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Chapter News





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Charles Frey Editor



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Yvonne Perrie Editor



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From the Editor



Editors

Charles Frey Steven Giannos Arlene McDowell Bozena Michniak-Kohn Yvonne Perrie Rod Walker

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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Controlled Release Society 3340 Pilot Knob Road St. Paul, MN 55121 U.S.A.

Telephone: +1.651.454.7250 Facsimile: +1.651.454.0766

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Bozena Michniak-Kohn Ernest Mario School of Pharmacy Rutgers–The State University of New Jersey, U.S.A.

The Value of Connecting at the Annual Meeting

A seach new school year begins, I think about the role of professors and more experienced industrial investigators in the career development of the young scientists in our laboratories and lecture halls. The more we are bombarded with emails, Facebook and LinkedIn invitations, webinars, and the latest iPhones and iPads, the more I see value in face-to-face interactions and professional society meetings.

Many of us have attended a meeting or two in recent months, including the CRS Annual Meeting in Chicago. Even though we all use interactive electronic media and agree there is value in its use, there is something special about "people interactions." We frequently hear about people who tried to set up collaborations through all kinds of virtual media, but these partnerships only flourished after the collaborators made personal contact at a professional society meeting.

I have experienced this many times. I meet with my colleague over coffee; perhaps I miss the lecture in the ballroom, but I walk away invigorated with new ideas and plans for additional interactions. After a personal meeting, it seems so easy to plan it all out.

Is this just for us, the "seniors"? What about students and postdocs? Is it worth sending them to such conferences, especially in these days of limited funding? I think the answer is an overwhelming YES! We should send our young investigators to meetings whenever we can afford it to experience real "people interactions," get away from behind the computer and iPhone, and learn how to present themselves and their science well. At a meeting, they pluck up the courage to ask a question in a crowded lecture hall after a leading scientist's plenary talk. They learn to organize a presentation in a meaningful way, so that the audience can understand their contribution and appreciate its impact. All these are people skills, real communication skills that iPhones and iPads cannot possibly provide.

So the next time you think that a CRS meeting is a little expensive for the student or postdoc in your lab or your new hire in pharma, think of the value of the meeting and what the young scientist will come away with: new ideas, new contacts, new collaborations, new approaches for old methodologies... Let's start to save those funds for Edinburgh!

In case you did not make it to the CRS Chicago meeting, the *CRS Newsletter* will feature Scientifically Speaking articles based on some of the excellent posters presented this year. Xie *et al.* investigated siRNA delivery to activated T cells using transferrin-polyethylenimine conjugate for treatment of asthma. With this conjugate, they demonstrated that there was a specific and increased uptake as well as a gene silencing effect *in vitro* in primary activated T cells. In addition, Ivanova *et al.* are addressing the challenge of formulating inhaled therapeutics for idiopathic pulmonary fibrosis. Their initial data suggest that an approach using dual drug/ siRNA nanoparticles may lead to successful inhalation formulations.

Wishing all our newsletter readers good reading and a productive year.



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

CRS: Connected and Relevant

A s many of us spent time together at our annual meeting in July, a common topic was, "What was your first meeting?" Mine was 1989 in Chicago—and this year it was a pleasant memory to be in Chicago again 25 years later. During those 25 years I have averaged four or five conferences a year, but CRS has always been my "home conference," and I have attended 22 of the last 25 years of annual meetings.

We have all seen changes over those 25 years. This year, for example, you registered for the meeting online; you used email, Twitter, or LinkedIn, to set up meetings with colleagues ahead of time; maybe you even used Uber for your ride in from the airport. Those and other tools have enriched our lives but also changed how we think about, design, benefit from, and enjoy annual meetings.

My personal memories of the meeting this year included some spectacular plenary lectures (who knew about WikiPearl[™] foods?), great sessions on protein delivery, learning more about pharmacokinetics in dogs, and listening in on a great Women in Science lunch session. But, as always, the connections and reconnections—whether at Kitty O'Sheas in the Hilton, over incredible tapas at Mercat a la Planxa just next door, or an enjoyable trip down memory lane at the Tuesday President's Banquet where all in attendance tested their knowledge of CRS history—are at the heart of the CRS Annual Meeting.

So my first request to you is to help think about making ours the best annual meeting. You likely noticed that attendance was down—a trend throughout most industries as an effect of the global economy over the last six years but also a reflection of how we now all obtain data and collaborate. The request is a simple one: provide feedback. As someone eloquently said to me at the meeting, "Help design a conference you wouldn't miss!"

As I mentioned, I have attended 22 CRS Annual Meetings. For 20 of those, a primary purpose of attending for me was being an exhibitor. Our exhibitors are primarily from the industrial sector, an important part of CRS both today and historically. Everyone attends the CRS Annual Meeting for great science; our industrial attendees are also thinking about products and

customers (as are many academic attendees). So my second request is this: because the Board has a priority this year of increasing industrial relevance, provide ideas on how we can do this for you.

CRS is a year-round organization, but our signature event remains our annual meeting. There are many people to thank and acknowledge, and here is a partial list. Past presidents Sandy Florence and Diane Burgess were acknowledged for years of scientific leadership and service, Sandy through the CRS Foundation's 2014 postdoctoral fellowship in his honor and Diane as the recipient of the Distinguished Service Award. Ian Tucker completed his term as president in Chicago; he has provided many years of leadership, culminating in his very successful tenure and setting up CRS for years of future success. Many, many volunteers make CRS work throughout the year and produce a successful annual meeting, in particular the Annual Meeting Program Committee, chaired for Chicago by Ick Chan Kwon and cochaired by Justin Hanes. Also, you may know them as Susan or Linda or Megan or Sue or Amy, but a hearty thank you to our headquarters staff who work tirelessly throughout the year, especially around the annual meeting.

If you have any concerns on the future of CRS, just attend a student event, which I got to enjoy on Monday night in Chicago. Then you will be quite comfortable with the next generation of CRS leaders!

With a great Board I look forward to this coming year. In this note you see two of our major objectives: building on years of successful annual meetings to make future annual meetings even better, and reaching out to and increasing relevance for the industry of delivery science.

As we look forward to a wonderful meeting next July in Edinburgh, I am starting a collection of relevant jokes and close with one here:

Question: When you see people playing the bagpipes, why are they always marching? Answer: They are trying to get away from the noise.

Remembering Marcus E. Brewster III,1957–2014



Leader, Mentor, Colleague, Friend

It is with great sadness that we note the untimely passing of our Controlled Release Society President-Elect, Marcus Brewster. Marcus passed away at his home in Belgium on Monday, September 15, 2014. Marcus had a great many friends and collaborators, and the Board asked one of them, Martyn Davies, to provide some thoughts on Marcus, including his great commitment to our field and our society.

This is a real tragedy; it was such a sad day when we heard the news at CRS. Marcus had shown such wise council and strong leadership in many roles within CRS, including Treasurer, Director-at-Large, and Chair of the Board of Scientific Advisors. We all believed he was going to be an excellent President in 2015–2016. Marcus loved his work, and he contributed to many other scientific societies. He was an editor of one the leading journals in the field, the *Journal of Pharmaceutical Sciences*. He published more than 270 papers, book chapters, and presentations and was co-inventor on approximately 75 patents. Not only was he universally admired by his peers in the international pharmaceutical community, he was deeply respected by his colleagues at Janssen for his contribution to the development of new innovative medicines.



John J. Dingerdissen, Global Head of Drug Product Development, says of him, "It is, perhaps, the biggest loss that I have experienced in my career in a colleague, friend, employee, and co-worker. He was so well respected inside and outside the company. His work was his life, and we will surely miss him. He touched us all with

im, have e, vas

his jovial laugh and mesmerized us with his scientific knowledge and prowess."



On a personal level, I feel shocked to have lost a friend and collaborator in such a sudden and unexpected way. I am sure many of you within CRS will feel the same. I was with him on the previous Friday in Leuven at the public defense of a Ph.D. student with whom we had both worked. He was warm, supportive, scientifically curious and knowledgeable—and, of course, funny. He seemed in great form, taking time to introduce me to key people in his group and also to congratulate the student's family, taking an interest in their lives. So typically Marcus, a person of great warmth and integrity, and scientifically top class—one of the good guys. He mentioned that his type 1 diabetes was slowing him down a little and, typically of him, made little of it. He generously asked how my daughter was doing (she struggles with the disease) and gave me gentle encouragement.

The CRS Board intends to recognize at a future meeting the wonderful contribution that Marcus made to our society and to the development of commercial products that are improving the lives of patients worldwide. In the meantime, we should all stop and remember this remarkable man, quietly reflect on his life of friendship and service, and warmly salute the achievements of this most outstanding of scientists. CRS sends our sincerest condolences to Marcus's family for their loss.



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What Is the Real Need in Low-Income Countries?

Roderick B. Walker, Professor of Pharmaceutics, Rhodes University, South Africa



I must thank Theresa Allen for starting the debate in her article titled "Debating CRS's Role in Low-Income Countries," which was published in the last edition of the *CRS Newsletter*. Theresa raises a number of important questions respecting the role of CRS in developing new products for low-income countries and briefly touches on some of the realities of attempting to do that.

Theresa specifically indicates that India, Brazil, and Cuba are not included in her areas of concern, as these countries have a "growing research and pharmaceutical manufacturing presence" that has allowed progress to be made in these countries. South Africa is no different in some of these respects but has major issues in respect to health delivery in a society ravaged by "apartheid" and one that is among the most unequal in the world in terms of those who have and those who have not. In this respect it is not the only country in which the legacy of historical empire building by nations in Europe and elsewhere has left a scar that will take decades to heal.

The role of a society such as CRS in developing therapies for countries in need, the role of major funding agencies in directing research into diseases that only occur in poor countries, and the role of scientists in pursuing these goals are admirable; however, I believe that there is a fundamental misunderstanding about some of the real needs of persons living and working in such countries.

Quite rightly, the costs of interventions need to be reasonable, and simple solutions to these challenges are required. Most significantly, a preventative intervention such as the distribution of mosquito nets, for example, is a valuable and successful approach to reducing malaria. The current focus on the treatment and eradication of malaria seems to me to be approaching the issue from the wrong end. Why not look to developing a technology to deliver a compound that destroys the mosquito larvae without impacting water quality? As CRS has roots in agricultural and consumer products, this may well be a viable approach.

There may also be a role in the context of developing aids to drug therapy. Young asthmatic patients often require use of a spacer to enhance therapy, and the cost may prohibit the purchase of one. However, I have seen the clever manipulation of a 500 mL plastic cold drink (soda) bottle by a health care professional in a rural community solve this problem. Is this a potential area of innovation for CRS device researchers?

A major concern in all countries is the so-called brain drain. Many highly trained and well-educated health care professionals and scientists have left their countries of origin to pursue careers in the "first world." The reasons for this migration are numerous, and some are understandable. However, the active recruitment and retention of these persons from low-income countries is unacceptable; it can and does have a major impact on the ability of these countries to find solutions through their own endeavors.

Perhaps there is an alternate approach that CRS can follow rather than only being product focused. There are many bright, intelligent, and passionate scientists who cannot pursue their dreams of tertiary education or postgraduate studies as a consequence of poverty. Rather than relocate these candidates to the United States or Europe, place them with eminent scientists in their home countries to find solutions to the challenges facing their fellow citizens. This could be a capacity development programme that would yield the next generation of academics and scientists that will have a direct impact on the health care system in their home country.

Despite the issues, there are and have been many successes. Examples include the issue of manufacture of generic antiretroviral drugs under license in several countries, and the investment of funds in South Africa to discover lead compounds for tuberculosis has yielded a molecule that is going into the clinic. There are numerous other examples of simple solutions to the challenges facing low-income countries, including a rapid diagnostic and simple test to detect faecal contamination in water and a low-cost grey water treatment unit, among others.

In short, issues such as the lack of cold-chain control, corruption, the lack of health care professionals, shortage of medicines, poverty, hunger, the inability to move medicines from manufacturer to clinic effectively, and transport costs must be understood in order to identify solutions to some of the issues Theresa raised. Theresa asked that we do not "stray too far into the political realm"; however, this is inevitable and must be considered when dealing with the issue of health in "developing" and low-income countries.

What is the real need in low-income countries? I suggest that the priority is to ensure that CRS facilitate the development of the next generation of scientists in these countries.

1,250

attendees gathered for the 41st Annual Meeting of the Controlled Release Society in Chicago, Illinois, U.S.A.



RS

Check out our two-minute slideshow for a taste of the meeting at controlledreleasesociety.org/meeting



LEARN

CRS chapters were represented at the Chapter Networking Hour, including Shiow Fern Ng (third from left), from the newest chapter in Malaysia (MyCRS)

> CRS members and attendees can view recorded presentations from the Webcasts page (controlledreleasesociety.org/webcasts)

speakers came to the podium to deliver scientific expertise, discuss trends, and encourage discussion ENGAGE



76 exhibitors introduced cutting-edge technology, products, and services

NETWORK



attendance continues to grow, offering critical international perspective



50

women shared knowledge (and business cards) during the Women in Science Luncheon

"Whatever you are studying, or developing, the CRS Annual Meeting will have individuals and organizations that can offer assistance or insight into your particular field."

-2014 Annual Meeting attendee



attendees from the Consumer & Diversified Products Division enjoyed a networking lunch at the Hilton

"The CRS Annual Meeting offers an excellent overview of technology and opportunities for out-of-the-box thinking."







50

representatives from the Preclinical Sciences & Animal Health Division met at Buddy Guy's Legends Blues Club "The international attendance and smaller meeting size (compared to some conferences) enhance opportunities to network and contribute."



COLLABORATE

103

young scientists rocked the boat on a cruise from Chicago's Navy Pier



Thank You to the Exhibitors of the 41st Annual Meeting & Exposition

These are the organizations that not only support the research and development needs of delivery science with products and services, but many of the exhibitors also sponsored refreshments and prizes in the exposition hall. Thank you, 2014 CRS exhibitors.

3M Drug Delivery Systems Adhesives Research, Inc./ARx, LLC Advanced Polymer Materials, Inc. Agilent Technologies Akina, Inc.: PolySciTech Division American Pharmaceutical Review Anton Paar USA Avanti Polar Lipids, Inc. Bend Research, Inc. BioPharm Solutions, Inc. **BUCHI** Corporation Catalent Pharma Solutions Celanese EVA Polymers Colorcon CordenPharma Croda Inc. Delta Industrial Services, Inc. Destination Edinburgh **Dissolution** Technologies Distek, Inc. Drug Development & Delivery DURECT Corp./LACTEL Absorbable Polymers Elsevier EMD Millipore Erbo Spraytec AG Evonik Corporation Fluid Imaging Technologies, Inc. Formex LLC Freund-Vector Corporation Gattefossé Gaylord Chemical Company Hanson Research Hovione Intec Pharma Ltd. Izon Science Limited KORSCH America, Inc. LCI Corporation Ligand Pharmaceuticals Incorporated Lipoid LLC Logan Instruments Corp. Lubrizol Advanced Materials, Inc.

Malvern Instruments NanoSight Medimetrics Personalized Drug Delivery B.V. Nanocopoeia, Inc. NanoImaging Services, Inc. Nisso America Inc. NOF Corporation Northern Lipids Incorporated, Inc. Noven Pharmaceuticals Novozymes Biopharma OctoPlus, a subsidiary of Dr. Reddy's Laboratories Ltd. ONdrugDelivery Magazine Optofluidics, Inc. Patheon Pharmaceuticals Services Inc. Pharmaceutical Technology PharmaCircle PolyMicrospheres-Advanced Nanotechnologies Polymun Scientific Immunbiologische Forschung GmbH Polysciences Inc. ProMed Pharma LLC Purac Biomaterials Shin-Etsu Chemical Co., Ltd. Siegfried USA, LLC Simulations Plus Inc. Sirius Analytical, Inc. SOTAX Southwest Research Institute Springer Surface Measurement Systems Suven Life Sciences Limited Sympatec Inc. Technology Catalysts International Texture Technologies Corp. Thermo Scientific UKICRS Local Chapter Vision Processing Technologies, Inc. VxP Pharma Wyatt Technology Corporation









2014-2015 CRS Board

The following CRS members make up the 2014-2015 Board. Sadly, President-Elect Marcus Brewster passed away September 15. The Board is following protocol in the bylaws and will make an appointment to this position soon. Members wishing to interact with Board members can find contact information in the member directory or can simply e-mail crspresident@scisoc.org.



President Art Tipton Southern Research Institute U.S.A.



Immediate Past President Ian G. Tucker University of Otago New Zealand



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Secretary Christine Allen University of Toronto Canada



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Director-at-Large Ben Boyd Monash University Australia



Director-at-Large Andrew Lewis Ipsen France



Director-at-Large James Oxley Southwest Research Institute U.S.A.



Director-at-Large Yvonne Perrie Aston University United Kingdom

Volunteer Spotlight: Planning the CRS Annual Meeting

Welcome back from the 2014 CRS Annual Meeting! For many years, our yearly meetings have served as a great way to reconnect with old friends and colleagues while making new connections and diving into innovative science, keeping participants physically exhausted but mentally recharged. This year was not an exception.



Ruth Schmid

However, we must remember that the

organization of this meeting, intercalating great science from all around the globe and wonderful social events, requires the commitment and hard work of a group of talented people who are eager to contribute their time and efforts. A big component of this team—the dream team—comes from volunteers.

In this Volunteer Spotlight, we will gain insights into the "kitchen" of the annual meeting from Ruth Schmid, one of the most prominent behind-the-scenes players responsible for the meeting's success. Ruth is vice president of marketing at SINTEF Materials and Chemistry in Trondheim, Norway, with special responsibility for the area of medical technology, including nanomedicine. Her research focuses on design and characterization of micro- and nanoparticles for nanomedical applications. She has been a member of CRS since 1998, a member of the Board of Directors since 2009, and is the current treasurer. We invite you here to take part in the conversation Biana Godin (deputy chair of the Volunteer Recruitment Committee) had with Ruth about her involvement with CRS.

Q How did you get involved in CRS?

A I attended the CRS meetings in 1998 and 1999, but always together with coworkers, so we did not really mingle and network much. After a break without projects in the area of delivery science, I came back to the CRS meeting in 2004, this time alone. Because meals alone are boring, I was prompted to get involved with other attendees. I attended all the Consumer & Diversified Products (C&DP) sessions, as our client requested. The C&DP Division marketed their luncheon actively during the sessions, and I decided to attend this event. There I was asked whether I would like to join the division and attend the monthly calls, which I thought was interesting and not too time consuming. Since then, I have been a member of the C&DP Division.

Q Tell us about your current and past volunteering experiences and leadership roles with CRS.

A As I mentioned earlier, I started as a member of the C&DP Division (back then, it was the C&DP Committee). One year, I was a member of the Industrial Award Committee. In 2008, I was asked to run for the Board of Scientific Advisors (BSA) but did not get elected. In 2009, I was asked to run for a director-at-large position on the Board of Directors and was elected. On the Board, I was the secretary (2012–2013) and treasurer-elect (2013–2014), and I am currently the treasurer (2014–2015). I was also part of the Annual Meeting Program Committee (AMPC) for the Chicago meeting. During my involvement with CRS, I have also been a part of several task forces: Women in Science Task Force, Annual Meeting Task Force, and Communication Task Force.

Q What are the main benefits and rewards in volunteering for the society?

A The main benefit is widening my network but also learning a lot about leading a not-for-profit organization. Also, because CRS is very diverse, being involved as a volunteer gives me insights into the various segments and differences that are part of CRS—for example, the various industrial application areas and translation from academia to industry—as well as into the cultural differences between people from various geographic areas. I have not only widened my professional network but also made a lot of personal friends.

Q What are the main considerations in shaping the annual meeting program, and which CRS bodies are involved?

A Programming for the annual meeting is mainly done by the AMPC, which is composed of 11 members representing the diversity of CRS (academia, industry, young, experienced, and representing various geographic areas and both genders). It is important to have all groups of CRS members represented in the AMPC, because the meeting program should reflect the diversity of the organization. The AMPC also works together with the BSA, the Satellite Meeting Committee (responsible for the workshops), the C&DP and Preclinical Sciences & Animal Health Divisions, and the Young Scientist Committee to get input in the various scientific areas for the programming. Additionally, there is an Annual Meeting Committee (AMC) that is not involved in the programming but is looking into the future of the annual meeting on a strategic level, and input from the AMC to the AMPC will also be more and more important in future years.

Q How do you feel our society stands out from other organizations?

A CRS covers a broad and diverse scientific and technological field: delivery science and technology. The organization is not focused on a narrow scientific topic but on the diversity and all the benefits that entails. The possibility of technology transfer at the various interfaces—academia and industry, young and experienced scientists, different focuses (including pharma, vet, cosmetics, food, beverages, textiles, and industrial applications), and geographic locations all over the globe—is one of the strengths of our organization. Today's big challenges in the world need multidisciplinary approaches, and CRS brings together all the different scientific fields to contribute to solutions.

Q What is your advice for new members and volunteers?

A Do a lot of networking, and do not be afraid to talk to all the other attendees, regardless of age and experience. Be curious. Tell the Volunteer Recruitment Committee your areas of interest and expertise, and let them know if you would like to get involved. Be realistic about your time management. Do not accept volunteer positions you do not have time for, because that would be a negative experience for both CRS and you. Ask how much time a certain job will take, and then make a decision.

Q What is your volunteering schedule during the year, especially the preparations for the CRS Annual Meeting?

A The preparations for the annual meeting started at the last annual meeting for me as a member of the AMPC, and they

took quite a lot of my time. Peaks were late autumn, when the sessions had to be finalized, and early spring, when all the abstracts had to be reviewed and oral presentations assigned. The Board job is more evenly spread over the year, with monthly calls and one or two face-to-face meetings each year. Additionally, there are committee calls to attend and prepare for. During the meeting, my volunteer schedule is packed: I have Board meetings, attend several committee meetings as a Board liaison, and also attend many of the social events, because networking is my first priority during the meeting. I also enjoy the wonderful science, and this year I contributed a lecture at a workshop, an oral presentation, and a poster.

Ruth, thank you very much for your tremendous involvement in CRS and for giving us a glimpse into your volunteer experience. We hope this interview will inspire many potential volunteers to join the "active forces" of CRS.



CRS Young Scientist Committee Events at the 41st CRS Annual Meeting & Exposition in Chicago

Adam Bohr,¹ Kaushalkumar Dave,² Emmanuel Ho,³ Joke Meeus,⁴ Yewande Oni,⁵ Jorrit Water,⁶ Jinzi Zheng,⁷ and Patrick Lim Soo⁸

At this year's CRS Annual Meeting in Chicago, the Young Scientist Committee (YSC) organized a series of events geared toward young scientists (graduate students, postdoctoral fellows, young academics, and industrial professionals). These events included scientific workshops and roundtables, a professional development workshop, a mentor/protégé get-together, and a social event. The chair of this year's committee was Josh Reineke (Wayne State University, U.S.A.), and the deputy chair was Patrick Lim Soo (Blend Therapeutics, U.S.A.). This year's team was composed of an enthusiastic and dedicated group of young scientists (www.controlledreleasesociety.org/community/YSC/ pages/meettheteam.aspx) who helped to generate, develop, and lead the various initiatives that took place at the annual meeting and throughout the year. Briefly, we describe the different YSC events and activities in Chicago.

The Saturday morning workshop was an interactive educational session titled "The Science of Publishing" and was chaired by Jorrit Water (University of Copenhagen, Denmark, YSC member) and Adam Bohr (University of Paris-Sud, France, YSC member). This workshop was intended to educate young scientists on the different aspects of publishing and peer review in scientific journals. It consisted of presentations by several editors of journals, including Ronald Borchardt (*Journal of Pharmaceutical Science*), Achim Göpferich (*European Journal of Pharmaceutics and Biopharmaceutics*), Vinod Labhasetwar (*Drug Delivery and Translational Research*), Ick Chan Kwon (*Journal of*



Group picture of the attendees of the YSC meeting in Chicago with a special guest appearance by President-Elect Arthur J. Tipton.

¹ University of Paris-Sud, France.

- ² South Dakota State University, U.S.A.
- ³ University of Manitoba, Canada.
- 4 KU Leuven, Belgium.
- ⁵ University of Nottingham, United Kingdom.
- ⁶ University of Copenhagen, Denmark.
- 7 Princess Margaret Cancer Centre, Canada.
- ⁸ Blend Therapeutics, U.S.A., CRS YS Chair.

Controlled Release), and publisher Anne Marie Pordon (Elsevier), with Thomas Rades (University of Copenhagen, Denmark) as moderator. The workshop started with a lecture on the history of publishing and the current publishing process followed by presentations by each of the editors about their respective journal and on topics such as publishing of negative data, peer reviewing, importance of impact factor, starting a new journal, plagiarism, and unethical behavior, and it ended with a presentation on the future of publishing. The workshop attracted young scientists interested in the publishing and peer review process and engaged them in a lively discussion on the presented topics. The invited speakers were particularly passionate about the topics, gave excellent talks, and participated actively in the discussion on each topic. The discussion was further sparked by challenging questions from Dr. Rades to each of the editors, making the event extremely interactive during the roundtable discussion. The attendees gained great insight on the thoughts and decisions of an editor of a journal, received useful information on how to publish and what the journals are looking for, and finally learned what the near future will bring within publishing. It was a successful educational event for all attendees and participants.

The Young Scientist workshop on Saturday afternoon covered the topic "Novel Technologies in Solubility Enhancement" and was chaired by Marcus Brewster (Johnson & Johnson, Belgium) and Joke Meeus (KU Leuven, Belgium, YSC member). With many solubility-enhancing strategies available, this workshop aimed to provide a context for deciding whether formulation enablement is necessary and which technique is most appropriate to apply to which problem. Moreover, novel screening, analytical, and manufacturing approaches were within the scope of this training forum. These diverse topics were



Science of Publishing Workshop. Left to right: Anne Marie Pordon, Jorrit Water (cochair), Adam Bohr (cochair), and Thomas Rades (moderator).

discussed by an international panel of specialists from industry and academia. Dr. Brewster discussed screening and decision making in formulation enablement with his presentation on "Automated and Downscaled Approaches to Select Enabling Formulation Strategies." The industrial perspectives of upscaling the manufacturing process once a suitable formulation strategy has been selected was commented on by Geert Verreck (Johnson & Johnson, Belgium). Ben Boyd (Monash University, Australia) gave an up-to-date overview of the use of lipids as solubilizers for poorly water soluble drugs. Desktop 3D printing as a novel manufacturing method for drug delivery systems was illustrated by Clive Roberts (University of Nottingham, United Kingdom). Finally, the use of solid-state NMR as an analysis technique to study miscibility and stability of solid dispersions was discussed by Joe Lubach (Genentech, U.S.A.). The event was well attended for a premeeting workshop. The workshop closed with a Q&A session that stimulated a lively discussion.

The Young Scientist Professional Development Workshop on "Communication and Networking: How to Develop and Utilize These Skills for a Successful Career" took place on Sunday morning. The chairs for this workshop were Kaushal Dave (South Dakota State University, U.S.A., YSC member) and Josh Reineke. Shahriar Absar (FDA, U.S.A.) also helped organize this event but was unable to attend the workshop. This interactive workshop was aimed toward discussing strategies to improve communication and networking skills. Three excellent speakers including Mark Prausnitz (Georgia Institute of Technology, U.S.A.), Marilyn Martinez (FDA, U.S.A.), and Mark Tracy (Tracy BioConsulting, U.S.A.) conducted interactive and educative lectures, discussion, and exercises on written communication, verbal communication, and professional networking. During the exercise on verbal communication, young scientists were given an opportunity to prepare an impromptu elevator speech followed by immediate feedback from the panel of speakers. Similarly, during the networking session, a mock networking scenario was practiced after the speech and the discussion. Overall, it was a lively and useful event with a high level of participation and positive feedback from all the attendees.

The "Imaging in Drug Delivery: Current Practice, Regulatory Challenges, and Future Trends" Sunday afternoon roundtable was chaired by Patrick Lim Soo and Jinzi Zheng (Princess Margaret Cancer Centre, Canada). This 1.5 hour roundtable session was well attended with approximately 85 participants. The session started with two introductory talks by Christine Allen (University of Toronto, Canada) and Twan Lammers (Aachen University, Germany, and University of Twente, the Netherlands). During these two talks, the audience learned about why imaging is needed for drug delivery systems design, what some significant past and current advances are, and where the field is likely headed in the near future. Helen Lee (Merrimack Pharmaceuticals, U.S.A.) presented the exciting journey that her team embarked upon three years ago with the generation of the concept that development of a diagnostic-therapy pair has the opportunity to increase the success of clinical trials of new liposome-based therapeutics. Specifically, a ⁶⁴Cu-liposome

formulation developed for positron emission tomography imaging entered a phase I clinical trial late last year. Neesha Dhani, a medical oncologist at Princess Margaret Cancer Centre (Canada), followed with an overview of the current use of imaging and molecular imaging agents in clinical trials of new and targeted drugs. She outlined the benefits derived from the incorporation of imaging biomarkers in therapy trial evaluation but also specified limitations of currently existing methods and the many challenges associated with effective clinical implementation. Keyvan Farahani (National Institutes of Health, U.S.A.) concluded by discussing the number of NIH research support programs in the area of image-guided drug delivery that are available to academic groups both in the United States and worldwide, as well as funds to support academicindustry collaboration and early clinical trials. During the Q&A session, a number of interesting points were comprehensively addressed by the speakers, including the high cost associated with image-guided strategies, the feasibility for widespread clinical implementation and adoption, and what the community as a whole can do to accelerate commercialization and clinical translation. Overall, this roundtable session facilitated the learning of the image-guided drug delivery field and provided a productive forum for academic and industry scientists to exchange opinions on viable strategies to increase the clinical impact of image-guided drug delivery technologies.



Imaging in Drug Delivery Roundtable. Left to right: Patrick Lim Soo (cochair), Christine Allen, Neesha Dhani, Helen Lee, Keyvan Farahani, Twan Lammers, and Jinzi Zheng (cochair).

The Mentor/Protégé Meet & Greet was organized for Sunday afternoon. The timing was not fortuitous, as it coincided with the finals of the World Cup football match between Germany and Argentina. Regardless, mentors and eager protégés gathered to meet their respective counterparts for the first time. Patrick Lim Soo gave an overview of the program and described potential guidance for both the mentor and protégé. Louise Rosenmayr-Templeton (Tower Pharma Consulting, Austria) provided her perspective as a mentor, and Kaushal Dave gave insight into his experiences as a protégé in last year's program. Both Louise and Kaushal highlighted the rewards and challenges of being a mentor and protégé, respectively. Then the mentor/protégé pairings began their initial introductions, and discussions quickly were on their way. The pairs were asked to set up specific achievable goals that the protégé could reach with the help of his/her mentor as well as to plan for their second meeting to occur within the first month of their initial encounter. The event wrapped up just in time for some of the attendees to gather and witness the game-winning goal scored by Germany. So all in all, a successful event!

The first "Get Up! Get Educated!" session of this year's annual meeting took place early Monday morning and covered the topic "Writing a Successful Grant Application." The session was chaired by Joke Meeus and Yewande Oni (University of Nottingham, United Kingdom), both members of the YSC. This session consulted an experienced academic, Clive Roberts (University of Nottingham, United Kingdom), and a funding body representative, Keyvan Farahani (NIH, U.S.A.). Both presenters shared their experience with and bestowed knowledge to more than 70 keen attendees on how to set their grant application apart and increase their chances of securing funding. The interactive Q&A session ended the session with invaluable tips and tricks from the presenters.

The Young Scientist Networking Event was held on the Mystic Blue Boat Ride on Monday evening. This year's event was organized by YSC members Emmanuel Ho (University of Manitoba, Canada) and Adam Bohr. In addition to the beautiful sunset view of the Chicago Harbor, the 100+ participants consisting of individuals from academia, industry, and government had a chance to mingle over great food and great company. How do you encourage networking among 100+ participants? It is easy when you have an ice-breaking event that involves dancing! This year we broke up the participants into small groups with each group containing one established scientist with the remaining members consisting of trainees. In a typical networking event, trainees tend to ask questions of the established scientist. This time around, we decided to turn the tables and allow the established scientists to ask questions of the trainees. Furthermore, the established scientist would then volunteer a trainee to compete in a dance off! With first place consisting of a photo with Ian Tucker (CRS President), Art Tipton (CRS President-Elect), and a few of the other established scientists on board, it is not a surprise that this networking event was a great success!

The Tuesday "Get Up! Get Educated!" session was chaired by Yewande Oni. It was feared that after a successful Young Scientist Networking Event the night before that this session might lack in numbers. How wrong we were! This year's session pulled over 90 attendees, keen to hear and discuss the "Evolution of Controlled Release R&D: From Pharmaceutics to Biopharmaceutics" with Ali Rajabi-Siahboomi (Colorcon, U.S.A.) and Irwin C. Jacobs (Jacobs Controlled Release Consulting, U.S.A.). The speakers discussed the breadth and scope of oral controlled release, with the need to tune the *in* vivo-in vitro correlation in biorelevant media, develop new systems to modulate the release of poorly soluble drugs, and understand patient needs. A discussion was sparked, including questions from a special guest, Paolo Colombo (University of Pavia, Italy). It was an all-around success and a delight to be a part of this workshop.



Evolution of Controlled Release R&D "Get Up! Get Educated!" session: Left to right: Irwin Jacobs, Yewande Oni (chair), and Ali Rajabi-Siahboomi.

The YSC acknowledges the valuable contributions of chair Josh Reineke and of CRS headquarters program manager Megan Pagel over this past year, as well as the guidance of board liaison Christine Allen. We welcome new deputy chair David Chen (Pfizer, U.S.A.) as well as new board liaison Maria José Alonso (University of Santiago de Compostela, Spain). Finally, we look forward to collaborating with the current and new members as we plan events for next year's meeting in Edinburgh, Scotland, continue to grow our Mentor/Protégé program, and strengthen our ties with the other CRS divisions and committees.

CRS Awards: Nominate a Colleague

One of the ways in which CRS supports its members and the advancement of delivery science is by recognizing those who have made significant contributions to the science and the society. Each year CRS seeks nominations for these prestigious awards. Please take a moment to read the profile of each award, and consider nominating a colleague who you believe deserves to be recognized. The awards will be presented at the 42nd CRS Annual Meeting taking place on July 26–29, 2015, in Edinburgh, Scotland. A list of past awardees can be found on the CRS website (controlledreleasesociety.org). Details of the nomination process, the committee responsible for award selection, and the benefits received are available on the CRS website. Awards can include a substantial honorarium and complimentary registration to the CRS Annual Meeting & Exposition. All nominees must be CRS members. Questions about the nomination packet or selection process should be directed to CRS headquarters, attention Linda Schmitt at lschmitt@scisoc.org. Nominations for all awards must be received by January 31, 2015.

College of Fellows Award

The most prestigious level of membership in CRS, a maximum of five new Fellowships will be awarded each year. To date, 91 CRS members have received this award. The College of Fellows recognizes CRS members who have made outstanding contributions to the field of delivery science and technology over a minimum of ten 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.



Paolo Colombo received the 2014 CRS Founders Award for his outstanding contributions to the science and technology of controlled release. Left to right: Art Tipton, Paolo Colombo, and Ian Tucker.





Tsuneji Nagai (right) congratulated Lin Zhu (center) and his advisor, Vladimir Torchilin (left), on receiving the 2014 CRS T. Nagai Postdoctoral Research Achievement Award.

CRS Young Investigator Award winner Suzie H. Pun presented at the CRS Annual Meeting.

CRS 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.

CRS T. Nagai Postdoctoral Research Achievement Award

Cosponsored by The Nagai Foundation Tokyo

Established to recognize those who have made an outstanding postdoctoral research achievement in controlled release science and technology, the CRS T. Nagai Postdoctoral Research Achievement Award recognizes an individual postdoc who has recently completed postdoctoral research and the postdoc's advisor, who played an integral role in the nominee's achievements. Candidates for the award may be from academia, industry, or government.

CRS Young Investigator Award

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

RECOGNIZE CONTRIBUTIONS TO DELIVERY SCIENCE

CRS award nominations accepted through January 31, 2015

controlledreleasesociety.org/awards

Targeted Delivery of siRNA to Activated T Cells by Using Transferrin-Polyethyleneimine for Therapy of Asthma

Yuran Xie,¹ Na Hyung Kim,¹ Venkatareddy Nadithe,¹ Archana Thakur,^{1,2} Lawrence G. Lum,^{1,2} David J. P. Bassett,¹ and Olivia M. Merkel^{1,2}

Introduction

Asthma is a chronic inflammatory lung disorder that is a major public health problem. It has been shown that activated Th2 cells play an important role in the pathology of asthma and overexpress transferrin receptor that can mediate endocytosis after binding with the ligand.^{1,2} Our therapeutic reagent, small interfering RNA (siRNA), which is involved in RNA interference, could perform promising and potent therapeutic effects by inducing transient sequence-specific gene silencing.^{3,4}

However, lymphocytes are well known to be hard to transfect or efficiently target by siRNA delivery. Also, reaching the desired cells with minimum toxicity remains a challenge.^{3,5} So we designed a targeted siRNA delivery system containing transferrin (Tf) and low-molecular-weight polyethyleneimine (PEI, 5 kDa), which is one of the most extensively studied cationic polymers for siRNA delivery.

Our hypothesis is that the Tf-PEI conjugate can efficiently target and deliver therapeutic siRNA to activated T cells via pulmonary administration for the therapy of asthma.

Here, we optimized Tf-PEI conjugation, tested *in vitro* Tf-PEI/ siRNA uptake and gene knockdown efficiency in human primary activated T cells, and measured the distribution of Tf-PEI/ siRNA *in vivo* after intratracheal administration in a murine asthma model.



Figure 1. Scheme of Tf-PEI conjugate synthesis.

- ¹ Wayne State University, Detroit, MI, U.S.A.
- ² Karmanos Cancer Institute, Detroit, MI, U.S.A.

Synthesis and Characterization of Tf-PEI

PEI was conjugated to Tf by using N-succinimidyl 3-(2-pyridyldithio) propionate (SPDP) as a cross-link reagent (as shown in Figure 1). The Tf-PEI conjugate was purified by ion exchange chromatography and membrane ultrafiltration. The resulting Tf-PEI conjugate contained a disulfide bond, which could help the Tf-PEI/siRNA escape from the endosome and release siRNA after internalization in cells. The molar ratio of Tf and PEI was approximately 1.5.

As shown in Table 1, Tf-PEI/siRNA polyplexes had suitable sizes around 50 nm, which could promote their uptake into cells, and had neutral zeta potentials, which could prevent plasma protein binding and toxicity.

siRNA Condensation of Tf-PEI

siRNA condensation efficiency of the polymer/conjugate was quantified by using an intercalating dye, SYBR Gold, to which nucleic acids condensed with polymers are not accessible (Figure 2). The free siRNA was decreased with increasing N/P ratios. Tf-PEI showed full condensation of siRNA at N/P 7. The condensation efficiency of Tf-PEI was comparable to PEI.

Uptake of siRNA in Activated T Cells

Tf-PEI mediated Alexa Fluor 488-labeled siRNA uptake in human primary activated T cells was significantly higher than achieved with PEI or Lipofectamine (LF), both of which are

Table 1. Zetasizer NanoZS Result of Polyplex of Tf-PEI and PEI with siRNA

	Diameter (nm)	PDI	Zeta Potential
PEI/siRNA	396.1	0.276	7.6
Tf-PEI/siRNA	51.76	0.202	-0.71



Figure 2. Condensation of siRNA by using SYBR Gold binding assay.

common commercial transfection reagents (Figure 3). It confirms that lymphocytes are hard to transfect, whereas our targeted delivery strategy can achieve efficient cellular uptake. In naïve T cells, however, siRNA delivery cannot be achieved with Tf targeting either. This confirms the specific delivery to activated rather than naïve T cells.

In Vitro Gene Knockdown in Activated T Cells

To investigate the gene knockdown efficiency of Tf-PEI, human activated T cells were transfected by Tf-PEI or PEI with housekeeping gene GAPDH siRNA or negative control siRNA. Specific knockdown of GAPDH mRNA was measured by quantitative real-time PCR (qRT-PCR). Tf-PEI/siRNA polyplexes were able to significantly knock down GAPDH gene expression compared with the positive control group PEI/siRNA and the untreated group (Figure 4).

siRNA Delivery in a Murine Asthma Model

The protocol for the murine asthma model is shown in Figure 5. After intratracheal administration, Tf-PEI/siRNA showed significantly higher uptake in CD4+ lung cells of ovalbumin (OVA) treated mice (Figure 6). Further subdifferentiation of CD4+ cells and identification of uptake in other cells of the lung are currently underway.

A siRNA uptake in activated T cells (high TfR) B siRNA uptake in naive T cells (low TfR)



Figure 3. Flow cytometry results. (A) Uptake of Alexa488-labeled siRNA in primary activated T cells. (B) Uptake in primary naïve T cells. (*** indicates P < 0.001 compared with blank.)



Figure 4. *qRT-PCR results of GAPDH gene knockdown in human activated T cells.*



Figure 5. Process of an OVA-induced murine asthma model.



Figure 6. Flow cytometry results of Alexa647-labeled siRNA uptake in CD4+ cells in the lung mediated by PEI, Tf-PEI, or after administration as free siRNA. (*** indicates P < 0.001 compared with free siRNA.)

Conclusions

Our study showed the successful conjugation of transferrin with PEI and efficient siRNA condensation of the Tf-PEI conjugate. With the Tf-PEI conjugate, we demonstrated the enhanced and specific uptake and gene silencing effect in primary activated T cells *in vitro*. Tf-PEI can successfully target and deliver siRNA to CD4+ cells in a murine asthma model. These results suggest that our Tf-PEI conjugate could be a promising and efficient delivery system for targeted delivery of therapeutic siRNA to activated T cells for therapy of asthma.

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Local Lung Codelivery of siRNA and Drug

Vera Ivanova, Olga B. Garbuzenko, Ruslan Rustamov, Kenneth Reuhl, Gediminas Mainelis, and Tamara Minko Rutgers–The State University of New Jersey, U.S.A.

Introduction

Inhaled therapeutics have recently played an important role in local therapy of various lung diseases including lung cancer and idiopathic pulmonary fibrosis (IPF). However, the efficiency of therapeutic agents delivered via inhalation is limited by the complexity of devices used and difficulties in formulation of suitable dosage forms.^{1,2} Furthermore, unlike asthma drugs, biological therapeutics including siRNA cannot be administered without an appropriate dosage form because of their fast degradation and poor cellular penetration.³ Prostaglandin E2 (PGE2), a cyclooxygenase-derived lipid mediator, has attracted considerable attention for its role in the development and progression of IPF and as a possible therapeutic agent for this disease.^{4,5} Previously, we found that chemokine CCL12, matrix metalloproteinase MMP3, and hypoxia-inducible factor HIF1A are key proteins responsible for the development of inflammation and IPF.⁵ We hypothesized that inhibition of these proteins by the local inhalation codelivery of PGE2 and multiple siRNAs



Figure 1. (A) Intratracheal instillation of bleomycin. (B) Structure of lipid nanoparticles (LN) based delivery system. (C) Installation for inhalation delivery of LN-based delivery system. (D) Particle size distribution by dynamic light scattering. (E) Atomic force microscope (AFM) images of nanoparticles.

targeted to mRNA encoding these proteins can be successfully used for effective treatment of IPF. The present investigation is aimed at developing an appropriate nanoscale-based complex of drug and siRNAs for such inhalation codelivery and verifying the hypothesis.

Experimental Methods

Lipid nanoparticles (LN) were used as a vehicle to deliver PGE2 and siRNAs. Precirol® ATO5, PGE2, and lecithin were dissolved in methanol with addition of butanol as a cosurfactant and preheated to 70°C under stirring. Then temperature was decreased to 37°C, and aqueous solution was added. Aqueous solution was prepared by mixing DOTAP with siRNA in 10 mL of Tween 80/MeOH/H₂O. The mixture was homogenized, sonicated, and allowed to stir for 8 h for precipitation. LNs were characterized by atomic force, transmission electron, and fluorescence microscopy and differential scanning calorimetry. Size and zeta potential of LN were also measured. Cyto- and genotoxicity of nanoparticles were assessed with MTT and comet assays, respectively.

In vivo experiments were carried out on SKH1 mice. Bleomycin was administered intratracheally to the mice in a 1.5 U/kg dose. Mice were treated for three weeks with a complex delivery system by inhalation or IV injection. PGE2 delivered by liposomes (Lip-PGE2) via inhalation route was used for the comparison. Mice were sacrificed and lungs, liver, kidney, spleen, heart, brain, and serum were collected for histological analysis. In addition, lungs were used for the histopathological evaluation, hydroxyproline and collagen measurements, TEM, immunohistochemistry, and TUNEL apoptosis assays. RNA was isolated, and quantitative PCR analysis of 84 key genes involved in the development of lung inflammation and fibrosis was carried out. Distribution of LN in lungs and other organs after intravenous or inhalation administrations was examined with an IVIS imaging system. Magnetic resonance imaging (MRI) was used to visualize fibrotic tissues.

Results and Discussion

The data presented in Figure 1 show that the developed LN had a spherical form with a narrow size distribution. A four-port nose-only exposure chamber was used for inhalation by mice as previously described.⁶ It was found that the chamber provided a uniform distribution of nanoparticles between the ports and did not influence significantly the size and shape of LN. Data showed that the developed nanoparticles were noncytotoxic and nongenotoxic and provided for an efficient protection of active components from degradation during the nebulization. The development of IPF and lung injury in experimental animals after the instillation of bleomycin was confirmed by the histopathological evaluation, body and lung weight, as well as lung hydroxyproline (a major component of the protein collagen) concentration measurements (Figure 2). In addition, MRI revealed a dense tissue in the lungs. Development of IPF also led to the overexpression of inflammatory and mesenchymal transition genes and protein that destabilized homeostasis and



Figure 2. Validation of IPF mouse model and treatment of mice by inhalation with liposomes (Lip-PGE2) or lipid nanoparticles (LN) (LN-PGE2 and LN-PGE2-siRNA). (A) Selection of bleomycin dose. Influence of inhalation treatment of IPF with Lip-PGE2 or LN-PGE2 on body weight (B) and lung weight (C). (D) Hydroxyproline content in the lungs. (E) Representative MRI images of healthy mice and untreated and treated animals with fibrosis. (F) Lung tissue histology. Animals were treated on day 15 after instillation of bleomycin. 1 = healthy animals (control); 2 = animals with IPF (bleomycin); 3 = animals with IPF treated with empty liposomes; 4 = animals with IPF treated with empty LN; 5 = animals with IPF treated with Lip-PGE2; 6 = animals with IPF treated with LN-PGE2; and 7 = animals with IPF treated with LN-PGE2-siRNA (targeted to HIF1A mRNA). Means ± SD are shown in the bar charts. * indicates P < 0.05 when compared with healthy untreated animals (control). † indicates P < 0.05 when compared with untreated animals with IPF (bleomycin).



Figure 3. Inhalation versus intravenous delivery of lipid nanoparticles (LN). (A) Relative tissue content of LN nanoparticles delivered to mice by intravenous injection or inhalation. LN content was registered in different organs 24 h after inhalation. Means are shown. (B) Localization of LN in the mouse lung tissues after the inhalation delivery. Representative transmission electron microscope image is shown.

induced apoptosis in lung tissues. Mice with IPF were treated by the developed delivery system via inhalation and IV injections. Biodistribution and TEM studies clearly showed that LNs were predominately accumulated in the lungs and penetrated lung cells after inhalation (Figure 3). Combinatorial treatment of mice with IPF by LN containing PGE2 and siRNAs had a synergistic effect in attenuating lung fibrosis by downregulating inflammatory factors, preventing alveoli collapse through synthesis of surfactant, downregulating myofibroblast proliferation, limitation of lung hydroxyproline, and restoring body and lung weights in experimental animals. These positive effects were significantly more pronounced after inhalation compared with IV treatment. Finally, inhalation treatment by PGE2 and siRNAs significantly decreased mortality of mice with IPF.

Conclusions

Our results showed that IPF can be effectively treated by local inhalation lung delivery of PGE2 and several specific siRNAs by LN. The data provided evidence that dual drug/siRNA nanoparticle-based inhalation treatment led to the overcoming of fibrogenesis, making this composition attractive for treatment of inflammation and IPF.

Acknowledgements

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Multidisciplinary Controlled Drug Delivery Research with Edith Mathiowitz

Vishwas Rai¹ and Bozena B. Michniak-Kohn²



Edith Mathiowitz is a professor of medical science and engineering and director of the biotechnology graduate program in the Department of Molecular Pharmacology and Biotechnology at Brown University, Providence, Rhode Island, U.S.A. One research highlight of her career has been the successful oral delivery of insulin to the body using an encapsulation approach. Her research led to the development of a bioadhesive delivery system with which

she was able to show the potential of increasing the oral bioavailability of nonadhesive nanoparticles from 4 to 65%. She was the founder of biotech company Spherics in 1997 and cofounder of a second biotech company, Perosphere.

She received her B.Sc. in chemistry followed by an M.Sc. and Ph.D. in physical chemistry at the Department of Structural Chemistry at the Weizmann Institute of Science in Israel. After finishing her Ph.D., she received the prestigious Bantrell Postdoctoral Fellowship at Massachusetts Institute of Technology (MIT) to pursue her research in the field of surface science. She finished her postdoctoral training at Dr. Robert Langer's lab working on development of erodible systems for drug delivery. She started her career with Enzytech as a senior scientist in drug delivery. She then moved to academia and took a position as an associate professor and then professor (1999) of medical science and engineering at Brown University.

Dr. Mathiowitz's current research interests include development and characterization of novel bioadhesive delivery systems, oral delivery of proteins such as insulin and growth factors, development of nanotechnology approaches for therapeutic applications, development of bone repair delivery systems, development of drug-eluting vascular grafts, use of progenitor cells to redirect healing of vascular grafts, development of novel liquid crystals as smart sensory devices, and gene/DNA delivery. She has published over 120 research articles, acquired 75 patents, and acts as a consultant to multiple biotech companies.

She has won multiple awards, including the Delek Prize (1982) for distinctive research work at Weizmann Institute, Whitaker Foundation Award (1991–1993), and Eurand Award for excellence in research in the area of oral drug delivery systems (2000). She has served as a member of the editorial boards of the *Journal of Biomaterials* (1996–2003), *Journal of Controlled Release* (1993–2003), and *Journal of Microencapsulation* (2000–2003) and

serves as a reviewer for multiple peer-reviewed journals. In addition, she has been involved in organizations such as the National Institutes of Health (NIH), American Chemical Society, American Association for the Advancement of Science, and others. She served on the CRS Board (1997–2001). She is an AIMBE fellow. For her outstanding contributions, she was recently inducted into the National Academy of Inventors. She has graduated about 30 Ph.D. students and about the same number of master's and honors students at Brown.

- **Q** What was the scientific basis of the bioadhesive delivery systems that ultimately may increase the bioavailability of insulin-like molecules?
- A Research in my laboratory started by developing novel bioadhesive polymers, which were different than the traditional hydrogels. It was the understanding that polymers such as polyanhydrides are more adhesive in general and better delivery systems for certain drugs, since they retain hydrophilic and hydrophobic drugs more effectively than hydrogels such as poly(acrylic acid). Specifically, we observed that bioadhesion with those new polymers elongated the residence time in rats, dogs, and pigs as well as enhanced the bioavailability of hydrophobic drugs.

The question my group then asked was what would happen if we made nanoparticles and delivered insulin and DNA. The results were astonishing and were initially received with a lot of criticism, yet *Nature* accepted the evidence and published the data. From there, my group has focused on studying the mechanism of action and more specifically what type of polymers will be both useful and nontoxic. By utilizing bioadhesive nanoparticles, we increased the residence time of these nanoparticle delivery systems in the gastrointestinal



Mathiowitz with members of her lab at Brown University in 1997, the same year she founded her first biotech company, Spherics.

¹ Chrono Therapeutics Inc., Waltham, MA, U.S.A.

² Ernest Mario School of Pharmacy, Rutgers–The State University of New Jersey, U.S.A.

tract, thereby producing a greater chance of uptake of these particles by both Peyer's patches as well as by the enterocytes of the intestine with subsequent release into the blood.

- Q Which polymeric entities were involved in the development of nanoparticles? Did the delivery system also successfully encapsulate and perform (i.e., deliver molecules to targeted sites during in vivo studies) for other biomolecules such as DNA and RNA? What encapsulation efficiencies did you achieve with different polymeric units tested?
- A Bioadhesion was one tool that we used, but the other challenge was developing efficient encapsulation techniques for each specific therapeutic. So we have focused on developing specific methods for encapsulating biologic molecules. As long as the development was in our lab, the efficiency of encapsulation was about 70%. Once the product was transferred to a company (Spherics) the efficiency of encapsulation reached over 95%.

Translation to a company setting from the lab focused the research more on development, which was why we were able to achieve high encapsulation efficiency. A variety of polymers have been used by my lab—from polyanhydrides to polyesters—while retaining protein bioactivity with molecules such as insulin, growth hormone, IL-12, VEG-F, and GM-CSF, to name a few. The nanoparticles were used for parenteral as well as oral delivery.

- Q Your research group performed a lot of in vivo animal studies for the polymeric nanoparticles. What drug delivery challenges did you face going from in vitro lab experiments to in vivo testing?
- A I was lucky to have motivated, outstanding students in the biotechnology and biomedical engineering programs. Each of my graduate students took a unique course, Experimental Surgery, which is taught at Brown by a dedicated team. Thus, almost all of my graduate students were able to perform preclinical studies that, depending on funding from institutions such as NIH and JDRF, were performed on mice, rats, dogs, and pigs. The transfer from the lab to a startup company went smoothly because of the experience my graduate students had in proficiently performing animal studies. In addition, I like to create a dedicated team of scientists who, once they graduate, can move seamlessly to a company setting. My first and second companies' employees were students or postdocs trained in my lab.

Q Please tell us about the idea behind the development of liquid crystals and its current status.

A The idea of developing liquid crystals or liquid crystal-like materials is in progress. Most of the efforts of my students are currently directed toward understanding the morphological changes we induce to create birefringent polymers and how to use them as drug delivery systems.



Mathiowitz lab members in 1999.

- Q Please tell us about the drug-eluting vascular grafts. What kind of polymeric properties do you look for in a vascular graft material? What drugs have you loaded and tested for release?
- A The idea behind this work was to develop a process for the inclusion of polymer microspheres in microporous polyurethane tubes and membranes. The artificial organs laboratory developed a unique way to make porous vascular grafts before I came to Brown. This work focused on the development of small-diameter vascular grafts by optimizing the process based on phase separation phenomena, one of my favorite topics. These composites were fabricated via a spray, phase-inversion technique using Cardiothane[™] 51, a medical-grade polyurethane, and either spray-dried poly (D,L-lactide-co-glycolide 50:50) microspheres or commercially available fluorescent polystyrene-latex microspheres. We intended to release heparin to prevent clotting, as this is a major hindrance with the development of small-diameter vascular grafts. This project reflected my desire not only to work on traditional dosage forms but to develop complex systems for tissue engineering.

Q Which bone repair research approaches are being investigated in your lab?

A The work on bone regeneration was a collaboration between my previous graduate student Ana Jaklenec and Roy Aaron, Bahar Bilgen, and Deborah Ciombor. The role of my team was to develop sequential growth factor release, which we achieved by fusing microspheres containing various growth factors. Growth factors have become important for tissue engineering and regenerative medicine alike. Insulin-like growth factor-I (IGF-I) and transforming growth factor- β 1 (TGF- β 1) in particular have great significance in cartilage tissue engineering. We described sequential release of IGF-I and TGF-B 1 from a composite made of poly(L,D-lactic-coglycolic acid) (PLGA) scaffolds. Growth factors were encapsulated in PLGA microspheres using a spontaneous emulsion technique. The bioactivity of released IGF-I and TGF- β 1 was determined using the MCF-7 proliferation assay and HT-2 inhibition assay, respectively. Both growth factors were released for up to 70 days in their bioactive form.

Interview with Mathiowitz continued from page 23

Scaffolds were fabricated by fusing bioactive IGF-I and TGF- β 1 microspheres. The fusion of microspheres occurred by using dichloromethane vapor, which lowered the glass transition of each microsphere at the surface, thus causing fast attachment of the spheres while still leaving a very porous structure. This approach allowed for developing scaffolds with tailored release kinetics: IGF-I and TGF- β 1 released continuously, or TGF- β 1 with IGF-I released sequentially after 10 days, or IGF-I with TGF- β 1 released sequentially after 7 days. The ability of these scaffolds to release IGF-I and TGF- β 1 sequentially made them useful for cartilage tissue engineering applications.

- Q Please tell us about postdoctoral research in Robert Langer's lab at MIT. What were your experiences working in such a large research group? How did this experience shape your future career?
- **A** I was always fortunate to have the best mentors in my life. It began with my parents, who always encouraged me to do whatever I desired. This paved the way for my future success. However, when my mother realized how serious I was about planning to become a scientist, she quietly told me that it was unacceptable to get a Ph.D. without having at least one child. In the end I had two wonderful children, one who was born during my master's degree program and another just before my Ph.D. defense. I arrived at Prof. Langer's lab and was sure that he would not be happy about my family. In my first meeting with him, he assured me that he supported me leaving early if necessary and that as a Bantrell recipient he expected me to choose my own topic for research in his lab. This first meeting changed my entire personality. Prof. Langer had just changed my "phenotype." I came to his lab with two young children, shy and timid, and here was this great scientist telling me to design my own research. How wonderful! The time I spent in his lab taught me how to interact with peers, graduate students, and undergraduates as well. He was the first mentor who taught me how to start companies and how *never* to get discouraged from negative criticism from any distinguished institute—just fight to address all comments and improve my results for the next round. What an amazing time! All the postdocs and graduate students during my time in the Langer lab are still today my best friends.



Mathiowitz with her current lab members.

- Q You spent a very short time in industry before returning to academia. What shaped that decision?
- A I loved working in industry. I liked the focus and the enormous energy, which is why I joined Enzytech, Prof. Langer's first startup company focusing on protein delivery. However, being a workaholic, I found myself easily bored and felt that I could probably run my own group in an academic setting. I still work in industry as a consultant, but working in a university, teaching, and inventing with bright young scientists is my passion, and it is impossible to resist.
- Q Please tell us about Spherics. How was it founded? What was the main technology? Also, tell us a little about the science versus business aspects.
- A Spherics was the first company I founded after publishing the *Nature* paper in 1997. I had minimal experience but a lot of enthusiasm. My entire lab that developed the bioadhesive polymers moved to the startup, and had we managed to get more money, we probably would have three products on the market. The company was focused on CNS drugs, making large dosage forms based on bioadhesive polymers. We raised more than \$40,000,000 and had about 60 employees at one time. Unfortunately, Spherics is no longer in existence due to lack of funding; however, it is my dream to start a similar company in Rhode Island with my current students.

Q What challenges did you face while handling a startup biotech, and how did you manage it?

- A The first experience with Spherics taught me that the most important parts of starting a company are to have a compelling story and to get a dedicated team of scientists. In my case, the dedicated team of scientists began with my students and postdocs. The focus then is to get enough preliminary animal study data and, once the funding is secured, to choose an appropriate CEO. I like to start companies, but I run them only as long as they are virtual. Once the funding is secured, I usually identify a capable CEO who has the knowledge to run the company toward development of a product. My role in the company then changes to a consultant. The challenge nowadays is to work hard on funding for your lab, where most ideas are created, and then generate funding for a startup in case commercial potential is created.
- Q Please list the most important publications from your research group to give a broad understanding of your research achievements to readers.
- A Here are the most important papers that have come out of my lab:

Mathiowitz, E, Jacob, JS, Jong, YS, Carino, GP, Chickering, DE, Chaturvedi, P, Santos, CA, Vijayaraghavan, K, Montgomery, S, Bassett, M, Morrell, C. Biologically erodable microspheres as potential oral drug delivery systems, Nature 386: 410-414 (1997).

Pekarek, KJ, Jacob, JS, Mathiowitz, E. Double-walled polymer microspheres for controlled drug release, Nature 367: 258-260 (1994).

Reineke, J, Cho, DY, Dingle, YL, Cheifetz, P, Laulicht, B, Lavin, D, Furtado, S, Mathiowitz, E. Can bioadhesive nanoparticles allow for more effective particle uptake from the small intestine? J. Controlled Release 170: 477-484 (2013).

Reineke, JJ, Cho, DY, Dingle, YT, Morello, AP, 3rd, Jacob, J, Thanos, CG, Mathiowitz, E. Unique insights into the intestinal absorption, transit, and subsequent biodistribution of polymer-derived microspheres. Proc. Natl. Acad. Sci. U.S.A. 110: 13803-13808 (2013).

However, to better understand my research, I recommend reading the papers I have published with my graduate students, research assistants, and postdocs.

- On bioadhesion and oral delivery of microspheres: Jules Jacob, Stacia Furtado, Don Chickering, Jerry Carino, Joshua Reineke, Arthur Morello, Camilla Santos, Danielle Abramson, Bryan Laulicht, Peter Cheifetz, James Chen, Ben Hertzog, Haitao Qian, and Christopher Thanos.
- On gene delivery and stem cell recruitment: Diana Ferris, Yong Jong, Verida Leandre, and Sasha Bakhru.
- On parenteral delivery and fibers: Jennifer Godbee, Michael Harrison, Nasheen Rahman, Maryellen Sandor, Wendy Webber, Danya Lavin, Ana Jaklenac, Nicola Bailey, and Mark Kreitz.

OUTSTANDING ACHIEVEMENT DESERVES THE SPOTLIGHT

CRS award nominations accepted through January 31, 2015

Here's your chance to recommend a colleague for a prestigious CRS award:

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

The CRS website includes eligibility requirements, nomination process, and online nomination form at controlledreleasesociety.org/awards

- On polymeric liquid crystal-like materials: Edwin Edwards and Christopher Baker.
- Q What are the most important oral delivery systems that you think have had the greatest impact on the oral drug delivery field?
- A The osmotic pumps by Alza, the first injectable system the Lupron Depot by Takeda, and the new protein oral delivery system by Oramed.
- **Q** On a lighter note, if you have any free time left, how do you like to spend it? Do you like traveling? What are your favorite destinations?
- A In my free time, I would like to take my two dear children and their families around the national parks in the United States. In addition, I would like to visit all the opera houses in Europe and the Metropolitan Opera House more often.

Welcome New CRS Members

Hyemi Ahn Hassan Almoazen Mitch Antoon Minjung Bae Mallory Banholzer Merav Blanca Nusrat Chowdhury Bill Deierlein Sandra Ekdawi John Elicker Randall Engler Marianna Foldvari Thomas J. Franz Keith Harris Shawn Hou Michael E. Hudson Hanjun Hwang Shirish Ingawale Matthew J. Jackson Mini Jan Gonto Johns Min Kyung Joo Sekhar Kanapuram Seongkyu Kim Hiroyuki Konishi

Umar Latif Marc Lavertu Yongkyu Lee Jerry Xiaofei Liu Lei Liu William McCarthy Ronald Meijboom Sterghios A. Moschos Melissa Olds Edward Orton Tim Peterson Krishna Raman Clive Roberts Amit Sagi Eun Young Seol Hui Shao Pattisue Simpson Se-Il Sohn Ching-Chiang Su Anand S. Ubhe Kurt G. Van Scoik Puratchi Vanangamudi Trinh Phuong Vo Xueying Yan Wenmin Yuan



Malaysia CRS Local Chapter Inaugural Meeting 2014

Mohd Cairul Iqbal Mohd Amin, Universiti Kebangsaan Malaysia

MyCRS successfully conducted its inaugural meeting on August 23, 2014, in conjunction with the Controlled Release & Drug Delivery Symposium 2014 (CRDDS2014) jointly organized with the Faculty of Pharmacy, Universiti Kebangsaan Malaysia, in Kuala Lumpur. The small meeting attracted over 50 participants from all over Malaysia with various academic and professional backgrounds in the area of controlled release and drug delivery.

At the meeting, the pro-tem committee members were unanimously reelected to lead MyCRS for the 2014–2016 session. The MyCRS executive council is as follows: president, Mohd Cairul Iqbal Mohd Amin; vice president, Allan Coombes; secretary, Tuan Mazlelaa Tuan Mahmood; treasurer, Shiow Fern Ng; and postgraduate representative, Haliza Katas. The following people will serve on the nonexecutive council: Mohd Hanif Zulfakar, Wong Tin Wui, Ahmad Fuad Shamsuddin, Farahidah Mohamed, Peh Kok Khiang, Kartini Noorsal, Ida Idayu Muhamad, and Azmy A. Hamid.

In his inaugural speech as president, Mohd Cairul Iqbal Mohd Amin presented his vision to the members and invited everyone to work with him to ensure the success of MyCRS as a platform for exchange of ideas, knowledge sharing, networking, and advancing research in the area of controlled release and drug delivery.

The symposium featured a plenary lecture on the history of drug delivery and the Controlled Release Society (CRS) given by CRS Immediate Past President Ian Tucker via live televideo conference from Dunedin, New Zealand.



Ian Tucker gives his plenary lecture.



A group photo of CRDDS2014 participants.



Participants view the poster presentations during a tea break.



Newly elected MyCRS President Mohd Cairul Iqbal Mohd Amin addresses the members.

CRS Nordic Local Chapter Symposium on Drug Transport and Delivery

Christel Bergström,¹ Bente Steffansen,² Leena Peltonen,³ and Ingunn Tho⁴

The Faculty of Pharmacy at the University of Helsinki, Finland, hosted the biannual CRS Nordic Local Chapter meeting August 26–27, this year with the theme "Drug Transport and Delivery." The meeting took place back-to-back with the Globalization of Pharmaceutics Education Network (GPEN) meeting. This enabled the committee to invite a large number of world leaders, being in Helsinki for the GPEN meeting, to also contribute to the CRS Nordic Local Chapter meeting. The high level of the scientific program resulted in 90 participants coming from 10 countries.

The meeting was opened by chair Ingunn Tho (University of Oslo, Norway) and Jouni Hirvonen (University of Helsinki, Finland) and had four sessions. The first session had the title "Drug Delivery of Poorly Soluble Compounds" and was chaired by Christel Bergström (Uppsala University, Sweden). Three invited speakers (Thomas Rades from University of Copenhagen, Denmark; Patrick Augustijns from University of Leuven, Belgium; and Ben Boyd from Monash University, Australia) gave talks on amorphous drug and drug products of multicomponent systems, biorelevant dissolution profiling, and colloidal structures present in the gut after administration of formulations or a meal. These talks provided an extensive state-of-the-art overview of the complex environment that poorly soluble compounds get exposed to at several levels, ranging from production/manufacturing over storage and physical stability to intestinal dissolution and absorption. The talks were inspiring, and the participants were



Invited speaker Steven Schwendeman from the University of Michigan.



Sven Engström from Chalmers University of Technology presents his research.



Delegates listening to the scientific program.

active during the time given for questions. After the three invited speakers, two abstracts selected for oral talks were presented. Matthew Crum (Ph.D. student from Monash University, Australia) presented a new model combining digestion of and drug absorption from lipid-based formulations. Marcus Brewster (Johnson & Johnson, Belgium) thereafter presented a small-scale method for production of stable liquid nanosuspensions. The session was closed by a panel discussion in which Matthew Crum and Marcus Brewster jointly discussed questions related to their studies, a format that worked well. The session was followed by a joint lunch.

The second session, with the topic "Novel Drug Development Technologies," was chaired by Leena Peltonen (University of Helsinki, Finland). Unfortunately, Niklas Sandler, who was scheduled to give a talk on "Printing Technologies in Fabrication of Drug Delivery Systems," had to cancel his participation. The session therefore had one invited speaker, Erem Bilensoy (Hacettepe University, Turkey), who talked about delivery of cationic nanoparticles. Prof. Bilensoy presented studies of surface modification of importance to increase oral bioavailability, but other administration routes were also discussed. Four abstracts had been selected for oral presentation. Neha Shrestha (Ph.D. student from University of Helsinki, Finland) presented her findings on chitosan-modified PSi microparticles as an oral delivery system for insulin. Clare Strachan (University of Helsinki, Finland) presented recent investigations of the suitability of coherent anti-Stokes Raman scattering (CARS) microscopy as a tool for imaging of caco-2 cells grown on filter support. Paul Stein (University of Southern Denmark) presented an NMR technique to determine among others diffusion coefficient, the partition coefficient between octanol and water, and permeability. The last speaker of the session was

¹ Uppsala University, Sweden.

² University of Copenhagen, Denmark.

³ University of Helsinki, Finland.

⁴ University of Oslo, Norway.

CRS Nordic Chapter continued from page 27

Massimiliano di Cagno (University of Southern Denmark), who gave a talk on the solubilization capacity of novel β -cyclodextrindextran polymers and their possible applicability for parenteral administration. Again, at the end of the session, the panel discussion was lively. After this session was a coffee break and an active poster viewing session with 30 posters being presented.

The "Drug Transporters and Delivery" session, chaired by Bente Steffansen (University of Copenhagen, Denmark), had three invited speakers and two presentations selected from the submitted abstracts. The invited speakers, Carsten Uhd Nielsen (University of Copenhagen, Denmark) and Per Artursson (Uppsala University, Sweden), presented their latest results on intestinal transporter-mediated impact on oral drug absorption. Dr. Uhd Nielsen showed how the proton coupled amino acid transporter (PAT1) mediates the absorption of the hydrophilic GABA mimetics vigabatrin and gaboxadol. He highlighted the challenges in proving the impact of carrier-mediated absorption on intestinal absorption in vivo. Prof. Artursson discussed how his mechanistic model may be used to resolve under which conditions transporters influence the apparent intestinal absorption of drugs. Based on dose, solubility, passive permeability, and kinetic parameters from transporter-mediated permeability of 1,800 drugs, the model predicts the impact of transporter inhibition on absorption. The last invited speaker in this session, Joseph A. Nicolazzo (Monash University, Australia), presented his work on transporters in the blood brain barrier (BBB). He focused on possible roles of Pgp and OCT transporters and changes of the cerebrovascular basement membrane thickness in the development of Alzheimer's disease, and he suggested that membrane thickness rather than the transporter functionality influences medication of Alzheimer's disease. The two presentations selected from submitted abstract were given by Ph.D. students Nicolas Darville (University of Leuven, Belgium) and Sara Munk Jensen (University of Southern Denmark). Nicolas Darville presented his work on how CARS microscopy also can be used as a tool for investigating nanoparticle-cell interactions, and Sara Munk Jensen showed her work on extraction of ether-linked phospholipids from *Sulfolobus islandicus* with the intended use to stabilize liposomes for oral administration. There were generally fruitful scientific discussions and many questions from the audience, which made a nice atmosphere. In the evening, an informal get-together was organized in the student association's house with a nice salad buffet and drinks, followed by the opportunity to enjoy the Finish sauna.

The final session Wednesday morning was devoted to "Biomolecular Delivery" and was chaired by Ingunn Tho (University of Oslo, Norway). This session had four invited speakers (Gerrit Borchard, University of Geneva, Switzerland; Teruan Siahaan, University of Kansas, U.S.A.; Steven Schwendeman, University of Michigan, U.S.A.; and Christian Schöneich, University of Kansas, U.S.A.) covering different aspects of formulation and delivery of biomolecules. Prof. Borchard talked about the use of layer-by-layer technology for the delivery of biopharmaceuticals, and Prof. Siahaan focused on peptides derived from cell adhesion molecules and their potential use in autoimmune diseases such as multiple sclerosis. Prof. Swendeman's talk dealt with microencapsulation of various peptides and proteins into porous PLGA matrices by use of spontaneous self-healing at mild temperatures. This technology may overcome some of the challenges owing to protein damage during otherwise harsh process conditions. Prof. Schöneich offered new perspectives to understanding the conjugate-induced chemical instability of antibody-drug conjugates, the use of which is emerging because of the high selectivity. Also in this session, two submitted abstracts were selected for oral presentation: Fransisca Araújo (Ph.D. student University of Porto, Portugal/University of Helsinki, Finland) talked about chitosanbased nanoparticles aiming at improved oral delivery of GLP1, and Sven Engström (Chalmers University of Technology, Sweden) presented his research on how nanoparticles and proteins have been found to cross stratum corneum by means of waterresponsive liquid cubic phases. Also, this session featured questions from the audience and a nice panel discussion. The meeting was closed by acknowledging the local organizers and all contributions.



Networking at the evening event in the house of the Finish Pharmacy Students' Association.



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People in the News

Compiled by Steven Giannos, Independent Consultant

MicroCHIPS, Inc., Appoints Cheryl R. Blanchard, Ph.D., as Chief Executive Officer

Business Wire: July 21, 2014 – WALTHAM, MA, U.S.A. – MicroCHIPS, Inc., a developer of implantable drug delivery devices, today announced that its board of directors has appointed Cheryl R. Blanchard, Ph.D., as chief executive officer and member of the board of directors effective immediately. Blanchard was formerly senior vice president and chief scientific officer of Zimmer, Inc. Blanchard joins MicroCHIPS at a time when the company is preparing for the next stage of commercialization for its implantable drug delivery devices, with a near-term focus on applications for women's health.

"As the former chief scientific officer and general manager of the biologics business at a global medical device company, Cheryl brings a skill set critical for MicroCHIPS to commercialize its products. Her past experiences in bringing complex medical products through the FDA and global regulatory authorities, performing clinical trials, and obtaining reimbursement as well as building the biologics business at Zimmer make her a great fit," said Richard Mott, executive chairman of the board of MicroCHIPS.

Blanchard replaces Bradley W. Paddock, who was appointed interim CEO in December 2013. "I've thoroughly enjoyed leading MicroCHIPS and am more excited than ever about the future for this revolutionary technology," says Bradley. He has accepted a role as general manager, Stryker Spine.

Blanchard has extensive experience in the medical device and biologics sectors. For the past 12 years, Blanchard served in roles of increasing responsibility at Zimmer, Inc., a medical device company focused on musculoskeletal products. Her roles at Zimmer included leadership of research and development, clinical, quality, and regulatory affairs, and health economics. She was also a member of Zimmer's executive committee and developed and led the biologics business at Zimmer through disciplined execution of an R&D pipeline coupled with significant partnering and business development activities. Previous to Zimmer, Blanchard built and led the medical device practice at Southwest Research Institute while also serving as an adjunct professor at the University of Texas Health Science Center, both in San Antonio, Texas. She has a B.S. in ceramic engineering from Alfred University and an M.S. and Ph.D. in materials science and engineering from the University of Texas at Austin.

"I am thrilled to be joining MicroCHIPS to lead the company to the next stage of commercializing game-changing products in women's health," Blanchard said. "A big part of my role will be to focus and build the company to commercialize products that address unmet needs for patients globally with this groundbreaking approach to delivering drugs." MicroCHIPS is currently developing its microchip-based implant to provide daily drug dosing ranging from 6 months to 16 years of therapy. The device can be programmed wirelessly allowing the physician to adjust the dosing for individual patient needs. It is implanted under the skin in a simple outpatient procedure using local anesthesia. MicroCHIPS is currently developing drug delivery devices in women's health applications for contraception and osteoporosis and in chronic diseases of multiple sclerosis and diabetes.

Depomed Announces Appointment of Srinivas G. Rao, M.D., Ph.D., as Chief Medical Officer

PRNewswire: July 16, 2014 - NEWARK, CA, U.S.A. -Depomed, Inc. (Nasdaq: DEPO) today announced the appointment of Srinivas G. Rao, M.D., Ph.D., as chief medical officer and senior vice president. Dr. Rao has extensive experience and background in pain and central nervous system diseases. He was the founder and chief executive officer of Kyalin Biosciences, a privately held biotechnology company developing a potential breakthrough therapy for autism, from its formation in 2011 through to its sale to Retrophin, Inc., in 2013. In 2014, he served as executive vice president and head of neuroscience at Retrophin. From 2011 to 2013, Dr. Rao also served as CMO and CSO of three companies through his association with Avalon Ventures. Finally, from 2001 to 2011, he was chief scientific officer of Cypress Bioscience, where he had a broad range of responsibilities, from business to clinical development. He was the innovator behind Savella[™], postulating that this drug's unique pharmacology would be effective for fibromyalgia. Savella[™] was approved by the FDA for this indication in 2009.

Dr. Rao received his M.D. from Yale School of Medicine and his Ph.D. in neurobiology from Yale Graduate School. Dr. Rao is a member of the American College of Neuropharmacology, the American Pain Society, International Association for the Study of Pain, and the Society for Neuroscience.

"We are delighted to have Srini join us as chief medical officer," said Jim Schoeneck, president and chief executive officer. "His deep expertise in the areas of pain and neurology and his experience in in-licensing and directing the clinical development and approval of medicines to treat important CNS conditions make him a great fit for Depomed as we seek to expand our franchise in pain and central nervous system diseases."

"I am extremely pleased to be joining Depomed at this exciting time in the company's history," said Dr. Rao. "I believe that Jim and the team at Depomed have accomplished a tremendous amount in the past few years and continue to move toward a leadership position in the field of pain and CNS related products. I look forward to helping the company achieve that goal."

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In the News

Compiled by Steven Giannos, Independent Consultant

August

Tris Pharma Selected as an Award Winner in the New Jersey Business & Industry Association's 2014 Awards for Excellence

PRNewswire: August 27, 2014 – MONMOUTH JUNCTION, NJ, U.S.A. – Tris Pharma, a specialty pharmaceutical company focused on developing innovative drug delivery technologies, today announced that it has been selected as an award winner in the New Jersey Business & Industry Association's 2014 Awards for Excellence competition in the Business Expansion category. Finalists were selected by an independent panel of judges from SCORE (Counselors to America's Small Business) and NJBIA member company volunteers. Award winners will be honored at a gala event to be held on October 15, 2014, at the Pines Manor in Edison, New Jersey.

The Business Expansion Award is presented to companies that have contributed to the state's economic growth through the expansion of their business. Tris was selected for its significant growth in the creation of new jobs over the past three years.

"We're thrilled to be an award winner for the NJBIA's 2014 Awards for Excellence competition" said president and CEO Ketan Mehta. "Tris has been part of the New Jersey landscape for 14 years, and we believe in supporting the prosperity of our local communities; on behalf of myself and our employees I'd like to thank the community for their support and the Awards for Excellence Committee for selecting Tris to receive this award."

Tris has several proprietary solubilization and bioavailability enhancing technologies as well as several generic extended release solid dosage products in development, under FDA review, and in the market. Tris's proprietary technologies and developed products are the catalyst for its dramatic growth over the past three years culminating in a 24-hour operation and the addition of almost 250 jobs.

Tris Pharma is a specialty pharmaceutical company focused on the research and development of technologies-driven products. 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[™] technology provides abuse deterrence for opioids and other abuse-prone drugs. Tris's R&D and manufacturing facilities are located in Monmouth Junction, New Jersey, U.S.A. For more information, please visit www. trispharma.com.

Depomed Prevails in Gralise[®] ANDA Litigation Blocking Generic Entry Until 2024

PRNewswire: August 19, 2014 – NEWARK, CA, U.S.A. – Depomed, Inc. (Nasdaq: DEPO) today announced Judge Joel A. Pisano of the U.S. District Court for the District of New Jersey has ruled in favor of Depomed in the company's patent litigation lawsuit against Actavis, Inc., related to Actavis's Abbreviated New Drug Application for generic versions of Depomed's Gralise[®] (gabapentin) tablets for the management of postherpetic neuralgia.

Judge Pisano's ruling finds that Actavis infringes all seven Depomed patents asserted and upholds the validity of the patents. The latest expiration of the infringed patents is February 2024.

"We are pleased with this decision, as it confirms the innovation of Gralise and the strength of our patents. This ruling provides for nearly 10 years of additional market exclusivity," commented Jim Schoeneck, president and chief executive officer of Depomed. "We look forward to providing Gralise to postherpetic neuralgia patients and their physicians well into the next decade."

Depomed previously announced settlements with two other Gralise ANDA filers providing for generic entry on January 1, 2024.

EastGate Acquisitions Augments Its Submicron Self-Nanoemulsifying Platform Technology

PRNewswire: August 18, 2014 – SALT LAKE CITY, UT, U.S.A. and TORONTO, Canada – EastGate Acquisitions Corporation (OTCBB: ESAQ), an emerging pharmaceutical company exploring drug delivery innovations in the development of novel formulations and alternative dosage forms of existing biologically active molecules, announced that it is augmenting its self-emulsifying submicron platform technology to include a broad spectrum of delivery options. The various technologies are applicable to the company's current pharmaceutical products in development and can also be employed as effective platforms for delivery of other biologically active compounds. The company recently expanded its new product development to include large molecules as active compounds that will address indications in diabetes, obesity, and the overall metabolic syndrome.

The company's technology platform led to the development of several improved novel formulations and alternative dosage forms for delivery of known biologically active molecules. The technology utilizes EastGate's submicron self-emulsifying delivery vehicle and facilitates the creation of harmonized

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formulations with better drug absorption. The company's technological approaches have demonstrated robustness and resulted in diversification of the drug delivery products. The variety of developed dosage forms includes liquid spray or droplets, semi-solid, compressed tablets, and capsules of different types.

The purpose of offering this spectrum of dosage forms is to provide patients with different treatment possibilities and bring products that will fit their lifestyle and improve patient compliance.

Currently the company is working toward acquiring the licensing rights to develop and manufacture an intraoral insulin formulation. The intraoral insulin dosage forms under consideration are liquid and solid dosage forms, such as a compressed tablet that can be delivered to the mouth for intraoral absorption.

"We have recognized the importance of expanding our submicron self-nanoemulsifying platform technology to include different dosage forms and delivery methods," said Anna Gluskin, EastGate's CEO. "The versatility of the submicron platform technology will continue to validate the company's submicron approach and provide a unique opportunity to offer different absorption-enhanced products to widen the target patient population," stated Gluskin.

EastGate Acquisitions Corporation with locations in Salt Lake City, Utah, and Toronto, Canada, is a pharmaceutical company aimed at utilizing drug delivery innovations for developing of improved novel formulations and alternative dosage forms of existing biologically active molecules. The company's model is based on a two-tier business approach that includes development of novel pharmaceutical products and innovative dietary supplements. Both pharmaceutical products and natural supplements are developed using highly effective contemporary technologies and demonstrated already proven usefulness in improvement of bioavailability and biological action of incorporated molecules. The company's product candidates address various pharmaceutical markets, including neurological disorders, such as epilepsy and panic attacks, infectious diseases, and diabetes. The company's natural dietary supplements, also an integral part of the R&D program, include compositions for glucose regulations, urinary tract health improvement, enhanced vitamin delivery, and skin conditions. EastGate is working to expand its current product portfolio through targeted investments in pharmaceutical research and development. EastGate is working closely with clinicians and patient advocate groups worldwide to identify existing health issues where EastGate's approach will be most beneficial for patient care. For more information, please visit the company's website at www. EastGatePharmaceuticals.com.

Sanofi and MannKind Announce Global Licensing Agreement for Afrezza® (Insulin Human) Rapid-Acting Inhaled Insulin

PRNewswire: August 11, 2014 – PARIS, France, and VALENCIA, CA, U.S.A. – Sanofi (EURONEXT: SAN and NYSE: SNY) and MannKind Corporation (Nasdaq: MNKD) announced today that they have entered into a worldwide exclusive licensing agreement for development and commercialization of Afrezza[®] (insulin human) inhalation powder, a new rapid-acting inhaled insulin therapy for adults with type 1 and type 2 diabetes. The companies plan to launch Afrezza in the United States in the first quarter of 2015.

Under the collaboration and license agreement, Sanofi will be responsible for global commercial, regulatory, and development activities. Under a separate supply agreement, MannKind will manufacture Afrezza at its manufacturing facility in Danbury, Connecticut. In addition, the companies are planning to collaborate to expand manufacturing capacity to meet global demand as necessary.

Under the terms of the agreement, MannKind Corporation will receive an upfront payment of \$150 million and potential milestone payments of up to \$775 million. The milestone payments are dependent upon specific regulatory and development targets, as well as sales thresholds. Sanofi and MannKind will share profits and losses on a global basis, with Sanofi retaining 65% and MannKind receiving 35%. Sanofi has agreed to advance to MannKind its share of the collaboration's expenses up to a limit of \$175 million.

"Afrezza is an innovative drug-device combination product consisting of a dry formulation of human insulin delivered through a small, discreet inhaler," said Pierre Chancel, Sanofi senior vice president, Diabetes Division. "Afrezza is a further addition to our growing portfolio of integrated diabetes solutions. It is uniquely positioned to provide patients with another insulin therapy option to manage their diabetes but does not require multiple daily injections."

"We are so very pleased and honored that Sanofi has joined with MannKind to bring Afrezza to patients with diabetes worldwide," stated Alfred Mann, MannKind's chairman and chief executive officer. "Sanofi is the ideal partner given their complementary product portfolio, their vast insulin market presence, and a leading global commercial infrastructure. Our profit-sharing agreement aligns the interests of MannKind and Sanofi to optimize development, commercialization, and manufacturing costs."

Sanofi's diabetes solutions portfolio includes medications as well as drug delivery systems and blood glucose monitoring devices. As a leader in diabetes management, the addition of Afrezza to Sanofi's leading portfolio of pharmaceuticals represents the latest opportunity for the company to bring another insulin option to people with diabetes around the globe.

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The closing of the transaction is subject to customary Hart-Scott-Rodino approval and completion of financing documentation.

Greenhill & Co. served as exclusive financial advisor to MannKind with respect to this transaction.

The U.S. Food & Drug Administration (FDA) approved Afrezza inhalation powder on June 27, 2014, to improve glycemic control in adult patients with diabetes mellitus.

Afrezza (uh-FREZZ-uh) is a rapid-acting inhaled insulin therapy indicated to improve glycemic control in adult patients with diabetes mellitus. The product consists of Afrezza inhalation powder delivered using an inhaler. Administered at the start of a meal, Afrezza dissolves rapidly upon inhalation to the deep lung and delivers insulin quickly to the bloodstream. Peak insulin levels are achieved within 12 to 15 minutes of administration, and decline to baseline by approximately 180 minutes.

Limitations of use: Afrezza must be used in combination with a long-acting insulin in patients with type 1 diabetes mellitus. Afrezza is not recommended for the treatment of diabetic ketoacidosis and is not recommended for patients who smoke. Full U.S. prescribing information, including boxed warning, medication guide, and instructions for use is available at Afrezza. com. Afrezza has been approved with a Risk Evaluation and Mitigation Strategy (REMS) required by the FDA to ensure that the benefits of Afrezza outweigh the potential risk of acute bronchospasm in patients with chronic lung disease.

Phosphagenics Completes First IND Enabling Study for TPM[®]/ Oxymorphone Patch

PRNewswire: August 11, 2014 – MELBOURNE, Australia – Australian drug delivery company Phosphagenics Limited ("the company") (ASX: POH, OTCQX: PPGNY) announced that the first of its additional studies designed to further characterise the TPM®/oxymorphone patch in support of an Investigational New Drug (IND) application with the FDA has been completed. The study was conducted on 15 healthy volunteers at Linear Clinical Research's facility in Perth. It assessed additional pharmacokinetic parameters associated with the safety and elimination profile that were not addressed in the previous multiple dose phase 1 study. The data generated will be used to help design the upcoming phase 2 study, support the IND application, and inform the eventual product label.

This single-dose study unequivocally reproduced the outstanding results obtained in the previous phase 1 study, both in terms of the oxymorphone delivery profile from the patch and the oxymorphone blood concentration in subjects. All 15 subjects achieved an oxymorphone blood concentration that was well above the minimum therapeutic blood level for the drug. The total number of subjects exposed to the TPM[®]/oxymorphone patch now stands at 27 with all patients attaining therapeutic oxymorphone blood levels.

Dr. Paul Gavin, chief scientific officer, said, "The TPM[®]/ oxymorphone patch has demonstrated reproducibility in two independent manufacturing and clinical trial campaigns with all subjects tested demonstrating blood concentrations equivalent to those produced by the commercially available oral dosage form. These studies clearly establish that the TPM[®]/oxymorphone patch has significant potential to be a remarkable product."

"The latest study also provides new information regarding the elimination phase of oxymorphone after patch removal, an important variable in patient safety that is needed to determine the phase 2 study design. As with any transdermal system, drug delivery ceased upon patch removal, and residual drug in the body was eliminated steadily over time. This represents one of the key safety advantages of a transdermal opioid system compared with the oral dosage form. Accidental overdose (i.e. due to the application of multiple simultaneous patches) rarely occurs with a transdermal patch because of the ease of intervention (i.e., removal of the unintended patches and immediate cessation of delivery)," said Dr. Gavin.

Phosphagenics'TPM[®]/oxymorphone patch development program for the next 18 months was previously described at this year's annual general meeting and reiterated in an announcement to the market on July 28, 2014. This result represents the successful and timely completion of the first stage of additional research that was communicated to the market. Phosphagenics will shortly commence the second planned study, which will compare the transdermal absorption of oxymorphone from application of the patch to different parts of the body. That study will inform the selection of appropriate sites for application of patches during phase 2. Both characterisation studies have been designed to provide valuable information for potential licensees as well as various global regulatory bodies.

Phosphagenics expects to begin the phase 2 trial in the United States during the first half of 2015 following the submission of an IND with the FDA.

Columbia Laboratories Announces Sale of IP and Technology for Legatrin P.M. to Lil' Drug Store Products

PRNewswire: August 6, 2014 – BOSTON, MA, U.S.A. – Columbia Laboratories, Inc. (Nasdaq: CBRX) today announced that Lil' Drug Store Products exercised its option to purchase the intellectual property rights and technology related to Legatrin P.M. Columbia licensed this product to Lil' Drug Store Products approximately 14 years ago and has received annual royalties. Based on a predetermined formula, Columbia will receive approximately \$2.2 million for the sale.

"Columbia has a long history of developing products for other companies and licensing the product and associated IP to commercial partners. We are pleased to have completed this transaction, which enables us to monetize our royalty stream and strengthen our balance sheet," said Frank Condella, president and chief executive officer of Columbia Laboratories. Columbia Laboratories, Inc. provides pharmaceutical development, clinical trial manufacturing, and advanced analytical and consulting services to the pharmaceutical industry. The company has a successful heritage in pharmaceutical research and development, particularly in women's healthcare and drug delivery. Its most successful product to date, CRINONE® 8% (progesterone gel), is marketed by Actavis, Inc., in the United States and by Merck Serono S.A. in over 60 additional countries worldwide. For more information, please visit www.columbialabs.com.

July

Columbia Laboratories' Subsidiary, Molecular Profiles, Strikes Alliance with XenoGesis

PRNewswire: July 31, 2014 - BOSTON, MA, U.S.A. and NOTTINGHAM, England - Columbia Laboratories, Inc. (NASDAQ: CBRX) today announced that its subsidiary, Molecular Profiles Ltd., and XenoGesis Ltd. have announced a collaboration that will support pharmaceutical and biotech drug developers during the preclinical and formulation development stage. Molecular Profiles' pharmaceutical development services will be supported by XenoGesis's expertise in preclinical drug metabolism and pharmacokinetics (DMPK) to give clients a smarter route into formulation development and a better understanding of a compound's bioavailability. This strategic alliance will allow the Nottingham-based companies to help drug developers in the initial design and selection of compounds for key DMPK and ADME (absorption, distribution, metabolism, and elimination) studies, as well as supporting lead candidates that have solubility issues during formulation development.

"We are very pleased to have struck this collaboration with the team at XenoGesis," said Frank Condella, president and chief executive officer of Columbia Laboratories. "We have complementary service offerings that allow us to apply a sciencedriven, collective approach to overcome the complexities of challenging molecules. It also adds a vital pK service to our enabling technologies package. For us, this will build upon the very successful drug development alliances we already have in place. We can now seamlessly offer a comprehensive service from initial drug discovery through to clinical supplies with best-inclass companies," concluded Mr. Condella.

XenoGesis was founded by its managing director, Richard Weaver, Ph.D., after a 15-year career at AstraZeneca. The company specializes in studying research compounds from a chemical and biological perspective to inform clients on how they will behave in the body.

Dr. Weaver commented, "Combining our skills in DMPK with the chemical knowledge at Molecular Profiles will provide a solid platform to support clients. We will be able to give them a better understanding of their compounds during preclinical work, which in turn will reduce cost and provide a quicker route to market." Working with leading drug development companies across the world, Columbia Laboratories' Molecular Profiles subsidiary specializes in advanced characterisation, pharmaceutical product development, clinical trials manufacturing, and analytical support. The company recently created a new enabling technologies team and invested in GMP hot melt extrusion (HME) technology at its clinical manufacturing facility to further enhance its expertise in the processing of difficult-toprogress molecules.

Alongside its development capabilities, its MHRA-licensed site enables the company to manufacture a range of dosage forms for clinical trials spanning solids, liquids, semi-solids, and inhaled products, including potent compounds and controlled drugs.

Columbia Laboratories, Inc., provides pharmaceutical development, clinical trial manufacturing, and advanced analytical and consulting services to the pharmaceutical industry. The company has a successful heritage in pharmaceutical research and development, particularly in women's healthcare and drug delivery. Its most successful product to date, CRINONE® 8% (progesterone gel), is marketed by Actavis, Inc., in the United States and by Merck Serono S.A. in over 60 additional countries worldwide. For more information, please visit www.columbialabs.com.

Molecular Profiles Ltd., a wholly owned subsidiary of Columbia Laboratories, Inc., is a contract development and manufacturing organization (CDMO) that specializes in early phase pharmaceutical development. Its early phase services extend from preformulation and formulation development to clinical trial manufacturing, with specialist knowledge on developing challenging molecules and complex compounds. Molecular Profiles is also renowned for its expertise and toolkit to analytically resolve some of the toughest issues during development and relating to intellectual property issues. The company's services are dedicated to pharmaceutical, biopharmaceutical, and healthcare companies across the globe. For more information, please visit www.molprofiles.co.uk

XenoGesis Limited, a contract research organization (CRO), specializes in expert DMPK/ADME laboratory services and interpretation and drug discovery consultancy. The XenoGesis team has significant experience and a track record of delivering candidate drugs to man from their careers at AstraZeneca R&D Charnwood. XenoGesis supports the drug discovery activities of biotechnology and pharmaceutical companies and academic units. For more information, please visit www.xenogesis.com

Boston Scientific Receives CE Mark for Agent™ Drug-Coated Balloon

PRNewswire: July 23, 2014 – MARLBOROUGH, MA, U.S.A. – Continuing to advance the development of innovative treatment options for coronary artery disease, Boston Scientific Corporation (NYSE: BSX) has received CE Mark and begun

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the European market launch of the AgentTM paclitaxel-coated PTCA balloon catheter. The agent drug-coated balloon (DCB) provides physicians with an additional alternative to treat both in-stent restenosis (ISR) and *de novo* small vessel coronary disease.

The agent DCB combines the deliverability of the Boston Scientific Emerge[™] balloon platform and the proven drug paclitaxel. The agent DCB also features proprietary TransPax[™] coating technology, which combines paclitaxel and a citrate ester excipient designed to maintain drug-coating integrity and maximize drug-transfer efficiency for consistent and predictable drug delivery.

"Boston Scientific is committed to providing the best treatment options for patients with coronary artery disease," said Kevin Ballinger, president, Interventional Cardiology, Boston Scientific. "We believe the addition of a highly differentiated DCB to our leading complex percutaneous coronary intervention portfolio strengthens the Boston Scientific position as a global innovator in interventional cardiology therapies."

Particle Sciences and Eyeon Therapeutics Receive Patent on Novel Dry Eye Technology

PRNewswire: July 22, 2014 – BETHLEHEM, PA, U.S.A. – Eyeon Therapeutics has received a Notice of Allowance on a novel dry eye treatment based on a charged hydrophilic polymer developed at Particles Sciences, a leading drug delivery CDMO. The product has been shown to be safe and effective in a small trial previously published. Mark Mitchnick, M.D., CEO, states, "This first set of claims around the polymer and its class will go a long way to moving this technology into the commercial phase. We have been using it in several development projects, and we believe it has promise in many ocular formulations as well as in other areas. Helping Eyeon gain a proprietary position in this very important market is a great example of what Particle Sciences offers its partners."

David Kleinman, M.D., CEO of Eyeon Therapeutics, commented, "Dry eye is a serious and growing problem for which there are few therapies. Our product offers a unique approach that is clinically validated and useful in a number of ocular applications. In the coming months we will be pursuing partnerships and expanded protection around this product and follow-ons."

Innocutis Introduces Sitavig[®] 50mg (ACYCLOVIR) Muco-Adhesive Buccal Tablet for Relief from Herpes Labialis (Cold Sores)

PRNewswire: July 21, 2014 – CHARLESTON, SC, U.S.A. – Innocutis is pleased to announce the introduction into the North American markets of Sitavig[®] (acyclovir) 50 mg buccal tablet. This tablet, developed by BioAlliance and licensed to Innocutis, represents a treatment breakthrough in the herpes labialis category, because of its unique vehicle and delivery system. Sitavig uses a proprietary delivery technology that consists of a tablet that sticks to the gum above the incisor tooth on the side of the lip that is infected with a cold sore. This white to slightly yellow tablet is tasteless and odorless; it is 8 mm in diameter and 2.2–2.6 mm in thickness. It dissolves to provide a sustained release of medicine.

A phase III, randomized, double-blind, placebo-controlled study including 775 subjects demonstrated that a single low dose of Sitavig acyclovir buccal tablet improved all clinical parameters of labial herpes when applied shortly after symptoms occurred. Most notable, Sitavig decreased duration of episode, increased the percentages of blocked lesions, and delayed by 105 days the recurrence of the next herpes episodes. It is well known that the standard of care, systemic antiviral drugs, are typically prescribed at high doses in the treatment of labial herpes (HL). However, acyclovir muco-adhesive buccal tablet (Sitavig) is an innovative drug delivery system that provides a high sustained-release local exposure of acyclovir in the oral mucosa, supporting its evaluation as single low dose in HL.

"We are very excited to bring Sitavig to the North American markets," said Charles Jenkins, vice president of marketing for Innocutis. "Up to 90% of Americans have been exposed to HSV by the time they are 50, but there hasn't been a real breakthrough product to address this problem in many years. Sitavig is revolutionary because unlike systemic drugs and topical prescription creams, Sitavig requires application to the gum only once per episode. It is available by prescription only at local retail pharmacies."

Sitavig provided clinical benefit to patients, reducing the occurrence of vesicular lesions, primary or nonprimary, which is the most important burden of the disease. It also prevented and delayed the recurrence of the next herpes episode, making Sitavig an attractive alternative option to systemic antiviral treatment for patients with recurrent HL, when applied within 1 hour after the occurrence of prodromal symptoms.

Sitavig[®] (acyclovir) 50 mg muco-adhesive buccal tablet is indicated for the treatment of recurrent herpes labialis (cold sores) in immunecompetent adults.

ViaCyte Files Investigational New Drug Application and Device Master File with FDA for Novel Cell Replacement Therapy Product Candidate Designed to Treat Patients with Type 1 Diabetes

PRNewswire: July 17, 2014 – SAN DIEGO, CA, U.S.A. – ViaCyte, Inc., a privately held regenerative medicine company developing a cell replacement therapy for the treatment of diabetes, today announced that it has filed an Investigational New Drug application (IND) with the U.S. Food and Drug Administration (FDA) seeking to initiate a phase 1/2 clinical trial in patients with type 1 diabetes. The trial would evaluate the safety and efficacy of ViaCyte's VC-01TM product candidate, a stem cell-derived, encapsulated cell replacement therapy. In a related development, ViaCyte submitted a Medical Device Master File (called MAF) to the FDA in support of the Encaptra[®] drug delivery system, the device component of the VC-01 product candidate.

"The filing of this IND represents the culmination of many years of research and development by a dedicated team focused on developing a cell replacement therapy for patients with type 1 diabetes and advancing our VC-01 product candidate to human clinical trials," said Paul Laikind, Ph.D., president and chief executive officer of ViaCyte. "The ViaCyte team has been assisted and supported by the California Institute for Regenerative Medicine (CIRM) a leading organization focused on advancing the field of stem cell-based technologies, and JDRF, the leading advocacy organization for patients with type 1 diabetes," added Dr. Laikind.

ViaCyte's VC-01 product candidate consists of pancreatic progenitor cells, called PEC-01[™] cells, which are derived from a proprietary human embryonic stem cell line. These cells are then encapsulated by use of ViaCyte's Encaptra device. When implanted under the skin, the PEC-01 cells are designed to mature and further differentiate into insulin-producing beta and other endocrine cells that regulate blood glucose in a manner similar or identical to the normal islets that comprise the endocrine pancreas.

Based on a pre-IND meeting with the FDA and subsequent consultations, ViaCyte is proposing to initiate clinical evaluation of the VC-01 product candidate directly in patients with type 1 diabetes who have minimal to no insulin-producing beta cell function. In addition to evaluating the safety of the product candidate in these patients, the study is designed to demonstrate the effectiveness of the VC-01 product candidate in replacing lost endocrine function that is central to the disease.

In the proposed clinical trial, insulin production from the VC-01 implant would be assessed by measuring C-peptide, a biomarker for insulin produced by beta cells that is expected to provide a sensitive measure of efficacy in these patients. As proposed, the trial would also evaluate secondary endpoints related to the need for administration of pharmaceutical insulin to control the disease and the incidence of hypoglycemia, a common side effect associated with pharmaceutical insulin usage.

ViaCyte's proprietary Encaptra device is designed to contain the implanted cells, preventing biodistribution, as well as shielding them from the immune system. Although PEC-01 cells are human cells, they are not the patient's actual cells. As such, they are considered an allogeneic graft, which typically requires immunosuppression in order for the recipient to tolerate the implant. However, the Encaptra device is designed to prevent the patient's immune system from accessing the implanted cells, thereby facilitating successful engraftment and subsequent maturation to islets.

The VC-01 product candidate is designed to be placed under the skin of the patient and can be monitored and readily removed, if or when required. The option to remove the cells is designed to provide an important safety benefit for this novel stem cell-derived cell therapy candidate. It is being regulated as a biologic through interaction with the Office of Cell, Tissue and Gene Therapy within CBER at the FDA. Given the combination product nature of the product candidate, the Center for Devices and Radiological Health at the FDA is also involved in its regulation.

ViaCyte is a private regenerative medicine company currently focused on development of a novel cell therapy for the treatment of diabetes. The company's VC-01 product candidate is based on the production of pancreatic progenitors derived from human pluripotent stem cells. These cells are implanted in a durable and retrievable encapsulation device called the Encaptra drug delivery system. Once implanted and matured, these cells are designed to secrete insulin and other regulatory factors in response to blood glucose levels. ViaCyte is funded in part by the California Institute for Regenerative Medicine (CIRM) and JDRF. For more information, please visit www.viacyte.com.

InSite Vision Announces the Issuance of Broad U.S. Patent Covering Bromfenac Formulations in DuraSite®

Business Wire: July 16, 2014 - ALAMEDA, CA, U.S.A. - InSite Vision Incorporated (OTCBB: INSV) today announced that the U.S. Patent and Trademark Office (USPTO) has issued a U.S. patent no. 8,778,999 covering bromfenac nonsteroidal ophthalmic compositions formulated in DuraSite. The allowed patent contains both composition and method of treatment claims that will broadly cover all of InSite's bromfenac product candidates, including BromSite[™] (bromfenac 0.075% ophthalmic solution formulated in DuraSite, ISV-303) for the treatment of inflammation and prevention of pain post cataract surgery. Additional bromfenac-containing products in InSite's pipeline covered under this patent include ISV-101 (bromfenac 0.01%-0.04% ophthalmic solution formulated in DuraSite) for the treatment of dry eye disease, back-of-the eye BromSite indications, such as the prevention of cystoid macular edema (CME), as well as the combination of bromfenac and dexamethasone containing products such as BromDex[™] (ISV-504). Due to USPTO delays, the patent term was extended by 155 days to provide protection for bromfenac formulations in DuraSite to August 2029.

InSite has successfully completed two phase 3 clinical trials of BromSite and plans to file a New Drug Application (NDA) with the U.S. Food and Drug Administration (FDA) in the second half of 2014. BromSite demonstrated statistically significant improvements versus vehicle across the primary and secondary endpoints of alleviating ocular inflammation, postsurgical reduction in pain, and reduction in inflammatory flare in InSite's pivotal clinical studies. InSite Vision recently announced that the Swedish Medical Products Agency (MPA) determined that the existing phase 3 clinical data for BromSite for the prevention of pain

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and inflammation in ocular surgery was likely sufficient to support the filing of a Marketing Authorization Application (MAA) with the MPA. InSite plans to pursue European regulatory approvals of BromSite following the submission of its U.S. NDA.

InSite Vision is advancing new ophthalmologic products for unmet eye care needs based on its innovative DuraSite[®] platform technologies. The DuraSite and DuraSite 2 drug delivery systems extend the duration of drug retention on the surface of the eye, thereby reducing the frequency of treatment and improving the efficacy of topical drugs.

The DuraSite platform is currently leveraged in two commercial products for the treatment of bacterial eye infections, AzaSite[®] (azithromycin ophthalmic solution) 1%, marketed in the United States by Akorn Inc., and Besivance[®] (besifloxacin ophthalmic suspension) 0.6%, marketed by Bausch + Lomb, a wholly owned subsidiary of Valeant Pharmaceuticals International. InSite Vision is also advancing AzaSite Plus[™], a novel ophthalmic therapeutics through phase 3 clinical studies for the treatment of eye infections, and is preparing two new drug applications (NDA) for the commercial approval by the U.S. Food & Drug Administration (FDA): BromSite[™] for the treatment of inflammation and prevention of pain associated with cataract surgery and DexaSite[™] for the treatment of blepharitis. For further information on InSite Vision, please visit www.insitevision.com.

FDA Designates Opioid Overdose Treatment for Fast Track Development Program

Business Wire: July 15, 2014 – LEXINGTON, KY, U.S.A. – A Kentucky company headed by a recognized expert in nasal delivery of medication says its intranasal naloxone spray, a drug designed to treat opioid overdoses, has received Fast Track designation from the Food and Drug Administration (FDA).

The Fast Track program of the FDA is designed to expedite the development and review of new drugs that are intended to treat serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs. Fast Track–designated drugs ordinarily qualify for priority review, thereby expediting the FDA review process. AntiOp and the FDA may also be able to employ additional tools to expedite the FDA review process such as "rolling submission," whereby AntiOp may submit portions of the new drug application (NDA) in a staged NDA submission process.

"The FDA has been very supportive of how we are developing our technology," said AntiOp founder and CEO Daniel Wermeling. "This Fast Track designation, combined with our recent collaboration with Reckitt Benckiser Pharmaceuticals Inc., validates our vision and belief that this drug has the potential to fulfill an unmet medical need in the United States." The latest data from the CDC, for 2011 data, demonstrated that the national opioid overdose death rate continues to climb. A new ready-to-use, needle-free, naloxone delivery system may provide medical providers and their patients more options to rescue a loved one. "We view the FDA decision to grant Fast Track designation to AntiOp for intranasal naloxone as an exciting and positive first step toward accelerating the commercialization of a simple, ready-to-use treatment needed to address the growing epidemic of opioid overdose," said Shaun Thaxter, CEO, Reckitt Benckiser Pharmaceuticals Inc.

Wermeling added that the company has received continuing support from the National Institutes of Health and its National Institute on Drug Abuse (NIDA), which recently approved grant funding of \$1 million annually for three years to advance development of AntiOp's naloxone spray. Total federal and state grant funding to date exceeds \$5 million, almost \$4.5 million of that from the NIDA.

In addition, the Kentucky Economic Development Cabinet has provided AntiOp with development funding. Wermeling added that the University of Kentucky Colleges of Pharmacy and Medicine and the National Institutes of Health Center for Clinical and Translational Science have provided critical support to AntiOp.

"We have had tremendous help from so many organizations and individuals who are motivated by the great potential of this product," Wermeling said, "and we are proud to have them on our team."

Deaths due to opioid overdose have tripled since 1990, according to the Centers for Disease Control and Prevention (CDC). The CDC's most recent data reveal approximately 16,500 deaths occur in the United States each year from prescription opioids. Studies have shown that approximately 800,000 ambulance runs occur each year in the United States in response to suspected opioid overdoses, involving both prescription medications and heroin. Commonly prescribed opioid painkillers include hydrocodone, methadone, oxycodone, and oxymorphone.

Neos Therapeutics Announces Positive Phase 3 Study Results for Its Methylphenidate Extended-Release (XR) Oral Disintegrating Tablet (ODT) in ADHD Patients

Business Wire: July 15, 2014 – GRAND PRAIRIE, TX, U.S.A. – Neos Therapeutics, Inc. ("Neos" or "the company"), a highly differentiated oral drug delivery company with a portfolio of proprietary technologies and a late-stage pipeline of innovative controlled release (CR) products for ADHD, announced today that it has completed a positive phase 3 study for its methylphenidate XR-ODT drug candidate, NT-0102, in children with ADHD.

The trial was a multicenter, randomized, double-blind, placebocontrolled laboratory classroom study in 87 children with a diagnosis of ADHD. NT-0102 met primary and secondary efficacy endpoints, showing statistically significant improvement on both the Swanson, Kotkin, Agler, M-Flynn, and Pelham Scale (SKAMP) and the Permanent Product Measure of Performance (PERMP) scale, through 12 hours postdose. No serious adverse events were reported during the study and the adverse event profile was consistent with the drug's mechanism of action.

"ADHD is a condition that causes significant distress for patients and caregivers. Although, there are a number of effective long-acting medications currently on the market, most formulations consist of tablets or capsules that can be difficult for children to swallow. The positive data from this study is exciting. Hopefully, soon we will have a once-daily oral disintegrating tablet option that is easy to administer to patients," said Dr. Ann Childress (Center for Psychiatry and Behavioral Medicine, La Vegas, NV), lead investigator for the study.

"We are very pleased to have worked with Dr. Childress on this study. Having a potential treatment option for those who cannot swallow other dosage forms is important, especially in a chronic disorder like ADHD, in which children may struggle to take their medication or develop pill fatigue," noted Dr. Carolyn Sikes, vice president of clinical development at Neos.

Stimulant medications, such as methylphenidate, have been available for the treatment of ADHD for decades. Extendedrelease formulations of these medications allow for once-daily dosing; however, recent data suggest that a significant percentage of children and adolescents struggle to ingest tablets or capsules. An XR-ODT formulation, which does not require swallowing an intact tablet or capsule and can be dosed once daily, may offer a practical alternative.

Dr. Vipin Garg, president and CEO of Neos, added that "we are delighted with these robust clinical results, as this data validates our XR-ODT technology. We believe that our methylphenidate and amphetamine XR-ODT formulations could provide a patient-friendly dosage form for both children and adults with ADHD. We are looking forward to filing the NDA for our NT-0102 drug candidate in the near future."

Neos Therapeutics, Inc., is a specialty pharmaceutical company focused on the development and manufacture of FDA-approved drug products that utilize the company's proprietary and patented delivery technologies. The Neos drug products are being developed using the Dynamic Time Release Suspension[®] (DTRS[®]) and Rapidly Disintegrating Ionic Masking[™] (RDIM[™]) technologies that deliver controlled release (CR) small molecule active pharmaceutical ingredients (APIs) in either liquid or oral disintegrating tablet (ODT) dosage forms. By utilizing APIs that are already FDA approved, Neos can reduce development and regulatory risk and efficiently advance targeted proprietary Rx products through the FDA's New Drug Application (NDA) approval process. For more information, visit www.neostx.com. ■

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AAPS Annual Meeting

and Exposition November 2–6 San Diego, CA, U.S.A. www.aaps.org/annualmeeting

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November 4–7 Taipei, Taiwan (ROC) www.7thwcprm.org

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