. is a global biotechnology company that develops therapeutic applications for the treatment and prevention of Alzheimer's disease and vascular dementia. The company is a subsidiary of Stemedica Cell Technologies, Inc. Stemedica International has an exclusive license to manufacture and distribute the parent company's allogeneic, ischemia-tolerant mesenchymal stem cell (itMSC) and ischemia-tolerant neural stem cell (itNSC) lines and stem cell factors for Alzheimer's disease and vascular dementia indications. The company also has Swissmedic licenses to import, export, and distribute Stemedica Cell Technologies' cell lines worldwide for human use in approved clinical trials. Manufactured in compliance with cGMP standards, the stem cell lines have a unique, proprietary technology based on the expansion of cells in constant hypoxia, which provides critical benefits in terms of safety, efficacy, and scalability. For more information, visit www.stemedica-intl.com.

Stempeutics Receives Japan Process Patent for Its Novel Stem Cell Drug Stempeucel®

PRNewswire: June 8, 2015 – BENGALURU, India – Stempeutics Research, a group company of Manipal Education and Medical Group and a joint venture with Cipla Group, announced today that it has been granted process patent from the Japan Patent Office (application no 2012-540529) for its novel stem-cell based drug Stempeucel®. The novelty covers the method of preparing master cell banks, working cell banks, and the final therapeutic product "Stempeucel" based on the novel pooling technology. Stempeucel® will initially be used for the treatment of critical limb ischemia (CLI), a breakthrough treatment option that directly addresses the root cause of the disease, unlike other drugs which typically treat the symptoms and not the disease itself.

Stempeucel® is derived from allogeneic pooled mesenchymal stromal cells extracted from the bone marrow of healthy adult voluntary donors. The company proprietary pooling approach allows an efficient manufacturing process with minimum wastage of resources in order to provide the product at an affordable cost to patients. This approach also allows more than one million patient doses from a single set of master cell banks, which is unique in regenerative medicine. The proprietary technology allows Stempeucel® to extend the therapeutic potential of the drug across multiple disease categories.

Commenting on the Japan patent, Mr. B. N. Manohar, CEO of Stempeutics, said, "The new patent strengthens our position in Japan, which has created an accelerated development path for stem cell therapies. The new regenerative medicine law implemented in Japan allows conditional approval of stem cell products, thereby enabling more rapid entry into the Japanese market. We are actively evaluating the potential for accelerated development of Stempeucel product for CLI and osteoarthritis indications in Japan with strategic collaborations."

Mr. Chandru Chawla, head of Cipla new ventures, said, "Japan is showing great leadership in innovating a regulatory framework for regenerative medicine, thereby addressing major unmet medical needs faster. We would like to leverage this new framework for rapid development of our Stempeucel product for the benefit of patients along with a potential partner."

Stempeutics is an advanced clinical stage biotech company based out of Bangalore. It was founded by Manipal Education and Medical Group (MEMG) in 2006 and later entered into a strategic alliance with Cipla in 2009. Stempeutics' strength lies in developing innovative stem cell products by nurturing cutting-edge research and clinical applications through dedicated efforts of its highly qualified team. Its goal is to develop novel stem cell drugs addressing major unmet medical needs with an India first, global next approach.

Mylan Launches First Bioequivalent Alternative to Combination Asthma Therapy Seretide® Evohaler® (Salmeterol Xinafoate/Fluticasone Propionate) Under the Brand Name Sirdupla™ in the United Kingdom

PRNewswire: June 8, 2015 – HERTFORDSHIRE, England, and PITTSBURGH, PA, U.S.A. – Mylan N.V. (Nasdaq: MYL) today announced that it has launched the first bioequivalent alternative to GlaxoSmithKline's Seretide® Evohaler® (salmeterol xinafoate/fluticasone propionate) under the brand name Sirdupla™ in the United Kingdom. Sirdupla is a pressurized metered-dose inhaler (pMDI) and is indicated to help treat or prevent symptoms of asthma in adults 18 years of age and older. The product is being manufactured by 3M Drug Delivery Systems.

The United Kingdom has one of the highest rates of asthma in Europe, affecting one in five households, and, on average, three asthma patients in the United Kingdom die every day from the condition. With 5.4 million people suffering from asthma in the United Kingdom, the condition costs the National Health Service (NHS) £1 billion (US$1.53 billion) annually.

Mylan president Rajiv Malik said, "Mylan is excited to be the first company to offer adult asthma patients in the United Kingdom the generic version of Seretide Evohaler, delivering on our mission to increase access to high-quality medicine. Sirdupla represents a significant advancement for the company that both strengthens our respiratory portfolio and pipeline and further demonstrates our ability to successfully execute on one of our key strategic growth drivers."

Mylan Europe president Jacek Glinka added, "The launch of Mylan's Sirdupla broadens patient access to an important treatment option and offers a familiar pMDI device experience to U.K. asthma sufferers. Asthma is a widespread illness in the United Kingdom and we are committed to contributing to ease this burden to both patients and the NHS."

"3M will fill, assemble, and package Sirdupla at 3M's manufacturing facility in Loughborough, United Kingdom. By partnering with Mylan, 3M has taken an important step forward in the generics space. This partnership combines 3M's expertise in inhalation drug development and manufacturing with Mylan's leadership position in the global generics market, including expertise in commercializing complex respiratory products," said Cindy Kent, president and general manager, 3M Drug Delivery Systems.

Sirdupla is a daily maintenance pressurized metered-dose inhaler that offers the same ease of use that patients expect from their asthma therapy. It is available in 125/25 mcg and 250/25 mcg with 120 doses.

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Invetech and Vaxxas Named Recipients of the 2015 Good Design Award for Development of Nanopatch Jet Coating Instrument for Needle-Free Drug Delivery

PRNewswire: May 29, 2015 – SAN DIEGO, CA, and BOSTON, MA, U.S.A. – Invetech, a leader in instrument development, custom automation, and contract manufacturing, and Vaxxas, a biotechnology start-up and developer of the Nanopatch™ needle-free drug delivery technology, have been named winners of the 2015 Good Design Award for development of the Nanopatch jet coating instrument, an advanced technology platform to support needle-free dermal drug delivery research and product development. The award was announced last evening at the Good Design Awards gala night held in Sydney, Australia.

Nanopatch™ is a next-generation drug delivery platform that consists of an array of thousands of coated microprojections able to perforate the dermal layer to deliver vaccine into the outer layers of the skin. Vaccine delivery using Nanopatch has the potential to offer significant advantages over traditional injections, including needle-free drug delivery, reduced pain, no need for refrigerated supply chain, improved vaccine effectiveness, and low cost of manufacture. A key consideration in product development is the ability to apply vaccine to the microprojections effectively. In this collaboration, design and engineering teams at Invetech and Vaxxas worked together to develop a unique drying protocol able to provide essential levels of precision and control in manufacturing and product replication. This, in turn, supports the potential use of Nanopatch in a range of vaccine clinical research programs.

"Our collaboration with Vaxxas is a great demonstration of how Invetech can complement the important work of emerging leaders in medical technology with additional insight and know-how to address very specific and complex challenges," said Richard Grant, global vice president at Invetech. "We are all very pleased that the Nanopatch jet coating instrument, which represents an important milestone in drug delivery innovation, has been named the recipient of a 2015 Good Design Award."

The collaboration between Invetech and Vaxxas resulted in development of an instrument that enables controlled coating of the micro-projections with drug compounds followed by specific drying protocols based on use of a unique gas jet technology. Usability was a key consideration throughout the development process, targeting a platform that is easy to use, maintain, and clean. With these advantages, manufacturers are better able to achieve target goals in terms of precision and product replication necessary to advance vaccines to clinical-stage research.

"Our goal with the Nanopatch has been to develop a technology that enables safer and more efficient vaccination versus administration via needle and syringe. The Nanopatch has the potential to provide a better patient experience, with better overall economics because there is no need to maintain costly cold chain. Of course, development of an advanced technology platform like this presented some challenges," said Dr. Angus Forster, Vaxxas's chief development and operations officer. "With our collaboration with Invetech, we brought together the range of expertise and insight to identify a new method to apply drug to microprojections that represents a major advance in our ability to deliver vaccines to patients."

Cerament™|G Shown to Increase Bone Formation and Decrease Infection

PRNewswire: May 27, 2015 – LUND, Sweden – Bonesupport, an emerging leader in injectable bone substitutes for orthopedic trauma, bone infections, and instrument augmentation related to orthopedic surgery, announced results from a pivotal preclinical study of Cerament™|G as presented at the 2015 Orthopedic Research Society (ORS) Annual Meeting. The study assessed the efficacy and safety of Cerament™|G, the first injectable gentamicin-eluting bone substitute, in the completeness of bone healing after surgery and in the eradication of chronic infection. Study results demonstrated that Cerament™|G increased new bone growth and decreased the rate of infection as compared to treatment without a bone filler and treatment with Cerament™|bone void filler without gentamicin.

"Treatment of chronic osteomyelitis often leaves a large critical defect that requires a bone void filler, yet current void fillers are inadequate because of donor site morbidity, expense, or their propensity to encourage infection," said Dr. Mathias P. G. Bostrom, orthopedic surgeon at Hospital for Special Surgery (HSS) in New York and co-author of the study. "This study showed Cerament™|G to be effective in decreasing the rate of infection and simultaneously increasing new bone growth, two essential functions for successful management of osteomyelitis."

Cerament™|G is an injectable, resorbable bone graft substitute designed to fill bone gaps and voids and to augment hardware and bone fractures during surgical procedures. Cerament™ has been shown to remodel into healthy native bone within 6 to 12 months. The efficient elution profile and the focused local delivery of gentamicin obtained with Cerament™|G are intended to prevent colonization of sensitive microorganisms, thereby protecting the bone healing, particularly in challenging cases of deep bone infection.

"This is the first animal study to evaluate Cerament™|G in a septic condition, and we were very pleased with the results," said Lloyd Diamond, CEO of Bonesupport. "Clinical investigation has always been the foundation from which we have built a robust portfolio, and it will continue to play an important role as we expand into new markets and new indications with our proprietary drug-delivery platform."

Osteomyelitis, or bone infection is a $1.7 billion market where prolonged, long-term antibiotic therapy, multiple surgical interventions, and the threat of amputation are the current standard of care. Rising prosthetic infections, diabetic ulcers, war injuries, sports injuries, and an increasing resistance to antibiotics contribute to this growing condition.

Generex Announces Collaboration with NHTherapeutics to Utilize the RapidMist™ Buccal Delivery Technology for Leuprolide

PRNewswire: May 26, 2015 – WORCESTER, MA, U.S.A., and TORONTO, Canada – Generex Biotechnology Corporation (www.generex.com) (OTCQB: GNBT) today announced that it has entered into a memorandum of understanding with NHTherapeutics, Inc. (www.nhtherapeutics.com, NHT) pursuant to which the companies will co-develop a formulation for the delivery of leuprolide into the human body via the buccal mucosa using the Generex proprietary RapidMist™ buccal drug delivery system.

The Generex proprietary RapidMist™ drug delivery platform technology administers active pharmaceutical ingredient via aerosolized metered dose spray into the mouth for rapid absorption by the buccal mucosa. The company's most advanced product in development using RapidMist™ is Generex Oral-lyn™, an insulin spray product for the treatment of diabetes mellitus.

NHTherapeutics holds intellectual property in respect to the dosing regimen and route of administration of leuprolide and other gonadotropin-releasing hormone (GnRH) agonists for the treatment of hypogonadism and other endocrine disorders.

Pursuant to a fee-for-service arrangement, Generex will develop a RapidMist™ formulation of leuprolide designed to achieve the safe, simple, rapid, dose-specific, and effective administration of the active pharmaceutical ingredient into the human body via the buccal mucosa. Thereafter, Generex will undertake local irritation and stability testing of the formulation.

It is contemplated that, pending the outcome of the RapidMist™ leuprolide formulation data, Generex will grant to NHT a license for the global commercial exploitation of the product in the field of endocrine disorders in exchange for royalties.

Leuprolide belongs to a class of medications called GnRH agonists. Traditionally, GnRH agonists are used at a high dose to chronically decrease hormonal release. Leuprolide is given by injection and is marketed to treat the symptoms associated with advanced prostate cancer, central precocious puberty (CPP), endometriosis, and anemia. Conversely, NHT intends to administer low-dose leuprolide and other GnRH agonists through an easy-to-use buccal spray to chronically increase hormonal levels. Proof of concept data already exists. "NHT recognizes that the Generex RapidMist™ drug delivery platform and attendant product development experience, together with NHT's expertise in the field of endocrine disorders, creates a unique opportunity to formulate leuprolide for rapid and effective administration through the buccal mucosa," commented Dr. David Brusegard, Ph.D., the company's chief operating officer. "Generex is pleased with this new opportunity to expand our RapidMist™ platform technology."

Dr. Aldemar Degroot, M.S., Ph.D., the president and chief executive officer of NHT, stated: "There is a real market need for a compound that can chronically increase hormonal levels, that is safe, can be easily administered, and that does not affect fertility. Unlike existing products that increase hormonal release, NHT's lead product (NH901) is nonscheduled and will not induce supratherapeutic hormonal levels, which can result in severe adverse effects. We look forward to working with Generex to make this product a reality. Its extensive experience with the buccal delivery of peptide drugs along with its RapidMist™ technology combined with our own experience in endocrine disorders and our intellectual property are bound to lead to success."

West Bolsters R&D Strategy with Global Site Expansions and Upgrades

PRNewswire: May 12, 2015 – EXTON, PA, U.S.A. – West Pharmaceutical Services, Inc. (NYSE: WST), a global leader in innovative packaging components and drug delivery systems, today announced a multiyear investment as part of the company's evolving research and development strategy. To better support pharmaceutical customers around the world, West will add capabilities to all of its global packaging systems R&D facilities and develop two new R&D centers of excellence—one in the Asia Pacific region and one in Europe—to leverage regional capabilities and expertise in parenteral drug packaging.

"For more than 90 years, West's focus on innovation, science, and service has made us a trusted partner for pharmaceutical and biopharmaceutical companies worldwide," said Karen Flynn, president, pharmaceutical packaging systems, West. "Our enhanced R&D development centers—in all regions of the globe—will further our commitment to our customers by providing world-class, science-based process and product development that enables us to quickly and efficiently anticipate and respond to changing market needs with new, innovative solutions."

The facility in Europe will be the company's center of excellence for drug vial and cartridge seals, plastic technology, and packaging component materials development and will be on line by the end of 2016. The company's location in the Asia Pacific region will serve as a center of excellence for innovation across all technologies specific to the emerging markets and is expected to be operational by the end of 2015.

In addition to the new facilities in the Asia Pacific region and Europe, a significant investment is being made in North America to expand the current R&D center located within the Exton, Pennsylvania, headquarters and to upgrade the St. Petersburg, Florida, facility.

West's comprehensive research and development global network also includes development centers for self-injection and drug delivery systems along with the company's contract manufacturing facilities in Tempe, Arizona, and Dublin, Ireland. A team focused on innovation in delivery systems is led from the West Innovation Center in Washington, New Jersey.

West's global investment in R&D demonstrates the company's focus on developing the most advanced packaging and delivery systems for its customers in order to meet the growing demands of the healthcare industry. ■

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

Calendar of Events

2015

13th International Nanomedicine and Drug Delivery Symposium (nanoDDS)
September 16–18
Seattle, WA, U.S.A.
www.nanodds.org

20th International Symposium on Microencapsulation
October 1–3
Boston, MA, U.S.A.
www.northeastern.edu/ims2015/contact

Formulation, Processing, and Testing of Functionally Coated Multiparticulates Workshop
Sponsored by CRS
October 24
Orlando, FL, U.S.A.
controlledreleasesociety.org

Drug Delivery Australia
Sponsored by CRS
November 19–20
Brisbane, Australia
www.crsaustralia.org

D4 – Devices for Diagnostics and Drug Delivery
Sponsored by CRS
November 25–26
Dunedin, New Zealand
www.nzcrs.org.nz

2016

XI Spanish-Portuguese Conference on Controlled Drug Delivery
Sponsored by CRS
January 21–23
Granada, Spain
www.splc-crs.org

Advances in Technology and Business Potential on New Drug Delivery Systems
Sponsored by CRS
February 23–24
Mumbai, India
www.crsic.org

2016 UKICRS Symposium
Sponsored by CRS
April 21–22
Cardiff, Wales
www.ukicrs.org