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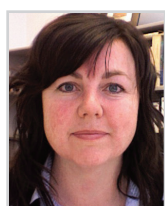
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Charles Frey
Editor



Steven Giannos
Editor



Arlene McDowell
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Bozena Michniak-Kohn
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Yvonne Perrie
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CRS Newsletter

Leading
Delivery Science
and Technology

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Editors

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

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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 Future Is Now

It may just be a coincidence, but here I am again in September writing the "From the Editor" section as I did this time last year.

As I write this, here in New Jersey it does not feel like September. We are having a heat wave with no rain and temperatures into the 90s Fahrenheit. The only hints of Fall are our calendars and the few yellowing leaves on the trees.

For those of us who still remember the original Star Trek series, you may remember how we marveled at the ingenious drug delivery devices, trackers, and monitors that were used—all handheld, small, and noninvasive. Well, we are slowly making progress toward this goal in the real world. This issue of the *CRS Newsletter* discusses microneedles as drug delivery devices. The concept is simple: make needles so small that they do not penetrate deep enough into the skin to reach the nerves (thus, no pain) or the blood vessels (thus, no bleeding) and that are small enough to have hundreds on a small topically applied microarray device. The challenges are to be able to manufacture these arrays cheaply and reproducibly and then be able to deliver the active(s) into the skin. There are many suitable compounds that may be used, including many drugs, proteins, peptides, vaccines, and other biomolecules. Currently, there is only one microneedle-based device on the market, called Soluvia (approved by the FDA in 2011) for the Fluzone influenza vaccine. However, there are over 25 companies working on this technology for both drug and vaccine delivery, and these include Corium International, Clearside Biomedical, Zosano Pharma (a Johnson & Johnson spinoff), Radius Health, Circassia, and NanoPass Technologies. In total, there are about 22 such microneedle-based products under development. In this issue of the *CRS Newsletter* you will read about the specific application of using such a device for intradermal vaccination based on research from laboratories at Cardiff University in Wales.

Also, as noted in the *DDTR* Update, a special issue on microneedles recently appeared. CRS members can access *DDTR* articles for free online as a member benefit.

Wishing you happy reading and a productive year. ■



*Debra Bingham
Valeo Partners
U.S.A.*

People, Products, and Science

It is an exciting time to take on the role of CRS President. I am pleased to have such a strong foundation to build on and sincerely thank Art Tipton for his vision and service. CRS is a vital organization, connecting science and delivery technology leaders from across the globe to foster new ideas, collaborations, and scientific breakthroughs. It is an honor to be a part of this organization, and I look forward to working with members in the coming year.

The Annual Meeting this year promised “more value,” which it certainly delivered, as you’ll read in the following pages. The CRS new strategic plan picks up on this sentiment, envisioning avenues to give members more value and more reasons to connect (and stay connected) to CRS. Over the next few months, the CRS Board will be working diligently to create a strategic plan that sets the course for the society over the next 2–4 years. I am energized by what has been developed thus far, as it is results-oriented with clearly defined, measurable outcomes. The ultimate impact of the plan is to increase value for members, better achieve the overarching goals of CRS, and create a more sustainable future. The strategies are framed by three key elements: people, products, and science. This year, the board seeks to achieve short-term objectives under this framework, such as:

- **People:** Elevate leadership, professional development, and networking opportunities for members.
- **Products:** Further the science, create a culture for product innovation through relationship building, and increase members.
- **Science:** Amplify board and committee opportunities to be thought leaders on future science, identify translational intersections, and be more intentional with communication to the greater industry.

The board and I will be proactive in our approach, partnering with other committees, members, staff, and related organizations to accomplish our goals. As an organization, we have achieved much in our history, and we are thankful for the many members who have volunteered their time to achieve this success. If what you are reading resonates with you and you would like to be part of this exciting implementation phase, please contact Biana Godin Vilentchouk, bianagodinv@gmail.com, chair of the Volunteer Recruitment Committee. To keep members apprised of our successes and challenges, the board will report on these activities during the course of the year.

In addition to becoming active with our strategic plan work, please consider submitting an abstract for the 2016 CRS Annual Meeting & Exposition taking place next July in Seattle, Washington. Plans for the innovative scientific program are underway, and we look forward to more opportunities to connect, engage, and explore new science. Abstract submissions open mid-November, and details can be found on the CRS website: controlledreleasesociety.org.

I truly look forward to working with such a distinguished group of colleagues and am motivated by the strong partnership, science, and growth opportunities to come. ■

The CRS Annual Meeting Program Committee kept their promise of “more than ever before,” with more learning and networking options, and more opportunities for participants to see the sights with the beautiful backdrop of Edinburgh, Scotland.

BY THE NUMBERS

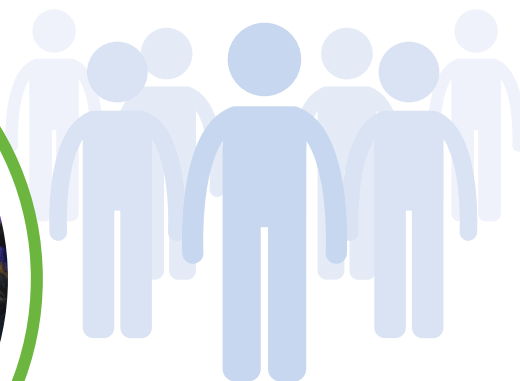
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attendees gathered in Edinburgh, Scotland, to gain new scientific insights, get the latest on delivery technology, and network with colleagues from around the globe



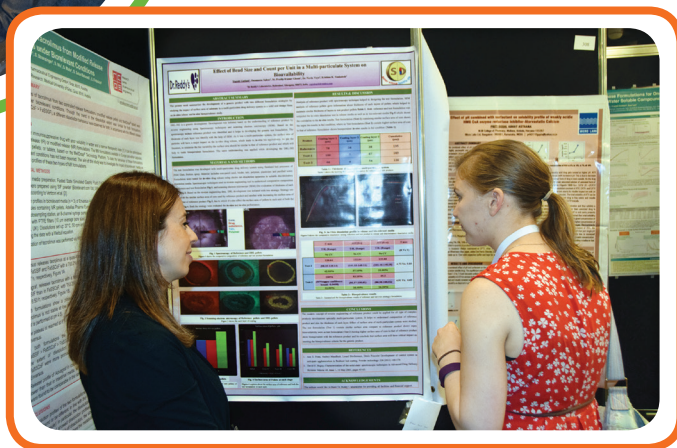
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people became new CRS members



50

women enjoyed a presentation from Begoña Carreño (Novartis) during the Women in Science Networking Event



613

scientific posters explained breakthrough research in delivery science

4 world-class plenary speakers inspired attendees, plus a bonus special address from the 2015 CRS Foundation Travel Grant Program namesake.



6 promising young scientists received the Nicholas Peppas Student Travel Awards



52 countries represented, with attendance continuing to grow, offering a critical international perspective



225 speakers engaged attendees in more thought-provoking presentations, workshops, and dialogue

Thank You to the Exhibitors of the 42nd Annual Meeting & Exposition

With the theme “Creating Value Through Customised Delivery,” we had a powerful meeting of the minds in Edinburgh, Scotland, which brought together over 60 exhibitors. These organizations support the research and development needs of delivery science and technology with innovative products and services, and they helped make the 42nd Annual Meeting a great success. Thank you, 2015 CRS exhibitors.

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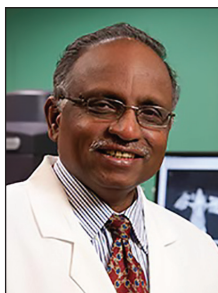
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Drug Delivery and Translational Research Update

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

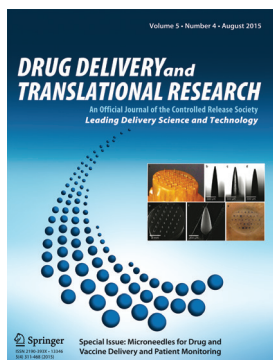


Vinod Labhasetwar

DDTR Editorial Board Meeting in Edinburg

This well-attended board meeting was quite constructive. Vinod Labhasetwar, Editor-in-Chief, reviewed the progress that *DDTR* has made since it began publication in 2011. We have achieved several milestones that are critical for long-term success of the journal. *DDTR* is now indexed in major databases including PubMed. The journal is also approved by

ISI, which means *DDTR* will receive its first impact factor in the summer of 2016. In addition, *DDTR* has published 12 special issues on various topics that are relevant to the science and technology of drug delivery. During the last four years, downloading has increased threefold. Dr. Labhasetwar also shared with the board members his vision for the journal in the next five years. One of the items discussed was capturing as much information as possible from the CRS annual and local chapter meetings in the form of publications in *DDTR*. To achieve this objective, Dr. Labhasetwar attended the CRS local chapter meeting with an appeal to consider developing special issues in *DDTR* based on conferences, workshops, and symposia organized by local chapters. The content published in *DDTR* is accessible to CRS members as a membership benefit.



DDTR Special Issue, Volume 5, Issue 4, pages 311–467

This special issue, Microneedles for Drug and Vaccine Delivery and Patient Monitoring, was edited by Ryan Donnelly and Dennis Douroumis. In this issue, there was a focus on novel applications of microneedles in drug, vaccine, and gene delivery, as well as in minimally invasive monitoring and diagnosis.

Given the inherent safety features of microneedle systems, it is easy to foresee a time within the next 10 years when vaccination programs in the developing world are based around microneedles. For most microneedle-formulated biomolecules, such as vaccine antigens in the dry state, the cold chain will be circumvented. Needle-stick injuries also will be obviated. Such an intervention could massively improve the quality of life, life expectancy, and economic productivity of developing countries. Accordingly, the potential impact of microneedle research and ultimate commercialization is vast. Once vaccine products are accepted by regulators, healthcare providers, and patients, other microneedle-based products for everyday patient and consumer use will become widely used to the benefit of the pharmaceutical, medical devices, and cosmetics industries and patients worldwide.

About the Guest Editors



Ryan Donnelly holds the chair in pharmaceutical technology at the School of Pharmacy, Queen's University Belfast, Ireland. A registered pharmacist, his research is centered on design and characterization of advanced polymeric drug delivery systems for transdermal and topical drug delivery, with a strong emphasis on improving therapeutic outcomes for patients. His bioadhesive

patch design was used in successful photodynamic therapy of over 100 patients with neoplastic and dysplastic gynecological conditions. This technology has now been licensed to Swedish Pharma AB, for whom Dr. Donnelly acts as a technical director. He is currently pursuing commercialization of novel microneedle systems with a range of international companies. Still at a relatively early stage of his career, he has authored over 400 peer-reviewed publications, including three patent applications, 19 book chapters, around 130 full papers, and four books, including the first textbook on microneedles. He has been an invited speaker at a wide range of national and international conferences, most notably the Gordon Research Conference on Mammalian Skin Barrier Function in 2011 and the LTS Academy, which brings together leading researchers in transdermal drug delivery from industry and academia, in 2012. He is the Editor-in-Chief of *Recent Patents on Drug Delivery & Formulation* and a member of the editorial advisory boards of *Expert Review of Medical Devices*, *American Journal of Pharmacology and Toxicology*, *Pharmaceutical Technology Europe*, and *Journal of Pharmacy and Bioallied Sciences*. He is also a visiting scientist at the Norwegian Institute for Cancer Research, where he is an associate member of the Radiation Biology Group. He was the Biotechnology and Biological Sciences Research Council Innovator of the Year for 2013, won the American Association of Pharmaceutical Scientists *Pharmaceutical Research Meritorious Manuscript Award* for 2011, the GSK Emerging Scientist Award in 2012, and the Royal Pharmaceutical Society's prestigious Science Award in 2011. He is a previous winner of the Queen's Improvement to Society Award, an Innovation Leader Award from the National Health Services Research & Development Office, a research scholarship from the Research Council of Norway, and the Pharmaceutical Society of Northern Ireland's Gold Medal.

Dennis Douroumis holds a chair in pharmaceutical technology and process engineering at the Faculty of Engineering and Science, University of Greenwich, United Kingdom. His research interests focus on the development of medical devices for transdermal delivery and coronary artery diseases. He is also interested in continuous manufacturing and process analytical technologies for the processing of oral solid dosage forms. He



has developed an inkjet printing proprietary technology for microneedle coating and design of novel metal arrays for the delivery of high-dose small molecules. He has joined the editorial boards of more than five international journals, including Wiley's editorial board for the series *Advances in Pharmaceutical Technology*. Dr. Douroumis has published more than 120 peer-reviewed publications,

including 65 full papers, two patents, two books, and five book chapters. He has chaired several sessions and delivered keynote lectures at national and international conferences. He has been awarded several EU grants for leading or participating in research consortia, and he is a member of the Advanced Pharmaceutical and Materials Technologies (AMPTEC) European group.

Submission for DDTR Special Issue on Ocular Drug Delivery

DDTR is accepting submissions for a special issue on Ocular Drug Delivery, which will showcase emerging pharmaceutical, engineering, and formulation approaches to efficiently treat both anterior and posterior segment diseases. Topics include topical formulations, ocular implants, and other delivery systems for both small and large molecules including proteins and genes with a focus on their application in disease conditions including preclinical and clinical data. Emphasis will be placed on ocular pharmacokinetics as well as short- and long-term ocular biocompatibility with a focus on clinical translation, new product development, and market opportunity. Guest editors are Ilva Rupenthal (i.rupenthal@auckland.ac.nz) and Michael O'Rourke (scotiavc@gmail.com). ■

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Using Human Skin to Understand Intradermal Immunisation Strategies

M. O. Ivory,^{a,b} S. Llewellyn-Lacey,^b D. A. Price,^b M. C. Kim,^c S.-M. Kang,^c V. Piguet,^b J. C. Birchall,^a and S. A. Coulman^{a,d}

Introduction

The emergence of minimally invasive transdermal delivery systems that can facilitate localised delivery of macromolecular therapeutics, in combination with increasing interest in the intradermal route for vaccination, has spawned significant research activity in the development of intradermal vaccines that can be delivered by microneedle devices.^{1,2} The perceived advantages of such systems include increased immunogenicity and a resulting dose sparing effect, as well as patient and public benefits related to the minimal invasive nature of the delivery system. Candidate vaccines for delivery by microneedle devices include both novel and established commercial vaccines, such as influenza.

When delivering intradermal vaccines, it is important to target the population of skin-resident immune cells best able to uptake, process, and present the vaccine to initiate an effective immune response. While animal models provide invaluable *in vivo* data, the distinct immunostimulatory properties of different skin immune cell subsets in human skin remain poorly understood. Human epidermis contains Langerhans cells (LCs), while the dermis contains numerous subsets of dermal dendritic cells (dDCs). These antigen-presenting cells (APCs) are able to uptake locally delivered antigen, migrate to lymph nodes, and interact with T-cells to initiate a systemic immune response. Antigen is then presented to CD8⁺ T-cells in the form of peptide fragments bound to major histocompatibility complex I molecules on the APC surface.

In the absence of direct infection, APCs are required to uptake, process, and present exogenous antigen via a “cross-presentation” pathway. This is particularly important in some cases (e.g., influenza infection) in which the CD8⁺ T-cell response is essential for viral clearance from the lungs. To maximise the cross-presentation of influenza virus antigen, it is vital that the vaccine is delivered to the correct population of APCs. However, the different cross-presentational properties of LCs and dDCs are under debate, and therefore we aimed to use our *ex vivo* human skin model to characterise these cells using an inactivated influenza virus vaccine and an influenza matrix-specific CD8⁺ T-cell clone restricted by HLA-A2.

Experimental Methods

Human skin samples were obtained with ethical approval and informed consent following routine mastectomy or breast reduction surgery. Excess lower dermis was removed using an electric dermatome to cut skin to a thickness of 300 µm. Skin was then incubated in collagenase A, DNase I, and Dispase II in RPMI medium for 30 min at 37°C to facilitate mechanical separation of the epidermis from the dermis. Dermis and epidermis were then incubated separately for 48 h, after which migratory (walkout) cells were collected from the media.

The principle of the primary cell culture experiment is detailed in Figure 1. Briefly, dermal and epidermal walkout cells expressing HLA-A2 were plated to give 2×10^4 dDCs or LCs per well prior to the addition of 1 µg of inactivated H1N1 influenza A/Puerto Rico 8/1934 virus. After incubation for 6 h, 6×10^4 HLA-A2-restricted CD8⁺ T-cells (ALF-3 clone) specific for the influenza A matrix protein (M1)-derived epitope GILGFVFTL (residues 58–66) were added to each well. ALF-3 cells were also treated with virus in the absence of APCs for control purposes. After 1 h, brefeldin-A was added to prevent cytokine release. Cells were then fixed after overnight incubation, and the CD3⁺ cell fraction was analysed for interferon-γ (IFN-γ) expression by flow cytometry.

Results and Discussion

Phenotypic analysis of skin walkout cells revealed that LCs comprise a single HLA-DR⁺ cell population expressing CD1a and langerin (CD207). Conversely, dDCs are a heterogeneous population comprising three subsets distinguished on the basis of CD11c and CD141 expression. The frequencies of each dDC subset varied between donors; mean values were CD141⁺/CD11c⁺, 22.6% (SD = 8.8); CD141⁺/CD11c⁺, 59.0% (SD = 8.4); and CD141⁺/CD11c⁺, 17.7% (SD = 9.0) ($n = 5$).

Mean purity of LCs and dDCs within total collected cells was 7.67% (SD = 4.7) and 34.93% (SD = 9.1), respectively ($n = 16$). Cell viability was consistently 80–90%, as determined by fixable viability dye staining. These results confirmed that usable numbers of skin immune cells could be obtained from *ex vivo* skin. Moreover, the detected dDC subsets conformed to previously reported patterns of marker expression.³

ALF-3 IFN-γ expression was greatest with virus-treated dDCs and was significantly different to untreated cells (Figure 2). LCs showed no significant cross-presentation of the matrix peptide. Importantly, HLA-A2⁺ APCs and ALF-3 cell controls failed to elicit IFN-γ expression (HLA-A2⁺ cells, $n = 5$; ALF-3 cells, $n = 6$; HLA-A2⁺ cells, $n = 1$). These results show that dDCs are able to present inactivated virus much more potently than LCs. This

^a School of Pharmacy and Pharmaceutical Sciences, Cardiff University, U.K.

^b Institute of Infection and Immunity, School of Medicine, Cardiff University, U.K.

^c Center for Inflammation, Immunity & Infection, Institute for Biomedical Sciences, Georgia State University, U.S.A.

^d Corresponding author. E-mail: CoulmanSA@cardiff.ac.uk

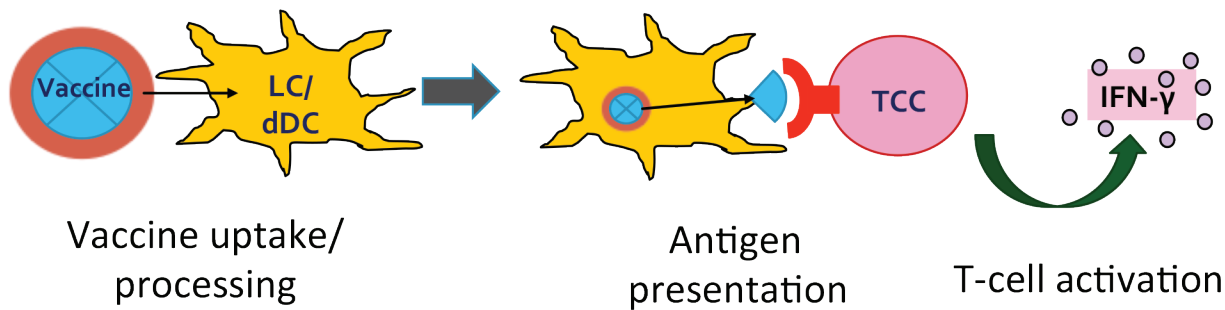


Figure 1. A schematic representation of the methodology, which used primary LCs and DC populations, isolated from human skin, to evaluate vaccine uptake, presentation, and activation.

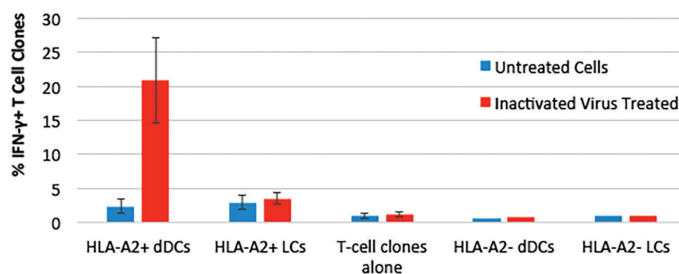


Figure 2. IFN- γ expression in ALF-3 clones, following coculture with HLA-A2+/- primary human dDCs/LCs or alone (error bars: \pm SEM).

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finding contrasts with studies in mouse models, in which epidermal LCs readily cross-present antigen.⁴ However, our data concur with other reports in human skin, demonstrating that dDCs, and more specifically the CD141⁺ dDC subset,⁵ are potent cross-presenting APCs.

Conclusion

The greater cross-presentational ability of dDCs over LCs suggests that these cells are important in processing intradermally delivered vaccine antigen. Further study is required to determine if this is the case with other influenza antigens involved in the CD8⁺ T-cell response, or indeed the importance of this for other intradermal vaccine candidates. However, with this information, vaccine delivery technologies such as the microneedle device can be tailored and optimised to target the most relevant cell populations.

These are exciting times for microneedle technology, and at the 4th International Conference on Microneedles, in May 2016, we will hopefully hear more about the design, development, application, and clinical translation of the technology, both for vaccination and other therapeutic applications.

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Polymeric Electrospun Scaffolds: Neuregulin Encapsulation and Biocompatibility Studies in a Rat Model of Myocardial Ischemia

M. T. Simon-Yarza,^a A. Rossi,^b K. H. Heffels,^b E. Garbayo-Atienza,^a F. Prósper,^c J. Groll,^b and M. J. Blanco-Prieto^{a, d}

Introduction

Cardiovascular disease remains the number one cause of death. Numerous studies try to identify new effective cell and/or growth factor (GF) based therapies for repairing damaged cardiac tissue. In the last decades tissue engineering has emerged as a promising therapeutic approach for restoring damaged heart tissue.¹ During myocardial ischemia, occlusion of the coronary artery causes ischemia and cardiac cell death. Damaged tissue is removed by macrophages, and it is subsequently replaced by a nonfunctional fibrotic scar through the activity of fibroblasts and endothelial cells.² This cardiac remodeling can produce cardiac insufficiency, resulting in a high risk of heart failure.³ In this context, the prospect of engineering a device that effectively incorporates cells capable of regenerating heart tissue along with GFs, which can promote cell recruitment, vasculogenesis, and/or cardiomyocyte replication, is attractive.⁴

Within the known cardioactive GFs, neuregulin (Nrg) has shown promising results in preclinical studies in regenerative medicine, and its therapeutic benefit in chronic heart disease is currently being investigated in several clinical trials. In a previous work we demonstrated that delivering polymeric microparticles encapsulating Nrg in a rat model of myocardial ischemia led to improved cardiac function.⁵ In fact, these microparticles decreased infarct size and fibrosis and efficiently promoted vasculogenesis, cardiomyocyte proliferation, and the recruitment of cardiac progenitors.

Researchers have employed several techniques to incorporate proteins, such as GFs, into fibrous biocompatible and biodegradable scaffolds that allow cell attachment. In this regard, electrospinning is an innovative method for generating scaffolds with ultrathin fiber diameters and large surface-to-volume ratios, favoring the delivery of bioactive molecules.⁶

The aim of this work was to evaluate the suitability of electrospinning to incorporate the cardioactive Nrg into polymeric fibers and to study the physiological response to the

implantation of this scaffold in the damaged heart, using a rat model of myocardial ischemia. The experimental overview is shown in Figure 1.

Experimental Methods

In Vitro Study: Nrg-Containing Fiber Scaffold. Preparation and Characterization. Microfibers were produced at room temperature. A high-voltage power supply was used to apply a 10 kV electrostatic field. The collector consisted of a rotating drum (6,000 rpm; length, 150 mm; diameter, 75 mm), which was placed at a distance of 140 mm away from the needle tip (19-gauge, blunt end). The polymer solution was electrospun at a rate of 1 mL/h, as controlled by a syringe pump, with a 30 min collection time. The resulting fibrous scaffold was cut and removed from the collector as a rectangular film (140 × 23.5 mm). To prepare optimal fibrous scaffolds, different parameters of the formulation and the electrospinning process were tested. Scanning electron microscopy was used to evaluate how polymer composition, presence of polyethylene glycol (PEG) in the formulation, addition of the electroconductive trifluoroacetic acid (TFA), or dissolution of Nrg in phosphate-buffered saline affected fiber structure. Protein loading in the fibers was evaluated by Western blot.⁵

In Vivo Study. A previously described rat model of myocardial ischemia was used for the *in vivo* studies.⁷ One week after artery occlusion, scaffolds were implanted covering the infarcted area. Animals were sacrificed at different times to study the inflammatory response and scaffold integration in the damaged tissue (24 h, 1 week, 1 month, and 3 months).

To perform histological analysis, hearts were cut into three pieces (apical, mid-ventricular, and basal) and embedded in paraffin for sectioning (5 μm). Haematoxylin-eosin staining was performed. Immunolabeling was employed to determine macrophage phenotype by using primary antibodies (anti-CCR7 for M1 and anti-CD163 for M2). M1 and M2 macrophages were visualized and quantified using a Zeiss Axioplan 2ie microscope equipped with epifluorescence optics. Six images per section were analyzed (eight sections per animal, 40× magnification), and digital images were processed using ImageJ software.

Results and Discussion

In Vitro Results: Nrg-Containing Fiber Scaffold. Preparation and Characterization. Homogenous smooth fibers with a diameter of around 5 μm were prepared with the following composition: PLGA 504H, 75 mg; NCO-sP(EO-stat-PO), 5 mg, TFA, 2 μg/mL; and Nrg, 10 μg. NCO-sP(EO-stat-PO) is a

^a Pharmacy and Pharmaceutical Technology Department, School of Pharmacy, University of Navarra, Pamplona, Spain.

^b Department of Functional Materials in Medicine and Dentistry, University of Würzburg, Würzburg, Germany.

^c Hematology Service and Area of Cell Therapy, Clínica Universidad de Navarra, Foundation for Applied Medical Research, University of Navarra, Pamplona, Spain.

^d Corresponding author. E-mail: mjblanco@unav.es

polymer synthesized by some of us that has been demonstrated to promote specific cell adhesion on the fibers.⁸ This formulation led to high encapsulation efficiency values (~85%).

In Vivo Results. The histology analysis revealed the interaction of the scaffolds with injured cardiac tissue over a period of 3 months (Figure 2). The scaffold efficiently adhered to and integrated in the cardiac tissue for up to 3 months. An inflammatory infiltrate appeared in the area of the implant, with cells penetrating and diffusing through the adhered fibrous scaffold (Figure 2, black double arrows). Specifically, acute inflammation was observed at 24 h and 1 week after implantation. This was followed by a phase of chronic inflammation, which was observed at 1 month and persisted until 3 months. At the later time points, fibrotic tissue could be seen adjacent to the biomaterial, with the inflammatory infiltrate in the scaffold visibly reduced compared to the first week. To analyze whether the Nrg-containing scaffold itself exerted

a positive or a negative impact on cardiac tissue remodeling we examined the M2/M1 macrophage ratio at 24 h, 1 week, and 1 month after implantation. M1 and M2 macrophages were recently shown to play distinct roles in tissue remodeling following injury.⁹ Thus, we employed immunofluorescence imaging to analyze the number of CCR7 and CD163 expressing cells in the injured cardiac tissue over time (M1 and M2 phenotypes, respectively). Notably, we found that the M2/M1 ratio significantly increased up to 1 month after implantation (Figure 3), suggesting that the Nrg-containing fibers themselves have a positive effect on cardiac remodeling.

Conclusion

We demonstrated that Nrg-containing fibers prepared via electrospinning and made of a mixture of PLGA/NCO-sP(EO-stat-PO) polymers displayed efficient adherence, integration, and biocompatibility with damaged cardiac tissue. Scaffold implantation yielded results consistent with constructive tissue

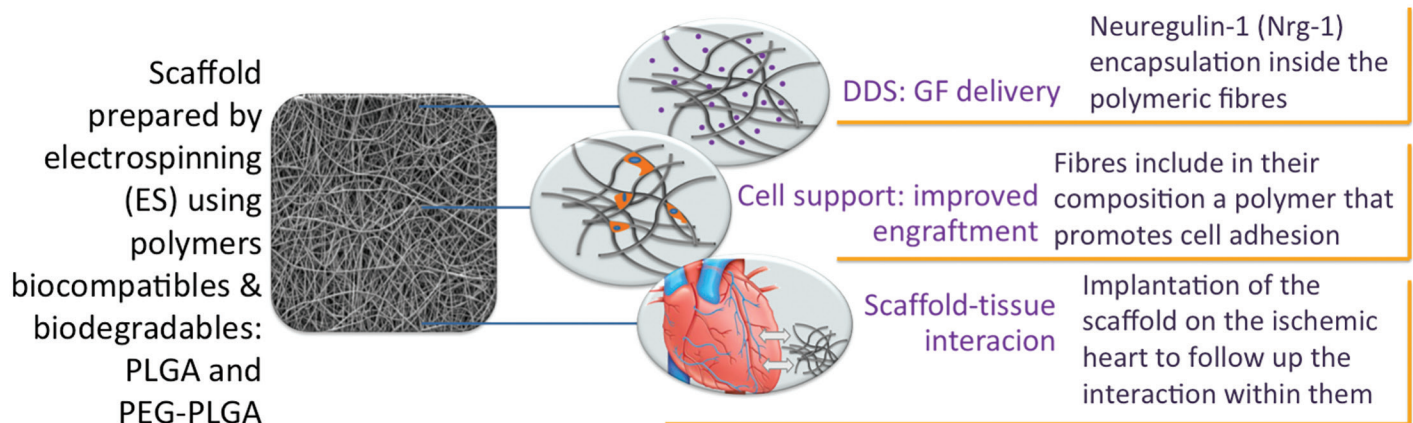


Figure 1. Overview of the experiment.

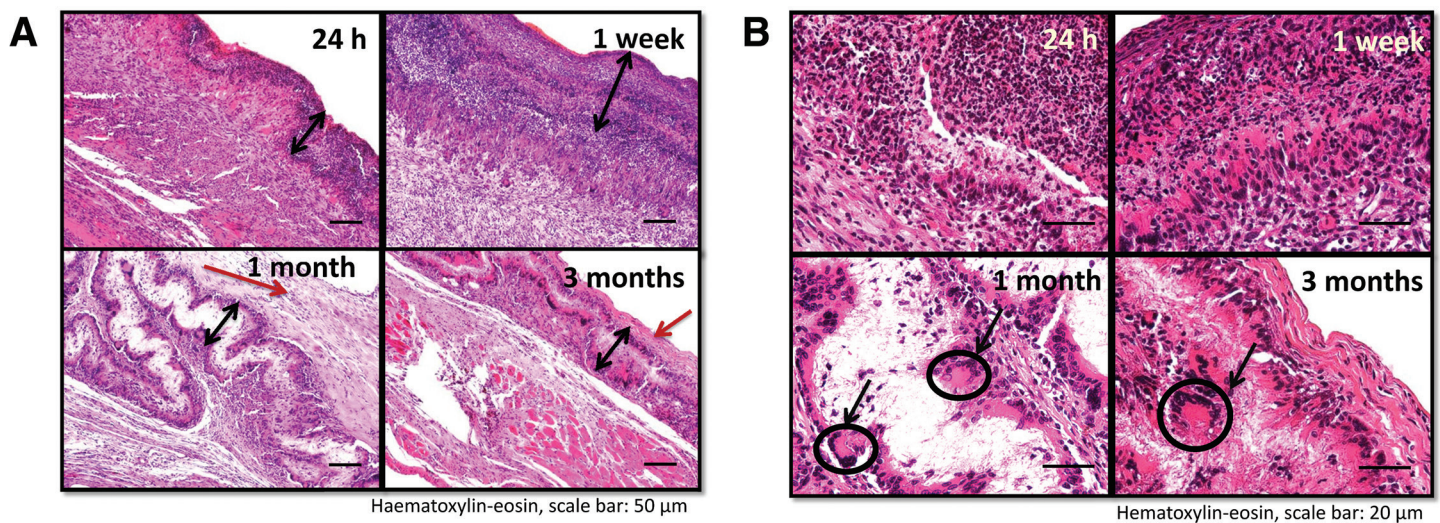


Figure 2. Biocompatibility of the nonloaded fibers. (A) The scaffold is detected in the heart even 3 months after implantation (double black arrows). After 1 month fibrotic tissue is deposited next to the biomaterial (red arrows). (B) Acute inflammation (24 h to 1 week) followed by chronic inflammation (1–3 months). Reduced inflammatory infiltrate and fibrotic tissue deposition and giant cells (black arrows, 1–3 months).

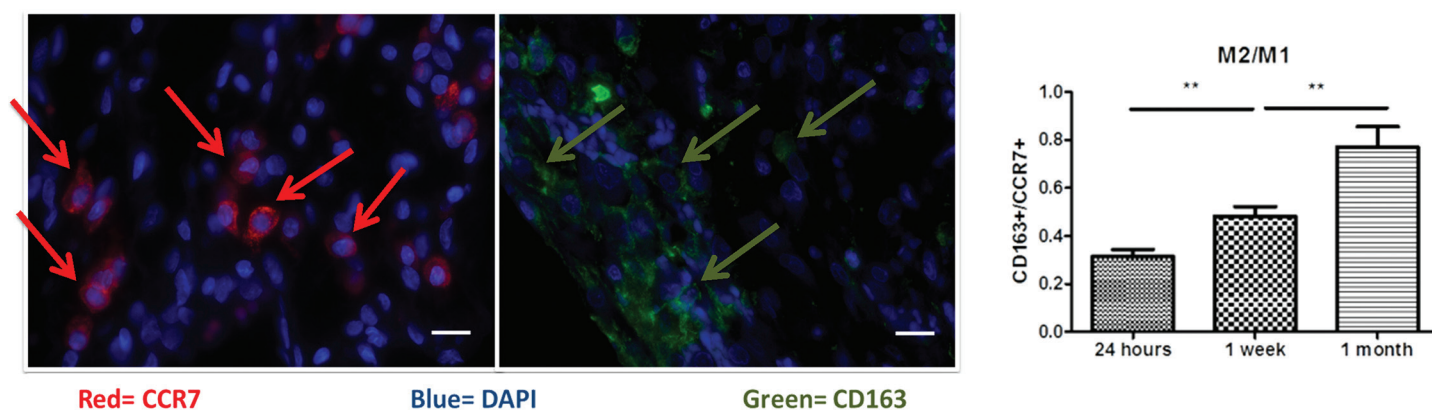


Figure 3. Immunofluorescent images showing host macrophage response to scaffolds after 1 month. Scale bars: 10 μ m. CCR7 (M1) = red; CD163 (M2) = green; and DAPI (nuclei) = blue. The graph shows the ratio of M2/M1 expressing cells (indicated as CD163+/CCR7+) at 24 h, 1 week, and 1 month after implantation (** indicates $P < 0.001$).

remodeling. These data suggest that the combination of Nrg-encapsulating scaffolds with cells able to induce cardiac regeneration might represent a promising therapeutic strategy for repairing damaged or diseased myocardial tissue in humans. This proof-of-concept study establishes the foundation for future efficacy *in vivo* studies using these Nrg-containing fibers.

Acknowledgements

This work was partially supported by ISCIII-RETIC RD12/0019/0031, MINECO PLE2009-0116 CARDIOBIO, SAF2013-42528-R, Program INNPACTO (PROCARDIO), European Union FPVII (INELPY), FUN (University of Navarra) Caja de Ahorros de Navarra (Programa Tu Eliges: Tu Decides). T. Simón-Yarza thanks the Spanish Ministerio de Educación (programa FPU) for the fellowship grant.

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From the Controlled Release Society and the American Association of Pharmaceutical Scientists

Formulation, Processing, and Testing of Functionally Coated Multiparticulates Workshop

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Patent Watch

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

This article briefly summarizes novel aspects of selected United States patents involving controlled release or delivery that were issued from January 1 to June 30, 2015. Selections have been loosely categorized into interest areas; however, many overlap into multiple categories. Greater detail on each can be found on the U.S. patent website at <http://patft.uspto.gov/>.

Abuse Deterrent

U.S. patents 9,060,976, 9,044,435, 9,040,084, 9,034,376, and 8,999,961 – Polyethylene oxide is introduced as a gelling agent to deter abuse of opioids from controlled release formulations.

U.S. patents 9,056,051 and 8,969,369 – Naloxone is incorporated in opioid formulations such that it blocks or attenuates the euphoric effects of sustained release opioids in therapeutic use and is above the amount needed to suppress those effects if released all at once.

U.S. patents 9,040,032 and 8,962,547 – An enzyme-cleavable oxycodone prodrug with the option to mediate release with a trypsin inhibitor is described for controlled release of the drug.

U.S. patents 8,927,014 and 8,927,013 – A superabsorbent is incorporated into the coating layers of a formulation to create a hard gelatinous composition when crushed and exposed to aqueous media.

Agriculture

U.S. patent 9,056,940 – By-products of industrial processes are used in the production of polyurethane and polyisocyanurate for potential use as controlled release coatings for fertilizers.

U.S. patent 9,055,722 – Fungicides, pesticides, fertilizers, and the like are prepared as a controlled release tablet and incorporated with an agricultural seed in a capsule to optimize plant performance after germination.

U.S. patent 9,051,222 – Slow and controlled release polymeric sulfur materials are described for more optimal sulfur delivery to plants.

U.S. patent 9,039,803 – Lignin and lignosulphonates from wood pulping waste streams are converted to methylol derivatives to create controlled release fertilizer compositions.

U.S. patent 9,010,338 – Cellulose esters with increased biodegradation speed are described as a means for controlled release of biocides or fertilizers.

Eye

U.S. patent 9,066,782 – An innovative stenting device for delivery of therapeutic agents to the eye is disclosed.

U.S. patent 8,945,602 – Drug-containing nanoparticles are employed for drug delivery into or onto the eye.

Food

U.S. patent 9,061,825 – A syrup-holding “capsule” system for controlled introduction of flavors to water from home carbonation systems is disclosed.

U.S. patent 8,932,708 – A multilayer coextruded film is described for immediate and extended release of sulfur dioxide in food or agricultural packaging to control spoilage for weeks or months.

Fragrance

U.S. patent 8,940,336 – Alkylene glycol acrylates are polymerized to form matrices for controlled release of flavors and fragrances.

Gastroretentive Systems

U.S. patent 9,060,930 – A gastroretentive system for controlled delivery based on buoyancy is formed by creating a porous granule from hydrophobic and gas-generating components.

U.S. patent 8,974,825 – Mucoadhesive materials are employed for gastric retention and prolonged bioactive release.

Implants

U.S. patent 9,005,649 – A means to fabricate micro-holes on tubes using photo-lithography and reactive ion etching techniques is used to provide zero-order and directional release in stents and the like.

U.S. patent 8,992,949 – A moldable implant composition consisting of crystallized hydrophilic polymer domains within an amorphous hydrophobic polymer matrix is described for controlled release in bone-healing applications.

U.S. patent 8,968,763 – Biodegradable polyesters, polyethers, and polyurethanes are described for controlled drug release from implants.

U.S. patent 8,962,008 – Biocompatible polyesters are crosslinked with functionalized polyalkyne oxides to create implants with enhanced hydrophilicity for controlled drug release.

U.S. patent 8,974,813 – A hydrophilic polyurethane derivative is disclosed for controlled release applications.

U.S. patent 8,956,640 – Methoxyethyl methacrylate is incorporated as a midblock polymer function to control the hydrophobicity of polymer coatings in controlled release implants.

U.S. patent 8,940,311 – An injectable system of drug-containing microspheres in a temperature sensitive hydrogel that gels upon injection is used for long-term release of agents in the microspheres and short-term release of agents in the gel.

Manipulations

U.S. patent 9,052,262 – Control of nanoparticle movement (count and velocity) through an aperture is achieved using electrical potential and pressure differential.

U.S. patents 8,992,511 and 8,968,274 – A delivery system employing acoustically controlled bioactive release from a reservoir to an organism or body of water is described.

U.S. patent 8,936,794 – Electrocontractile nanotubes are described for electrically controlled delivery of bioactives.

U.S. patent 8,931,114 – A charged tether on a redox-active conductive polymer provides porosity control through voltage application, which can be applied in several capacities including bioactive controlled release.

U.S. patent 9,008,770 – Current is applied to a metal component of an implant to release metal ions to mitigate infection.

Materials

U.S. patent 9,062,159 – A simple, “green,” low-cost method for synthesizing medical-grade poly(lactic-co-glycolic acid) is described.

U.S. patent 9,040,071 – Para-ylene polymer formulations are employed as controlled release layers on reservoir devices.

U.S. patent 9,034,373 – Glyceryl monostearate and binder in the absence of microcrystalline cellulose are used to create spheronized beadlets.

U.S. patents 8,999,389 and 8,936,809 – A method for creating a partially or fully hydrated ceramic for localized extended release from an implant is disclosed.

U.S. patent 8,968,784 – Hydro/organic gelators prepared from disaccharide sugars are employed for enzymatically controlled drug delivery.

U.S. patent 8,956,645 – An albumin coating is employed to allow transport of hydrophobic actives for controlled drug delivery.

U.S. patent 8,956,638 – A strategy for creating a biocompatible poly(amic acid) for controlled drug release in implants and tissue scaffolding is disclosed.

U.S. patent 8,945,551 – A means of creating and using a biopolymer gel composed of a polyaminosaccharide and/or protein; a biocompatible phosphate and/or sulphonamide compound; a biologically active agent; an aqueous insoluble alkaline earth metal phosphate; and a biocompatible glycan and/or proteoglycan as a controlled release depot are disclosed.

U.S. patent 8,940,392 – Pseudo-cubic titanium/polycarboxylate structures are disclosed for liquid absorption, liquid or gas separation, or controlled bioactive release.

Miscellaneous

U.S. patent 9,068,109 – Viscosity breakers for subterranean systems are incorporated into nanoparticle coated polyelectrolyte complexes whereby breaker release is controlled by disruption of the complex by alternative counterions.

U.S. patent 9,050,366 – Tissue-adhering copolyester derivatives are used to create liners on internal body lumen surfaces for controlled release of bioactives.

U.S. patent 9,005,355 – An aluminum phosphate nanoparticle coating system is described for controlled release of phosphate anions to control corrosion. ■

New Horizons in Nanomedicine Symposium

Dan Peer, Tel Aviv University, Israel

The New Horizons in Nanomedicine symposium organized by the CRS Israeli Local Chapter (ICRS) took place at Tel Aviv University June 24–25, 2015. Overall, 150 people attended this two-day symposium, and we were honored to host high-level experts on a range of topics of scientific interest.

Topics included supramolecular architectures for drug delivery, targeted platforms for drugs and RNA inhibition, antibody-drug conjugates, stem cells, bioengineering, and theranostic imaging probes—all of which represent the vast research, technical challenges, and achievements of scientists working in the immense fields of drug delivery and biomaterials in our hyper-connected world.

Among the plenary speakers, Peter Senter (VP of Chemistry, Seattle Genetics, U.S.A.) spoke about antibody-drug conjugates from concept to product and included all the challenges and

opportunities around this strategy. Jeff Karp (Harvard Medical School, U.S.A.) spoke about stem cells and bioengineering principles in inflammation. Twan Lammers (RWTH Aachen University, Germany) talked about cancer theranostics, potential artifacts in optical imaging, and the importance of quantitative measurements in imaging such as PET, SPECT, MRI, and CT modality. Finally, Yanjun Zhao (Tianjin University, China) talked about new polymer chemistry for drug delivery.

In addition, 17 local Israeli speakers including veteran world-renowned scientists such as Yechezkel Barenholz and Rimona Margalit gave talks on new strategies they are developing in the fields of malaria and cardiovascular diseases. Young investigators included Tal Dvir, who talked about cardiac tissue engineering, and Avi Schroeder, who talked about new concepts in personalized nanomedicine.

Finally, a session devoted to cancer nanomedicine included Ronit Satchi-Fainaro, former president of ICRS, and Ayelet David, an ICRS board member. Both talked about polymer therapeutics strategies developed in their labs.

Tel Aviv University endorses a broad range of science, technology, and international cooperation that forms the basis of this conference. Our interdisciplinary approach in matters of research, our researchers, and our innovative endeavors are critical in ensuring a continual flow of knowledge, innovation, and talent.

The successful organization of this event required the devoted commitment and time of the organizers, to all of whom I extend my grateful thanks, including Mickey Shenhar and Inbal Halevi. I also thank our sponsors—the Gertner Institute for Medical Nanosystems at Tel Aviv University and the Focal Technology Area on Nanomedicine for Personalized Theranostics—for supporting the two-day symposium.

Of note, on February 4, 2016, the CRS Young Israeli Chapter is organizing a symposium for graduate students and postdocs only (anticipated number is 350) at Tel Aviv University to discuss challenges and opportunities in the field. ■



Auditorium during lectures.



Plenary speakers Yanjun Zhao, Twan Lammers, Peter Senter, and Jeff Karp with ICRS president Dan Peer.



Graduate students during a coffee break.

CRS Nordic Local Chapter Preconference Symposium

Line Hagner Nielsen,¹ Bente Steffansen,^{2,3} Annette Bauer-Brandl,³ Tapani Viitala,⁴ and Ingunn Tho⁵

This year the CRS Nordic Local Chapter event was organized as a preconference symposium in Edinburgh on Saturday, July 25, the day before the opening of the 42nd CRS Annual Meeting in the Scottish world heritage city. The meeting gathered close to 40 participants in the Edinburgh Training and Conference Venue situated in the city's Old Town. The topic of the meeting was "Drug Transport and Delivery," and the program was divided into a morning session and an afternoon session, each of which were opened by two well-reputed keynote speakers followed by three oral presentations selected among the submitted abstracts. During the poster session 20 posters were presented. The meeting was opened by CRS Nordic Local Chapter chair Ingunn Tho (University of Oslo, Norway) welcoming the delegates.



Bente Steffansen presenting the award for best presented abstract to Heikki Saari.

The scientific part of the symposium was kicked off with a session of two invited speakers. The session was chaired by Tapani Viitala (University of Helsinki, Finland). The opening presentation was given by Christel Bergström (Uppsala University, Sweden) about predictive tools for delivery of poorly soluble drugs. The introduction of the talk gave an overview of how the connections and relations of different molecular descriptors of new chemical entities (NCEs) can be organized in an easily understandable graphical form. From there it was then easy to understand how calculated molecular properties can be used to provide information of what is restricting the solubility of poorly soluble compounds. Examples of computational approaches for predicting glass-forming ability and stability, as well as drug solubility in commonly used pharmaceutical lipids, were then

presented. Finally, Bergström discussed how an early assessment of these properties could help to take into account the processes that limit solubility in an early formulation stage, thus ultimately providing a road map for rapid identification of an optimal formulation approach for any NCE. The second invited presentation in the opening session was given by Anja Boisen (Technical University of Denmark). The talk focused on the development and applications of micro- and nanomechanical sensors and microfabricated systems for oral drug delivery. An interesting approach in which the optics and mechanics of a DVD player could be utilized as compact and sensitive sensor systems was presented. The use of this approach for manipulating liquid samples such as blood for performing operations such as separation, valving, and mixing was given as an example from life sciences. The talk also included examples of how microfabricated systems such as cantilevers, strings, and "nanograss" could be utilized for novel sensing platforms, for example, for detecting single nanoparticles or monitoring antibacterial treatments. Finally, she presented a future concept on how micrometer-sized



Networking among enthusiastic delegates.

¹ Technical University of Denmark.

² University of Copenhagen, Denmark.

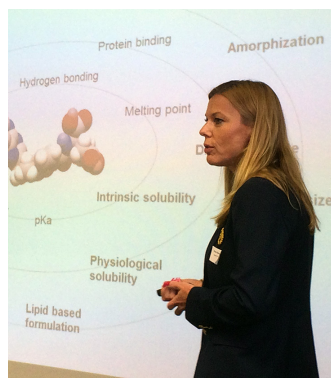
³ University of Southern Denmark.

⁴ University of Helsinki, Finland.

⁵ University of Oslo, Norway.



Invited speaker Yvonne Perrie.



Invited speaker Christel Bergstöm.

containers filled with drugs and sealed by an intelligent lid that opens at a specific location in the body could be utilized for improving oral drug delivery.

After the coffee break, three speakers selected for short talks from the submitted abstracts within the topic of drug delivery systems presented their research projects. The session was chaired by Bente Steffansen (University of Copenhagen and University of Southern Denmark). The first presentation was from Annika Jokinen (BioNavis Ltd., Finland), who presented how multiparametric surface plasmon resonance can be applied as a new and interesting optical method to characterize surface interactions between the cellular membrane and drug nanoparticulate delivery systems as well as for studying release kinetics of small drug molecules from controlled release formulation systems. Then Wye-Khay Fong from ETH Zürich (Switzerland) and Monash University (Australia) presented how external (thermal) irradiation with near-infrared light seems to trigger ^{14}C glucose release from phytantriol gold nanorod subcutaneous implants to rats. Finally, Karen Stephansen (University of Copenhagen and Technical University of Denmark) presented how electrospun fish sarcoplasmic protein-based nanofibers stabilize insulin against proteolytic degradation and promote transepithelial permeation of the intact insulin. At the end of the short talk session there was a shared discussion, with several interesting questions and comments from the audience.

Following the lunch break and poster session, the third session of oral presentations took place and was chaired by Line Hagner Nielsen (Technical University of Denmark). This session contained two invited speakers. The first invited keynote was given by Arto Urtti (University of Helsinki and University of Eastern Finland) and dealt with pharmacokinetics in ocular drug delivery and the need for better delivery systems to the eye. The talk included modeling of ocular pharmacokinetics, properties of blood–ocular barriers, and systemic drug delivery to the eye. An active discussion followed the talk. Yvonne Perrie (Aston University, United Kingdom) was the last among the invited speakers. She talked about delivery of vaccines with a special focus on the use of liposomal adjuvants. She showed how physicochemical characteristics of the functionalized liposomal surface play a key role in the modulation of immune response and vaccine efficacy. The liposomes were prepared by microfluidics, followed by decoration of the outer surface of the

liposomes by different ligands. By manipulation of lipid type (charge and transition temperature) and vesicle size, along with other parameters, the use of liposomal adjuvants can be optimized toward the ultimate goal of more efficient vaccines.

After the afternoon coffee break a fourth session consisting of selected oral presentations took place, chaired by Annette Bauer-Brandl (University of Southern Denmark). The focus of this session was on drug transport studies. As the first speaker, Massimiliano di Cagno (University of Tromsø, the Arctic University of Norway) introduced a new artificial and biomimetic barrier (Permeapad) and explained in examples how this barrier may be used to predict passive drug permeability. He mainly focused on the barrier's specific advantages in terms of functional stability, ease of use, and cost effectiveness compared with established assays. The next speaker was María García-Díaz (University of Copenhagen, Denmark). She summarized her studies about the contribution of mucus to the barrier function of the intestine. Using different cell-free *in vitro* models, she looked into possible mechanisms of permeation reduction by mucus: silica nanoparticles were used to study the steric contribution, and peptides were used to estimate interactions on the molecular level. She concluded that mucus contributes to the barrier function in both aspects. The last presentation of the day was by Ph.D. student Heikki Saari (University of Helsinki, Finland), who talked about a new approach to drug delivery using extracellular vesicles (EVs). These are membrane-bound particles excreted from cells that participate in the molecular communication between cells. As an example, Paclitaxel was used with cancer cell-derived EVs, and the transport of the drug into cells was depicted by, for example, live cell microscopy. The subsequent panel discussion with the three speakers addressed questions from the auditorium. These mostly concerned transport assays and their commercial availability, the biological barriers in general, and some experimental details.

To conclude the meeting, Heikki Saari was presented with the award for the best short presentation of the day for his clear and scientifically sound but critical presentation of his results. Ruth Schmid, the incoming President-Elect for CRS, was a welcome guest in the afternoon. She greeted the chapter, presented her view of the contribution of CRS to the scientific community, and shared her experience on how to get the most out of the CRS Annual Meeting in terms of contacts and networking. To close the scientific part of the program, Ingunn Tho thanked all the speakers, the organizers, and the auditorium for a fruitful meeting and the lively discussions. The day was completed with an informal dinner in Mr Basrai's World Cuisines restaurant. ■



CRS President-Elect Ruth Schmid (SINTEF, Norway) greeting the chapter.

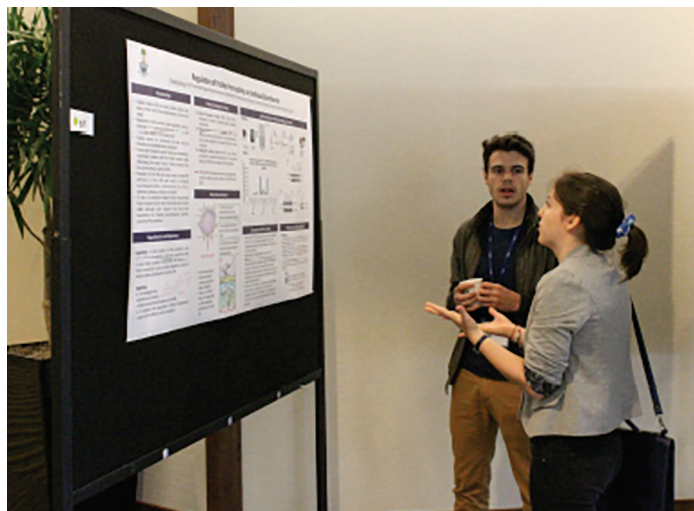
Drug Discovery and Development in the Post-Genomic Era: Canadian Chapter of the Controlled Release Society 2015 Symposium

Patricia Comeau¹ and Todd Hoare²

For the fourth time in the last five years, the CRS Canadian Local Chapter (CC-CRS) joined forces with the Canadian Society for Pharmaceutical Sciences (CSPS) to hold a joint annual symposium, this year in Toronto, Ontario. The theme of this year's symposium was "Drug Discovery and Development in the Post-Genomic Era," with topics ranging from leading-edge academic research to industrial product development to regulatory considerations. The focus throughout the symposium was to identify where future pharmaceutical science development should be directed, including how controlled release fits in to the goals and challenges of the pharma industry.

The conference started with a workshop showcasing the novel contributions of Canadian academic, industry, and government researchers focused on global vaccine development, including a discussion of the strengths and gaps in the Canadian vaccine landscape. Key speakers from the University of Alberta (Lorne Babiuk), the Mayo Clinic Vaccine Research Group (Gregory Poland), and the global head research and development of GSK (Rino Rappuoli) were featured in this daylong workshop. Overall, this first day was an invaluable learning opportunity for CC-CRS members to better understand where emerging delivery science technologies may best accommodate the current needs in Canadian (and global) vaccine development.

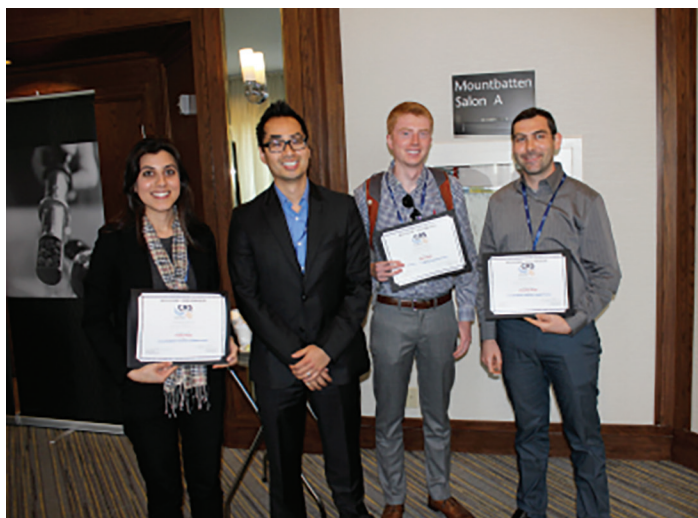
Following the conference welcome reception later that afternoon at the conference site, CC-CRS members—both old and new—met at a local rooftop bar to socialize, network, and really start



CC-CRS student member Warren Viricel gaining from the interdisciplinary conference at a CSPS poster.

the conference off on a good footing! The technical program of the conference officially started the following morning after an early trainee mentoring breakfast hosted by Agilent Technologies.

CC-CRS organized two sessions for this year's meeting: "Mucosal Drug Delivery" (cochaired by board members Emmanuel Ho and Marta Cerruti) and "Bioavailability of Novel Dosage Forms" (cochaired by board member Michael Doschak and Adrien Musuku of Pharmascience). In the "Mucosal Drug Delivery" section, Olivia Merkel (Wayne State University) gave a talk on targeting siRNA delivery to T cells in the lung, Justin Hanes (John Hopkins University) described mucus penetrating nanoparticles, and Haeshin Lee (KAIST, Korea) described adhesive paintable biomaterials inspired by marine mussels. In the "Bioavailability of Novel Dosage Forms" section, Michael Doschak (University of Alberta) described advances in peptide delivery formulation to impart bone specificity, Adrien Musuku (Pharmascience) provided an update on the bioanalytical sector, Kirshna Bhandari (Ashland Specialty Ingredients, Ashland Inc.) highlighted the role of excipients in design of solid amorphous drug dispersions, and Barbara Davit (Merck) discussed bioequivalence and pharmaceutical equivalence criteria for drugs acting locally within the gastrointestinal tract. CC-CRS members also benefitted strongly from a forward-looking session on "Imaging in Drug Delivery" (cochaired by board member Christine Allen and Jinzi Zheng from the University Health Network) that featured significant controlled release content, including presentations by Helen Lee (Merrimack Pharmaceuticals) on tumor deposition imaging as a predictive biomarker for personalized nanomedicine, Willem Mulder



CC-CRS 2015 poster award winners. From left to right: Sandra Ekdawi, CC-CRS incoming president Emmanuel Ho, Scott Campbell, and Michael Dunne.

¹ Dalhousie University, Canada.

² McMaster University, Canada.

(Mount Sinai School of Medicine) on imaging and nanomedicine in inflammatory atherosclerosis, Twan Lammers (Aachen University, Germany) on nanomedicines and theranostics, and Shyam Garg (University of Alberta) on traceable nanocarriers for targeted therapy of primary and metastatic breast cancer. As evidenced by the topics outlined above, the presentation sections were diverse from both a scientific and clinical perspective, giving insight into the potential for controlled release across multiple potential therapeutic targets and highlighting a variety of interesting materials and devices that may be applicable not only to the targeted application but other clinical applications.

Another key part of the conference was the poster session, which gave over 25 CC-CRS trainees from across Canada the chance to present their research to the conference audience. CC-CRS, with the assistance of local chapter funding from CRS, sponsored four travel awards to help facilitate travel of leading student researchers from across the country to present their posters at the symposium; such support is essential in a country as large as Canada in which travel can be a huge financial and logistical barrier to scientific collaboration. The winners of these awards were Jijin Gu (University of Manitoba), Kathy Tang (University of Alberta), Yufei Chen (University of Manitoba), and Huaifa Zhang (McGill University). In addition, five additional awards were given for abstracts of high merit to Petro Czipiel (University of Toronto), Daryl Sivakumuran (McMaster University), Madeline Simpson (McMaster University), Michael Dunne (University of Toronto), and Scott Campbell (McMaster

University). The two top-ranked student abstracts, from Yufei Chen (discussing the evaluation of drug release and *in vivo* biocompatibility of an intravaginal implantable device) and Petro Czipiel (discussing targeted delivery of siRNA by polymeric nanomolecules) were given the opportunity to also present their work during the oral presentation sessions organized by CC-CRS, with outstanding feedback from conference attendees. CC-CRS also sponsored three poster awards for the best posters presented at the conference. The winners of this year's competition were Scott Campbell, Sandra Ekdawi (University of Toronto), and Michael Dunne. Congratulations to these outstanding student researchers!

Finally, CC-CRS took the opportunity to hold its annual general meeting, at which outgoing chapter president Todd Hoare highlighted the current state of CC-CRS and incoming chapter president Emmanuel Ho discussed his vision for the chapter moving forward. Of particular note, the 2014–2015 academic year saw CC-CRS successfully host—for the first time—three “local” chapter events in different regions of Canada (Manitoba, Ontario, and Quebec). Given the immense size of Canada, these events are essential to build new local collaborations and ensure that controlled release science is active and flourishing across the country. Our hope is to maintain and expand the delivery of such events, featuring a mix of industrial and academic speakers, student poster or three-minute thesis competitions, and networking, throughout even more of Canada (e.g., from coast to coast!) in the coming years, aiming to spark additional collaborations between academics and industry on a more local level and improve the visibility and impact of CC-CRS across the country. In addition, these events have promoted (and will continue to promote) CRS membership and meetings as ideal avenues to build international contacts in the field.

While we took in a lot of science over the three days of the symposium, it was not all work. In addition to the chapter networking event on day 1, we also enjoyed a great conference banquet with CSPS and many networking breaks in the three-day program.

Overall, the conference was yet another example of how research and translation of controlled release science is alive and well in Canada! We invite everybody to join us at next year's annual symposium, to be held again in collaboration with CSPS in Vancouver, BC, May 31–June 3, 2016. Please mark your calendars and plan to join us! We will communicate our plans for this meeting as well as the local events coming up this year via the CRS News Capsule throughout the year. ■



Michael Doschak highlighting his research in controlling bone metabolism via controlled release strategies in Session 11: Bioavailability of Novel Dosage Forms.

MICRONEEDLES 2016

4th International Conference on Microneedles

23 - 25th May 2016
GSK House, London



The International Conference on Microneedles provides a unique international forum for academics and industry involved in the design, development, application and clinical translation of microneedle technology. The conference includes keynote presentations from leaders in the field interspersed with poster sessions and opportunities for networking when researchers at all levels can interact.

Registration and Key Dates

Registration includes access to both the Conference and Exhibition centres in addition to the Gala dinner event. Registration will be open in Autumn 2015 and will close in April 2016. The abstract submission deadline will be February 2016. For more information please visit www.microneedles2016.org.

Sponsorship

Sponsorship options offer the opportunity for your organization to benefit through enhanced visibility as an industry leader, brand recognition from your target market and direct exposure to prospective partners and customers. A variety of sponsorship packages are available. For more information please visit www.microneedles2016.org or contact the organizers at contact@microneedles2016.org.

In the News

Compiled by Steven Giannos, Independent Consultant

September

Generex Announces Formalization of Buccal Cannabis Codevelopment Plan

PRNewswire: September 2, 2015 – WORCESTER, MA, U.S.A. and TORONTO, ON, Canada – Generex Biotechnology Corporation (www.generex.com) (OTCQB: GNB) today announced that its previously announced intention to implement a buccal cannabis codevelopment arrangement with CannScience Innovations Inc. (www.cannsci.com) has been formalized.

Generex and CannScience have entered into a binding codevelopment and technology licensing agreement. Pursuant to the agreement, Generex has licensed its proprietary RapidMist™ drug delivery platform technologies to CannScience for the codevelopment of products for the buccal delivery of cannabinoids and cannabinoid-derived products and granted an exclusive license to CannScience for the commercialization of such products in Canada in exchange for royalty payments. Generex and CannScience will co-own the intellectual property created by this codevelopment effort and will share profits from the global commercialization of the products.

CannScience is a research and development biopharmaceutical company established to conduct research, and undertake the development of, therapeutic products based on the extracts from medicinal cannabis. The company is developing proprietary technologies and owns know-how related to the chemistry and pharmacology of medicinal cannabis. CannScience is working on integrating various medical devices and drug delivery technologies for the delivery of medications for various patient populations.

“With this codevelopment program, Generex and CannScience seek to benefit from the growing global trend towards legalization of cannabis, particularly for medicinal purposes,” commented Mark Fletcher, Generex president and chief executive officer. “Our goal here is to develop products combining proprietary formulations and devices for the buccal delivery of dose-specific cannabinoids into the human body with no deposit into the lungs, thereby offering a safe, simple, fast, and efficacious alternative to smoking or edibles with their attendant uncertainties in respect of onset of action and dose control.”

Generex is engaged in the research, development, and commercialization of drug delivery systems and technologies. Generex has developed a proprietary platform technology for the delivery of drugs into the human body through the oral cavity (with no deposit in the lungs). The company’s proprietary liquid formulations allow drugs typically administered by injection to be absorbed into the body by the lining of the inner mouth using the company’s proprietary RapidMist™ device. Antigen Express,

Inc., is a wholly owned subsidiary of Generex. The core platform technologies of Antigen Express comprise immunotherapeutic vaccines for the treatment of malignant, infectious, allergic, and autoimmune diseases. Antigen Express has pioneered the use of specific CD4+ T-helper stimulation technologies in immunotherapy. One focuses on modification of peptides with Ii-Key to increase potency, while a second relies on inhibition of expression of the Ii protein. Antigen Express scientists, and others, have shown clearly that suppression of expression of the Ii protein in cancer cells allows for potent stimulation of T-helper cells and prevents the further growth of cancer cells. For more information, visit the Generex website at www.generex.com or the Antigen Express website at www.antigenexpress.com.

Neurotech Announces First Patient Enrolled in Novel Anti-VEGF Encapsulated Cell Therapy Study

PRNewswire: September 2, 2015 – CUMBERLAND, RI, U.S.A. – Neurotech Pharmaceuticals, Inc., announced today the first patient has been enrolled in the multicenter phase 2 clinical trial of NT-503 encapsulated cell therapy (ECT) for the long-term treatment of recurrent subfoveal choroidal neovascularization secondary to age related macular degeneration (wet AMD). NT-503 is a unique vascular endothelial growth factor (VEGF) receptor protein continuously produced by Neurotech’s versatile ECT implant.

“This landmark proof-of-concept study will evaluate NT-503 ECT as a viable alternative to frequent intravitreal injections in wet AMD patients,” said Charles Johnson, M.D., chief medical officer. “We believe NT-503 ECT has the potential to maintain visual acuity in patients who have already exhibited a good response to intravitreal injections, while reducing the long-term treatment burden. This program will provide key information regarding the safety and efficacy of NT-503 ECT as we continue to make progress toward our goal of advancing treatment for wet AMD and other chronic posterior segment conditions.”

The phase 2 randomized, active-controlled, masked study will evaluate the safety and efficacy of NT-503 ECT compared with aflibercept (Eylea®) intravitreal injections. Approximately 150 patients who have previously been treated with at least three anti-VEGF injections and have demonstrated a good clinical response will be enrolled. This study will compare maintenance of vision in patients randomized to receive a single NT-503 ECT implant or aflibercept injections every 8 weeks. Efficacy will be evaluated using a combination of endpoints including change in visual acuity, change in retinal thickness, rate of treatment failures, and rate of rescue medication. A primary analysis will be conducted at one year, and patients will be followed for two years.

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“We are very excited to initiate this study,” said Arshad Khanani, M.D., managing partner of Sierra Eye Associates in Reno, Nevada, the first retinal surgeon to enroll a patient in the trial. “ECT represents the future of drug delivery. It has the capability to allow for the continuous delivery of therapeutics with a single surgical procedure. NT-503 ECT has the potential to maintain a therapeutic response in patients with wet AMD while eliminating the need for repeated injections.”

Neurotech anticipates enrollment to be completed by the end of 2015 and plans to report top-line data from their phase 2 program in the first half of 2017.

Neovascular or “wet” age related macular degeneration is the most advanced stage of AMD. It involves the growth of new, abnormal blood vessels (promoted by vascular endothelial growth factor or VEGF) and typically results in severe vision loss. Almost 2 million patients in the United States have wet AMD, and it is the most common cause of blindness in those over the age of 55. While there is no cure, the current standard of care is aimed at treating vision loss and the associated leakage of fluid from abnormal blood vessels through the routine administration of intravitreal anti-VEGF injections.

Anti-VEGF injections have dramatically improved visual outcomes in patients with wet AMD. However, improvements are dependent upon frequent injections and close monitoring, which places a large burden on patients, physicians, caregivers, and the healthcare system. As such, studies have shown that real world utilization rates of anti-VEGF injections are often suboptimal, and alternative approaches intended to reduce the treatment burden, including “as needed” regimens, are sometimes less effective than monthly or bimonthly administration. A long-term, continuous therapy with a low treatment burden remains a clear unmet need in wet AMD treatment.

Encapsulated cell therapy is an investigational, first-in-class, versatile delivery platform that promotes continuous production of therapeutics to the eye with the potential to treat a broad array of ocular diseases. It utilizes a proprietary, well-characterized retinal pigment epithelial cell line that has been genetically engineered to produce therapeutically active biologics. The cells are encapsulated in a semipermeable membrane that allows for selective passage of therapeutic proteins.

The ECT platform is implanted during a single outpatient surgical procedure through a small scleral incision and can be removed through the same incision, if desired. It has the potential to address the current limitations of intraocular drug delivery by allowing for single- and multiple-factor drug combinations and ensuring patient compliance and reducing treatment burden with one surgical procedure that can deliver drug for at least 2 years.

To date more than 280 patients have received ECT with either the NT-501 (CNTF) or NT-503 (sVEGF) producing constructs. Adverse events have been generally mild and

consistent with those expected from the surgical procedure or the secreted protein.

Neurotech’s lead clinical product, NT-503 ECT, continuously produces a soluble vascular endothelial growth factor receptor protein. Dose-escalation studies with NT-503 ECT have been successfully conducted in patients with wet AMD.

Neurotech Pharmaceuticals, Inc., is a private biotechnology company focused on developing transformative therapies for chronic eye diseases. Its core technology platform, encapsulated cell therapy, enables continuous production of therapeutic proteins to the eye. Neurotech is exploring several ECT candidates including its lead product for the treatment of wet AMD, DME, and RVO (NT-503), combination therapy for wet AMD (NT-506), and ciliary neurotrophic factor (NT-501) for glaucoma and macular telangiectasia (MacTel). To learn more, visit www.neurotechusa.com.

GNTbm Updates Developments in the Vaucarrin™ Nanogold Drug Delivery Platform

PRNewswire: September 1, 2015 – TAIPEI, Taiwan – Taiwan’s GNT Biotech & Medicals Corporation (GNTbm) held a press conference in Taipei on August 25th to update developments in its new Vaucarrin™ platform, a targeted drug delivery technology that uses nanoscale gold as the delivery vehicle.

This event was part of a joint press conference held by its parent company, Gold NanoTech Inc. (GNT), showcasing GNT’s latest edible gold-based food and beverage partners, together with another GNT spinoff GNT Biotech & Medical Device Corp (GNTbmd), developing medical devices and cosmetics.

By directing the drug to the disease site, a Vaucarrin™ drug-carrier-targeting molecule complex can improve a drug’s pharmacokinetics, increase its half-life, enhance its therapeutic effect, and decrease its adverse effect. Besides improving existing drugs, Vaucarrin™ can also be used to repurpose drug candidates that have been shelved due to the less-favorable targeting and pharmacokinetic profile.

The complex made up of nanogold, the therapeutic agent, and the targeting antibody molecule is formed through conjugation with a pH-sensitive proprietary linker developed by GNTbm that controls the release of the drug inside a diseased cell, making it a powerful delivery system with exciting possibilities. GNTbm has developed a library of linker molecules for different therapeutic applications.

Compared with other nanoscale targeted drug delivery technologies in use today, GNTbm nanogold as the delivery vehicle has certain advantages. These include superior biocompatibility, increased drug payload capacity, reduced drug resistance, and great flexibility to the varieties of drugs and ligands that can be utilized in the complex. The complex is small

enough to pass the blood brain barrier and also has potential to be used in oral dosage form, adding exciting possibilities to its potential application. GNTbm intends to focus initially on applications in cancer, rheumatoid arthritis, and neurodegenerative diseases.

“Gold is inert, so it’s very safe; GNT’s gold flake products have been approved as a food additive by the Taiwan FDA as well as European Regulation of Food Additives E175, and we expect our nanogold to share the same safety profile,” elaborated Dr. Alex Chen, president of GNTbm. “The nanogold particle is sized between 20 and 100 nanometers and can carry a drug payload up to 16% of its weight, compared with only 10–12% for other nanomedicines,” added Chen.

Concerns over toxicity or adverse effects observed in early stage trials are among the major reasons for a new drug’s development to be shelved or discontinued completely. Repurposing of such shelved assets is a sought-after alternative for pharmaceutical companies, which may have made significant but unrealized investments in such drugs. With Vaucarrin™, GNTbm intends to provide collaboration opportunities for drug repurposing to the pharmaceutical industry, whereby companies’ drugs, whether small or large molecules, protein drugs, siRNA and DNA, and so on, all can be repositioned as complexes with greater targeting efficiency, longer half-life, and lower toxicity or adverse effects.

Already the Vaucarrin™ platform is generating significant interest from the international pharmaceutical community.

“During the recent BioTaiwan 2015 exhibition, we signed confidentiality agreements with several major overseas pharmaceutical companies who wanted to learn more about Vaucarrin™,” said Dr. Yesu Chao, vice president of GNTbm.

GNTbm will offer a range of cooperation models to the pharmaceutical industry, including synthesis of nanogold plus linker complexes; tailored nanogold, linker plus therapeutic agent complex formulation; and nonexclusive and exclusive licensing of its platform for external use by pharmaceutical company partners.

Currently, GNTbm is working on two projects using the Vaucarrin™ platform: Gbm12401 for breast cancer and Gbm12407 for rheumatoid arthritis.

The development of the Vaucarrin™ platform has been rapid. Work on this technology—developed entirely in-house—only began in July 2014, about one year after GNTbm was formed. Currently undergoing PK/PD studies, GNTbm is confident enough in the safety and purity of its nanogold product to hold off on precise and comprehensive toxicology studies until next year at the earliest.

GNTbm nanogold is produced by a proprietary physical vapor deposition (PVD) process, developed by parent company GNT Inc. 23 years ago. Nanogold, being gold rendered by the PVD process of between 20 and 100 nanometers in size, is utilized in the Vaucarrin™ platform, whereas the visible much larger-sized gold flake created by the same process is used by GNT and GNTbmd for a wide variety of applications in the food, beverage, medical device, and cosmetic industries.

The process for combining the nanogold, therapeutic agent, and targeting antibody molecule complex with the pH-sensitive proprietary linker is another proprietary process developed and owned by GNTbm.

Formed in 2013, GNTbm (Taiwan GISA stock code 7427, IPO expected at the end of 2015) is currently focused on the development of the Vaucarrin™ drug delivery platform to create new drug complexes for applications in cancer, rheumatoid arthritis and neurodegenerative diseases. Drugs including small or large molecule, protein drugs, siRNA and DNA, and so on, all can be incorporated into this platform. GNTbm also provides contract pharmaceutical services developing drugs with different targets and new formulations. In addition, GNTbm is conducting the NDA and new indication development (breast cancer and non-small cell lung cancer, NSCLC) of chidamide in Taiwan. Chidamide, the novel epigenetic regulator for targeted cancer therapy, is a small molecule in-licensed from ChipScreen Biosciences Ltd. of Shenzhen, China. Chidamide is only the fourth histone deacetylase inhibitor (HDACi) approved in the world. GNTbm has in-licensed seven patents, including one for chidamide, and others from the parent company GNT Inc. for nanogold applications. GNTbm has submitted provisional filing and expects to submit a further six patent applications for the medical use of nanogold drug delivery technology one year from now.

Gold NanoTech Inc. (GNT; Taiwan stock code 1267) was established in 1993 by a team of electronic and materials experts focused on the R&D and manufacture of trace precious metals, including gold, silver, platinum, and palladium. GNT developed a unique physical vapor deposition (PVD) production process, a physical metal nanomanufacturing technology that is radically different from ordinary chemical nanometal processing. GNT’s physical processing produces nanoscale materials without the addition of other elements or dispersants. Resultant materials are collected and distributed using pharmaceutical grade water and with the purest nanomaterial processing technology available. PVD technology produces gold with a purity of 99.99%. This material has passed toxicology tests, making it safe for human consumption. Gold flakes produced by the PVD process and used in cosmetic, food and beverage applications have been approved as a food additive by the Taiwan FDA and the European Regulation of Food Additives (E175).

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August

Chrono Therapeutics Receives Second Fast Track SBIR Grant from National Cancer Institute for Patient-Individualized Smoking Cessation Therapy

PRNewswire: August 25, 2015 – HAYWARD, CA, U.S.A. – Chrono Therapeutics, a pioneer in digital drug therapy, today announced it has received a second phase 1 and phase 2 Fast Track Small Business Innovation Research (SBIR) grant award from the National Cancer Institute (NCI). This award of up to \$2.3 million will support final product development of the digital portion of Chrono's patient-individualized smoking cessation therapy as well as pilot efficacy trials of the system. This is the second Fast Track SBIR grant award Chrono has received from the NCI. Chrono successfully executed on a 2012 \$2.23M grant that funded early product engineering and a second in human pharmacokinetic study.

Chrono's smoking cessation solution is the first nicotine delivery system to time medication delivery to when smokers' cravings are predictably strongest. The wearable component automatically begins delivering nicotine before smokers wake up, helping to curb the strong morning craving most smokers experience—something other nicotine replacement products cannot do. Embedded with sensors and Bluetooth, the wearable monitors compliance and securely connects with a companion mobile application that provides real-time behavioral coaching in response to cravings and the nicotine-dosing regimen.

"Receiving our second grant award from the NCI is an endorsement of Chrono's cessation platform, which takes a fresh approach to a serious addiction that kills 5 million people worldwide each year," commented Alan Levy, the CEO and chairman of Chrono Therapeutics.

Dr. Michael Burke and Dr. Taylor Hays of the Mayo Clinic are among several of the world's leaders in nicotine dependence treatment working with Chrono to integrate tailored nicotine delivery with evidence-based, proactive, and personalized behavioral strategies to help smokers quit.

"Integrating a smart digital coach that leverages the best in behavioral science with a new and adjustable method to deliver nicotine replacement has the potential to save many thousands of lives by providing new hope and support to people struggling to become tobacco free. We are very excited to collaborate with Chrono on this innovation," stated Dr. Burke, assistant professor of medicine at the Mayo Clinic School of Medicine and program coordinator at the Mayo Clinic Nicotine Dependence Center.

The smoking cessation solution is the first product targeted to be commercialized from Chrono's platform, which represents the convergence of optimized drug delivery, embedded sensor technology to monitor compliance, and connected and personalized behavioral support to transform how medicine is delivered and how people achieve their health goals.

Guy DiPierro, the founder of Chrono and VP of intellectual property and governmental affairs, commented, "We appreciate NCI's ongoing support and leadership in helping Chrono combat one of the world's leading pandemics."

Effective care of the most hard-to-treat conditions requires approaches beyond simply taking medicine. Chrono's team is developing the first wearable transdermal drug delivery device that optimizes drug dosing, is embedded with sensor technology to track usage, and is connected via Bluetooth to an evidence-based smartphone application that delivers real-time personalized behavioral support to keep users on track to achieving their goals. Chrono's first application is in smoking cessation, enabling smokers to overcome the world's deadliest addiction. For more information, visit www.chronothera.com

Micell Technologies Announces Surgical Technologies Approved as MiStent SES Commercial Manufacturer for CE Mark Countries

PRNewswire: August 20, 2015 – DURHAM, NC, U.S.A. – Micell Technologies, Inc. announced that its application for a manufacturing partner, Surgical Technologies, Inc. (STI), was approved by British Standards Institution (BSI) to begin full-scale manufacturing of Micell's MiStent SES® sirolimus-eluting absorbable polymer coronary stent system for commercial distribution in the European Union and other countries where the CE Mark is accepted. STI will be the primary contract manufacturer of MiStent SES, a new drug-eluting stent with a bioabsorbable coating designed to promote optimal healing in patients with coronary disease.

"We are excited to join the team that is bringing this new class of medical device to people suffering with coronary artery disease," said Timothy M. Scanlan, president and chief executive officer of STI and its parent company, Scanlan International. "As a pioneer in medical contracting, STI is well suited to partner with Micell to execute commercial-volume manufacturing. Micell's uniquely efficient manufacturing process enables scalable, high-yield throughput within a small footprint."

Arthur J. Benvenuto, Micell's chairman and chief executive officer, said, "With STI's expertise and performance in full-service medical device contracting and Micell's highly efficient manufacturing process, we are accommodating the controlled commercial launch of MiStent SES in CE Mark countries as well as supplying clinical trials currently being conducted in Europe and China. We also are prepared to support a commercial launch in China once granted regulatory approval."

MiStent SES received a CE Mark in the European Union and is commercially available through Micell's distribution partner, STENTYS. STENTYS introduced MiStent SES earlier this year in Western Europe via a controlled launch and will expand availability of MiStent SES in the second half of 2015 to selected countries within the Middle East, Southeast Asia, and Latin America. Micell is currently pursuing regulatory approval in China, Hong Kong, and Macau. Upon completion, MiStent

SES will be distributed exclusively by Hefei Life Science Technology Park Investment and Development Co., Ltd. (Hefei Life Science). MiStent SES is not approved for sale or use in the United States by the Food and Drug Administration (FDA).

MiStent SES® is designed to optimize healing in patients with coronary artery disease. The rapidly absorbable coating of MiStent SES, which contains crystalline drug (sirolimus) and an absorbable polymer, is intended to precisely and consistently provide for local drug delivery and limit the duration of polymer exposure. These characteristics potentially reduce the safety risks associated with currently commercially available drug-eluting stents.

Using an approved drug (sirolimus) and polymer (PLGA), Micell's patented supercritical fluid technology allows a rigorously controlled drug/polymer coating to be applied to a bare-metal stent. MiStent SES leverages the benefits of a cobalt chromium coronary stent system—a state-of-the-art, thin-strut, bare-metal stent that has demonstrated excellent deliverability, conformability, and flexibility.

The European Union's approval of MiStent SES was supported by clinical data from two studies, DESSOLVE I and II. DESSOLVE II demonstrated superior in-stent late lumen loss rates and an excellent safety profile. Four-year DESSOLVE II data will be presented at TCT in October 2015. The three-year follow-up of the DESSOLVE clinical studies subjects was completed in 2014, and these patients continue to undergo long-term followup. In 2015, clinical sites in China began enrolling patients in DESSOLVE C, a prospective, single-blind, multi-center, randomized, controlled clinical trial to demonstrate MiStent SES's efficacy and safety. DESSOLVE C, intended to support regulatory approval of MiStent SES in China, is being sponsored by Hefei Life Science in conjunction with Micell. MiStent SES is not approved for sale or use in the United States by the FDA.

Nuvo Research® Announces U.S. Patent for Topical Foamed Formulations That Include DMSO

PRNewswire: August 20, 2015 – MISSISSAUGA, ON, Canada – Nuvo Research Inc. (TSX: NRI), a specialty pharmaceutical company with a diverse portfolio of topical and immunology products, today announced that the U.S. Patent Office has granted U.S. patent no. 9,107,823 ('823 patent) covering novel topical foam formulations that include dimethyl sulfoxide (DMSO) together with certain drug actives. Nuvo has pioneered the use of DMSO as a carrier in topically applied drug products, which is a key component of the company's U.S. Food and Drug Administration (FDA) approved products, Pennsaid® and Pennsaid 2%.

The claims of the '823 patent protect foamable formulations comprise (i) DMSO in a specified range; (ii) a pharmaceutically active agent that is an anti-inflammatory steroid, a nonsteroidal anti-inflammatory drug (NSAID) or a local anesthetic; and (iii) other specified ingredients. In particular, the patent covers Nuvo's

novel IBUFOAM drug candidate that contains DMSO and the NSAID ibuprofen. The anticipated expiry date of the patent is November 22, 2031.

"This patent provides broad intellectual property protection for foam formulations that use DMSO to enhance delivery of specified categories of known active drugs into or through the skin," said Tina Loucaides, Nuvo's vice-president, secretary, and general counsel. "The patent affords Nuvo another avenue to realize value from our investments and scientific accomplishments in topical and transdermal drug delivery. Our strategy is to make this patented dosage form platform, including IBUFOAM, available for development and out-licensing collaborations with partners who will fund completion of the development program."

IBUFOAM has been developed to treat acute and chronic pain conditions such as sprains and strains and osteoarthritis (OA). IBUFOAM is a topical ibuprofen foam formulation that combines a transdermal carrier DMSO with 5% the NSAID ibuprofen and delivers the active drug through the skin directly to the site of inflammation and pain. IBUFOAM has not yet been studied in clinical trials or approved by regulatory authorities for sale and is available for out-licensing to partners that would complete its development. Significant chemistry, manufacturing, and controls (CMC) information, including stability data, as well as nonclinical data are available to support an Investigational New Drug (IND) submission.

Pennsaid is used to treat the signs and symptoms of OA of the knee(s). The drug combines a transdermal carrier (containing 45.5% w/w DMSO) with 1.5% diclofenac sodium, an NSAID, and delivers the active drug through the skin directly to the site of inflammation and pain. Following FDA approval of Pennsaid 2%, Pennsaid is no longer marketed in the United States effective January 1, 2015. It is currently marketed in Canada by Paladin Labs Inc. and marketed under license and/or distribution agreements in Greece, Italy, and the United Kingdom.

Pennsaid 2% is a topical product containing DMSO and 2% diclofenac sodium compared with 1.5% for original Pennsaid. It is approved in the United States for pain of OA of the knee(s) and, like Pennsaid, contains 45.5% w/w DMSO. It is more viscous than Pennsaid, is supplied in a metered dose pump bottle, and has been approved in the United States for twice daily dosing compared with four times a day dosing for Pennsaid. Pennsaid 2% is protected by multiple U.S. patents that are listed in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations database or Orange Book. Pennsaid 2% has not yet received regulatory approval outside of the United States. Patents protecting Pennsaid 2% have been issued or are pending in multiple major international territories. Nuvo (TSX: NRI) is a specialty pharmaceutical company with a diverse portfolio of products and technologies. The company operates two distinct business units: the Topical Products and

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Technology (TPT) Group and the Immunology Group. The TPT Group currently has four commercial products, a pipeline of topical and transdermal products focusing on pain and dermatology, and multiple drug delivery platforms that support the development of patented formulations that can deliver actives into or through the skin. The Immunology Group has two commercial products and an immune system modulation platform that supports the development of drug products that modulate chronic inflammation processes resulting in a therapeutic benefit. For additional company information, visit www.nuvoresearch.com.

Elixir Medical Receives 2015 Innovator of the Year Award from EK-UNICO

Business Wire: August 18, 2015 – SUNNYVALE, CA, U.S.A. – Elixir Medical Corporation, a developer of products that combine state-of-the-art medical devices with advanced pharmaceuticals, announced that it has received the prestigious “Innovator of the Year” for 2015 at the annual conference of EK-UNICO in Germany. With a presence in more than 20 countries, Elixir Medical was selected for this honor by the 12 German university hospitals that make up the EK-UNICO purchasing pool headquartered in Münster.

EK-UNICO CEO Dr. Frank Obbelode awarded the coveted prize to Elixir Medical, a 10-year-old American company, in the presence of around 120 purchasers from the 12 associated member institutions. On behalf of these associated member institutions, Dr. Obbelode also thanked the representatives of Elixir Medical for their successful and faithful collaboration.

“We hope in this way to clearly express our recognition of a company that has, at its young age, proven able to combine excellence in medical technology and innovative skill with entrepreneurial success, thus making a significant contribution to improving health care for heart patients,” said Dr. Obbelode in his address. “Elixir Medical’s example clearly shows the importance of advances in research and development. This is where scientific pioneering spirit, entrepreneurial initiative, and marketing skill come together—to the benefit of all the EK-UNICO-associated university hospitals and their patients.”

“Elixir Medical is honored and excited to receive this prestigious Innovator of the Year award for 2015,” said Motasim Sirhan, CEO of Elixir Medical. “We are committed to presenting innovative and state-of-the-art products to our customers, and providing them with excellent service as well.”

Elixir Medical is the only company with three CE Mark-approved drug-eluting systems spanning all market segments: the DESolve Novolimus-eluting bioresorbable coronary scaffold system, the DESyne® BD Novolimus-eluting coronary stent system (with biodegradable polymer), and the DESyne® Novolimus-eluting coronary stent system (with durable polymer). Elixir Medical Corporation, a privately held company headquartered in Sunnyvale, California, develops products that combine state-of-the-art medical devices with advanced

pharmaceuticals to provide innovative treatment solutions to patients worldwide. The company’s next-generation drug-eluting stent systems and bioresorbable coronary scaffold are designed to optimize localized drug delivery to provide safe and effective treatments for cardiovascular patients. For more information, visit www.elixirmedical.com.

Aerie Pharmaceuticals and GrayBug Announce Research Collaboration

Business Wire: August 5, 2015 – IRVINE, CA, and BALTIMORE, MD, U.S.A. – Aerie Pharmaceuticals, Inc. (Nasdaq: AERI), a clinical-stage pharmaceutical company focused on the discovery, development, and commercialization of first-in-class therapies for the treatment of patients with glaucoma and other diseases of the eye, and GrayBug, Inc., a venture-stage pharmaceutical company developing microparticle controlled release drug delivery technologies for the treatment of ocular diseases including wet age-related macular degeneration (AMD) and glaucoma, today announced a research collaboration and license agreement to deliver certain of Aerie’s preclinical product candidates to both the front and back of the eye using GrayBug’s proprietary technology.

Initially, the partnership will focus on evaluating the ability of GrayBug’s polymer-based delivery technology to provide multi-month drug release capability for an Aerie small molecule for wet AMD. Preclinical *in vivo* studies showed that Aerie’s AR-13154 molecule reduced wet AMD lesion size more than the market-leading product Eylea® (aflibercept). AR-13154 targets Rho Kinase, Janus Kinase 2, and platelet-derived growth factor receptor beta.

The research collaboration also provides Aerie with the ability to evaluate long-term sustained delivery of the active ingredient in Rhopressa™ to the anterior chamber of the eye for patients with glaucoma and ocular hypertension.

The terms of the agreement provide for a one-year research collaboration and include an exclusive option for Aerie to obtain from GrayBug an exclusive license to use the GrayBug technology to develop and commercialize sustained-release versions of Aerie’s ophthalmic products.

“We are delighted to collaborate with GrayBug, and we believe their technologies will provide Aerie with the ability to make excellent progress in understanding the potential of Aerie’s small molecules to provide new treatment approaches to serious diseases of the eye. AR-13154 has shown impressive results preclinically, and we believe the best way to provide sustained delivery of this product to the back of the eye is through GrayBug’s unique delivery platform. We are also interested in further evaluating front of the eye applications for our glaucoma product set,” said Vicente Anido, Jr., Ph.D., Aerie’s chairman and chief executive officer.

Jeffrey L. Cleland, Ph.D., GrayBug interim chief executive officer, commented, “We believe Aerie is an excellent partner to apply

our unique delivery technologies for practical application in the treatment of serious ocular diseases. GrayBug has an extensive background in polymer-based delivery technologies including the ability to formulate different release profiles, and we believe we have unparalleled potential to drive sustained delivery of Aerie's products to both the front and back of the eye."

Under the terms of the license agreement, GrayBug will receive development milestone payments from Aerie and will receive royalty payments upon successful commercialization of any products arising from the collaboration. Initial commitments, including research and execution investments, are not considered material to Aerie's financial statements at this time.

Aerie is a clinical-stage pharmaceutical company focused on the discovery, development, and commercialization of first-in-class therapies for the treatment of patients with glaucoma and other diseases of the eye. Aerie is currently conducting a phase 3 registration trial in the United States named Rocket 2, for which the primary efficacy endpoint is to demonstrate noninferiority of IOP lowering for Rhopressa™ compared with timolol, along with a phase 3 registration safety-only trial, named Rocket 3, in Canada. Aerie completed its initial phase 3 registration trial, named Rocket 1, the three-month efficacy results of which were initially reported in April 2015, and expects to commence a fourth phase 3 registration trial, named Rocket 4, in the third quarter of 2015. Aerie also completed in 2014 a phase 2b clinical trial in which Roclatan™ met the primary efficacy endpoint, demonstrating the statistical superiority of Roclatan™ to each of its components, and plans to commence the first phase 3 registration trial for Roclatan™, named Mercury 1, in the third quarter of 2015.

GrayBug was founded in September 2011 as a spin-out of the Wilmer Eye Institute of the Johns Hopkins University School of Medicine. GrayBug is developing injectable controlled release technologies to reduce the frequency of ocular therapy to a few times per year (as few as twice per year). These technologies have solved the problems with tolerability and blockage of vision noted with many injectable sustained release ocular products. GrayBug is initially focused on developing its own products for the treatment of wet AMD and glaucoma. GrayBug's technologies were codeveloped by GrayBug founder Justin Hanes, Ph.D., who is the Lewis J. Ort Professor of Ophthalmology at the Wilmer Eye Institute of the Johns Hopkins University, in collaboration with GrayBug cofounders, and leading ophthalmology clinician-scientists from the Wilmer Eye Institute Peter A. Campochiaro, M.D., and Peter J. McDonnell, M.D. The technologies were licensed from Johns Hopkins University. For more information, please visit www.graybug.com.

CTX Acquires Promising Proprietary Drug Delivery Assets

Business Wire: August 4, 2015 – TUCSON, AZ, U.S.A. – CTX Technology Inc., based in Tucson, Arizona, has acquired the intellectual property, formulations, and related data of Convoy Therapeutics Inc.

Built on peptide-based skin-penetration platform technology developed in the laboratory of Samir Mitrugotri, Ph.D., at the University of California, Santa Barbara, the Convoy Therapeutics assets include proprietary formulations for both therapeutic and aesthetic applications.

The proprietary peptide platform technology is uniquely capable of transporting small and large molecules, with a wide range of molecular weights, including biologics, into the skin and ensuring that they remain at the site of local placement. The technology represents a new approach for improved topical delivery of a wide range of active ingredients.

Of the proprietary formulations acquired, Khalay HA™, a formulation of hyaluronic acid, has shown superior moisturizing and wrinkle-reduction performance for aesthetic applications. Cyclopsorb™ is a promising disease-modifying therapeutic that targets mild-to-moderate psoriasis. Both formulations utilize the CTX peptide-based skin-penetration platform technology.

CTX will commercialize the existing proprietary formulations through focused partnerships, continue to work on new applications, and out-license the platform technology for the therapeutic and aesthetic markets.

July

Neos Therapeutics Resubmits New Drug Application for FDA Review of Amphetamine Extended-Release Orally Disintegrating Tablets to Treat ADHD

Business Wire: July 30, 2015 – DALLAS and FORT WORTH, TX, U.S.A. – Neos Therapeutics, Inc. (NASDAQ: NEOS), a pharmaceutical company with a late-stage pipeline of innovative extended-release (XR) product candidates for the treatment of attention deficit hyperactivity disorder (ADHD), today announced that it has resubmitted a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) for its amphetamine XR orally disintegrating tablet (XR-ODT) product candidate, NT-0202, for the treatment of ADHD.

The NT-0202 NDA resubmission provides information to specifically address the FDA-issued Complete Response Letter received in September 2013. This includes the results from an additional pharmacokinetic study, which was conducted with NT-0202 that utilized a commercial-scale manufacturing process, and the requisite stability data. This submission is a class 2 resubmission, with a target six-month PDUFA review period. If approved, NT-0202 will be the first amphetamine XR-ODT for ADHD. Neos' methylphenidate XR-ODT candidate, Cotempla XR-ODT™, is currently under review by the FDA and, if approved, will be the first methylphenidate XR-ODT available for the treatment of ADHD.

"Our product candidates incorporate two of the most commonly prescribed medications for the treatment of ADHD, methylphenidate and amphetamine. Our proprietary modified-

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release drug delivery technology platform has enabled us to combine two key drug delivery attributes in each of these product candidates: an extended-release profile, which allows for once-daily dosing, and an ODT dosage form, which disintegrates in the mouth, without the need for water,” said Vipin K. Garg, Ph.D., president and CEO of Neos.

Stimulant medications such as methylphenidate and amphetamine are the standard of care for treating ADHD, and XR formulations of these medications allow for once-daily dosing. However, recent data suggest that a significant percentage of the pediatric population have difficulty swallowing solid dosage forms, and many remain uncomfortable doing so into adulthood. ODTs differ from traditional tablets and capsules in that they are designed to disintegrate on the tongue without the need for water, rather than being swallowed whole.

According to the National Institute of Mental Health, ADHD is one of the most common childhood disorders and can continue through adolescence and adulthood. Symptoms include difficulty staying focused and paying attention, difficulty controlling behavior, and hyperactivity (overactivity).

Neos Therapeutics, Inc. is a pharmaceutical company focused on developing, manufacturing and commercializing products utilizing its proprietary modified-release drug delivery technology platform. The company is initially focusing on ADHD and has developed three branded product candidates that are XR medications in patient-friendly ODT or liquid suspension dosage forms. In addition, Neos manufactures and markets its generic equivalent of the branded product Tussionex®1, an XR liquid suspension of hydrocodone and chlorpheniramine indicated for the relief of cough and upper respiratory symptoms of a cold.

Osmotica Announces Its Second Late Stage NDA Asset, OS-320 (Osmolex ER), Has Been Awarded Orphan Drug Status by the U.S. Food and Drug Administration

Business Wire: July 22, 2015 – MARIETTA, GA, U.S.A. – Osmotica Pharmaceutical Corp. (privately held), a global specialty pharmaceutical corporation developing best-in-class therapeutics for the treatment of CNS diseases, announced today that the U.S. Food and Drug Administration (FDA) granted orphan drug designation for the treatment of levodopa-induced dyskinesia (LID) for patients with Parkinson’s disease. Osmolex ER, a proprietary drug formulation of amantadine HCl extended release tablets utilizing Osmotica’s patented Osmodex technology platform, represents a novel approach to the treatment of LID for patients with Parkinson’s disease. “Receiving orphan drug designation for Osmolex ER in the treatment of LID for patients with Parkinson’s disease is an important milestone for this clinical development program,” commented Osmotica’s vice president of global clinical development, Dr. Gene Wright. Mark Stacy, M.D., professor of neurology, vice dean for clinical research, Department of Neurology, Duke University School of Medicine, and chair of

the Osmotica’s scientific advisory board also commented, “Osmolex™ ER is a once a day treatment for a highly unmet medical need for Parkinson’s disease patients with dyskinesia; we look forward to seeing this innovative formulation become available to our patients.” Osmotica anticipates filing the NDA for Osmolex in 2016.

The FDA’s office of orphan drug products grants orphan status to support development of medicines for rare disorders defined as diseases that affect fewer than 200,000 people in the United States. Orphan drug designation provides Osmotica with certain benefits, including limited market exclusivity upon regulatory approval when received, and exemption of FDA application fees and tax credits for qualified clinical trials.

In addition to Osmolex ER and a phase 3 trial recently completed for Ontinua ER, a treatment of spasticity in patients with multiple sclerosis, Osmotica’s pipeline contains multiple CNS projects in early stage development. Osmotica is focused on leveraging its proprietary Osmodex™ drug delivery technology to improve the lives of patients with high unmet needs. Osmotica Pharmaceutical and its related companies form an international group of companies with principal operations located in the United States, Argentina, and Hungary.

Acorda Awarded Grant to Study ARCUS® Technology in Respiratory Distress Syndrome

Business Wire: July 22, 2015 – ARDSLEY, NY, U.S.A. – Acorda Therapeutics, Inc. (Nasdaq: ACOR) today announced that the Bill and Melinda Gates Foundation has awarded the company a \$1.4 million grant to support the development of a formulation and delivery system for a dry powder version of lung surfactant, a drug used to treat neonatal respiratory distress syndrome (RDS). The formulation will be based on the company’s proprietary ARCUS technology and will be produced in collaboration with the Massachusetts Institute of Technology (MIT).

RDS is a condition affecting newborns in which fluid collects in the lungs’ air sacs; it most commonly affects infants born prematurely. It can be fatal or lead to severe, chronic health issues caused by a lack of oxygen getting to the baby’s brain and other organs. The syndrome is caused by the infants’ inability to produce enough surfactant, a liquid lining the inside of the lungs. Delivering liquid surfactant to the lungs via intubation is the standard of care. Intubation poses problems in the developing world due to resource and infrastructure limitations, including the need to refrigerate surfactant, access to sterile medical supplies, access to potable water, and a lack of healthcare professionals trained in intubation. This grant will support the development of a portable and easily administered inhaled form of surfactant, which may present a more practical alternative for use in developing areas of the world.

“Using the ARCUS technology to develop an inhaled formulation of surfactant has the potential to expand access to this life-saving treatment in developing countries. ARCUS-formulated medications studied to date have been self-administered and

stored at room temperature; these features have the potential to eliminate some of the barriers that prevent more widespread use of surfactant to treat infants with RDS,” said Rick Batycky, chief technology officer of Acorda Therapeutics. “The ARCUS technology has a wide range of potential applications. With the support of the Gates Foundation, we’re excited to explore this technology to improve health outcomes for infants in areas with constrained healthcare infrastructures.”

“Some of the early research that led to the ARCUS technology was conducted at MIT, so it’s very gratifying to see its continued development,” said Robert Langer, Ph.D., David H. Koch Institute Professor of the Massachusetts Institute of Technology. “We’re excited that it has the potential to help newborns with RDS, where there is a significant unmet medical need.”

ARCUS technology is used in CVT-301, an inhalable form of levodopa being investigated by Acorda in phase 3 trials to treat “off” episodes in people with Parkinson’s disease. It has also been used in formulating CVT-427, a treatment for migraines in preclinical testing. The ARCUS technology has been used to successfully deliver more than one million doses to patients in clinical trials of various products.

Acorda’s proprietary ARCUS technology platform is a dry-powder pulmonary delivery system that has potential applications in multiple disease areas. This platform allows consistent and precise delivery of significantly larger doses of medication than are possible with conventional pulmonary systems. The ARCUS inhaler is breath-actuated, operated by the user putting their lips to the device and simply breathing in.

The ARCUS technology has been used to successfully deliver more than one million doses to patients in clinical trials of various products. CVT-301 is the most advanced drug candidate using the ARCUS technology. Acorda has an extensive patent portfolio relating to CVT-301 and the ARCUS technology, which covers aspects of the formulated drug product, the inhaler, the method of drug delivery, and manufacturing processes for CVT-301.

CVT-301 is being developed as a self-administered, inhaled levodopa therapy for treatment of “off” episodes in Parkinson’s disease. This is an adjunctive therapy to a patient’s individually optimized oral L-dopa regimen. Acorda’s proprietary ARCUS technology provides a precise dose of a dry powder formulation of L-dopa to the lung to enable rapid and predictable absorption. CVT-301 is delivered through a pocket-size, breath-actuated inhaler designed to be patient-friendly. Based on the results of the phase 2b trial, Acorda has initiated a phase 3 clinical trial that is expected to enroll approximately 345 participants across three arms: 50 mg, 35 mg, or placebo. These are the same doses used in the phase 2b study. The primary outcome measure is improvement on the UPDRS III after administration of CVT-301.

More details about the study, including enrollment criteria, can be found at www.acorda.com or <http://clinicaltrials.gov/ct2/show/NCT02240030?term=CVT-301&rank=2>

CVT-427 is an inhaled triptan being investigated for the treatment of acute migraines. The company anticipates beginning a phase 1 clinical program in 2015. CVT-427 utilizes the ARCUS technology platform.

Founded in 1995, Acorda Therapeutics is a biotechnology company focused on developing therapies that restore function and improve the lives of people with neurological disorders.

Acorda markets three FDA-approved therapies, including AMPYRA® (dalfampridine) extended release tablets, 10 mg. The company has one of the leading pipelines in the industry of novel neurological therapies. Acorda is currently developing a number of clinical and preclinical stage therapies. This pipeline addresses a range of disorders including post-stroke walking deficits, Parkinson’s disease, epilepsy, neuropathic pain, heart failure, MS, and spinal cord injury. For more information, please visit the company’s website at www.acorda.com.

Lysogene and Alcyone Lifesciences Enter into a Collaboration for Mucopolysaccharidosis Type IIIA (MPS IIIA)

Business Wire: July 21, 2015 – LOWELL, MA, U.S.A. and PARIS, France – Alcyone Lifesciences, Inc., a leader in neural intervention systems for neurological conditions and targeted drug delivery, and Lysogene, a privately held biotechnology company and leader in recombinant adeno-associated virus (rAAV) based gene therapy for the CNS, have entered into a collaboration. Lysogene and Alcyone Lifesciences will join forces to evaluate the intraparenchymal delivery of Lysogene’s proprietary rAAV to treat patients with mucopolysaccharidosis type IIIA (MPS IIIA), also known as Sanfilippo A, utilizing the Alcyone MEMS Cannula (AMC) targeted delivery platform.

“We are excited about this collaboration. Lysogene is a unique company with incredible science and a strong culture. Karen Aiach and her team are truly impressive. We hope to be part of their success in treating patients with these debilitating conditions,” commented P. J. Anand, founder and chief executive officer of Alcyone Lifesciences.

“Alcyone and Lysogene represent synergy. This is a great opportunity for both companies to forward research in delivering gene therapy to the CNS,” said Karen Aiach, founder and chief executive officer of Lysogene. “Effective therapeutic and optimized delivery is an absolute requirement for successful therapy. This is an excellent match, and I look forward to the outcome of the collaboration,” added Dr. Olivier Danos, cofounder of Lysogene and scientific advisor to Alcyone Lifesciences.

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Dr. Michel Zerah, professor of neurosurgery at Necker Hôpital Enfants Malades, Paris, welcomed the collaboration and stated, “I look forward to working with Lysogene and Alcyone to further expand our research on effective gene therapy delivery to the brain.”

Lysogene’s most advanced product candidate is rAAV vector serotype rh.10 carrying the human N-sulfoglucosamine sulfohydrolase (hSGSH) for the treatment of MPS IIIA. The recently completed phase I/II study in four MPS IIIA children demonstrated that the gene therapy and neurosurgical procedure is safe, well tolerated, and exploratory efficacy profiles are encouraging.

The Alcyone MEMS Cannula (AMC™) targeted delivery system was developed using the company’s proprietary microelectromechanical system (MEMS) technology platform. Without burdening the neurosurgery community with unnecessary additional capital equipment, the AMC can be utilized with any existing commercial imaging and stereotactic system in conjunction with the work-flow friendly clinical use guideline designed by the company’s scientist and neurosurgery advisors. Neurosurgeons can select a target, navigate the AMC precisely to the target, and observe in real time the precision delivery of the therapeutic agent, all under intraprocedural MRI guidance. In addition to the MEMS tip that has dual microchannels, the AMC features a unique patented distal end design that helps prevent reflux or back flow along the cannula shaft, which can be a significant drawback with current devices. The AMC platform device is designed for optimal targeted biodistribution and neurosurgeon’s ease of use.

MPS IIIA presents in early childhood, causing progressive neurodegeneration associated with intractable behavioral problems and developmental regression. Life span is shortened, with death usually occurring in the mid teen years. There is currently no treatment.

Lysogene’s gene therapy is delivered directly to the CNS in one neurosurgical procedure. It is hoped that the delivery of the missing SGSH gene provides a permanent source of functional enzyme in the brain that reverses phenotypic abnormalities of CNS neural cells.

Lysogene is a global biotechnology company, leader in the basic research and clinical development of gene therapy for neurodegenerative disorders. Its mission is to radically improve the health of patients suffering from incurable life threatening conditions by developing AAV vectors that have demonstrated their effectiveness in safely delivering genetic material to the central nervous system. For more information, please visit www.lysogene.com.

Alcyone Lifesciences, based in Lowell, Massachusetts, is a privately held medical device company focused on development of novel treatment modalities for chronic neurological conditions. The company’s patented technology platform is based on a

uniquely engineered amalgamation of microfabrication technologies along with advanced biomedical engineering with core product focus on targeted drug therapy and hydrocephalus. Alcyone’s team of scientists, physicians, and advisers includes recognized leaders in the field of neurology and neurosurgery. For more information, please visit www.alcyonels.com.

Heron Therapeutics Resubmits SUSTOL® New Drug Application to FDA

Business Wire: July 20, 2015 – REDWOOD CITY, CA, U.S.A. – Heron Therapeutics, Inc. (Nasdaq: HRTX), a biotechnology company focused on improving the lives of patients by developing best-in-class medicines that address major unmet medical needs, today announced that it has resubmitted its New Drug Application (NDA) for SUSTOL® (granisetron) injection, extended release, for the prevention of acute and delayed chemotherapy-induced nausea and vomiting (CINV) associated with moderately emetogenic chemotherapy (MEC) or highly emetogenic chemotherapy (HEC) regimens, to the U.S. Food and Drug Administration (FDA). Heron expects confirmation of acceptance from the FDA and a Prescription Drug User Fee Act (PDUFA) goal date within the next few weeks. The company anticipates a six-month review by the FDA.

The NDA filing includes data from the MAGIC study, Heron’s recently completed, multi-center, placebo-controlled, phase 3 study in patients receiving HEC agents. The MAGIC study evaluated the efficacy and safety of SUSTOL as part of a three-drug regimen with the intravenous (IV) neurokinin-1 (NK1) receptor antagonist fosaprepitant and the IV/oral corticosteroid dexamethasone for the prevention of delayed nausea and vomiting in patients receiving HEC. The MAGIC study, which was conducted entirely in the United States using the 2011 ASCO guidelines for classification of emetogenic potential, is the only phase 3 CINV study to date to use the currently recommended, standard-of-care, three-drug regimen for CINV prophylaxis in an HEC population as the comparator: a 5-HT3 receptor antagonist, fosaprepitant, and dexamethasone.

The MAGIC study’s primary endpoint was achieved. Specifically, the percentage of patients who achieved a complete response was significantly higher in the SUSTOL arm compared with the comparator arm ($p = 0.014$). Significant benefit was also observed in the reduction in episodes of nausea, which has the greatest impact on patient quality of life. Data from a previous phase 3 study of more than 1,300 patients, which was previously submitted to the FDA, demonstrated SUSTOL’s efficacy in the prevention of acute and delayed CINV associated with MEC regimens and acute CINV associated with HEC regimens. “The rapid resubmission of the NDA for SUSTOL, the first and only 5-HT3 receptor antagonist with extended-release technology and five-day CINV prevention in both MEC and HEC, is a major milestone for Heron Therapeutics,” commented Barry D. Quart, Pharm.D., chief executive officer of Heron. “We look forward to working closely with the FDA during the SUSTOL NDA review period, as we believe SUSTOL has the potential to improve the lives of patients suffering from CINV

by significantly reducing both nausea and vomiting associated with MEC or HEC regimens.”

SUSTOL® (granisetron) injection, extended release, which utilizes Heron’s proprietary Biochronomer® drug delivery technology, is Heron’s novel, long-acting formulation of granisetron for the prevention of chemotherapy-induced nausea and vomiting (CINV). Granisetron, an FDA-approved 5-hydroxytryptamine type 3 (5-HT3) receptor antagonist, was selected due to its broad use by physicians based on a well-established record of safety and efficacy. SUSTOL has been shown to maintain therapeutic drug levels of granisetron for five days with a single subcutaneous injection. SUSTOL is being developed for the prevention of both acute (day 1 following the administration of chemotherapy agents) and delayed (days 2–5 following the administration of chemotherapy agents) CINV associated with moderately emetogenic chemotherapy (MEC) or highly emetogenic chemotherapy (HEC). While other 5-HT3 antagonists are approved for the prevention of CINV, SUSTOL is the first agent in the class to demonstrate efficacy in reducing the incidence of delayed CINV in patients receiving HEC, a major unmet medical need, in a randomized phase 3 study.

Affecting 70–80% of patients undergoing chemotherapy, CINV is one of the most debilitating side effects of such treatments, often attributed as a leading cause of premature discontinuation of cancer treatment. 5-HT3 receptor antagonists have been shown to be among the most effective and preferred treatments for CINV. However, an unmet medical need exists for patients suffering from CINV during the delayed phase, which occurs on days 2–5 following the administration of chemotherapy agents. Only one 5-HT3 receptor antagonist is approved for the prevention of delayed CINV associated with MEC, and no 5-HT3 receptor antagonists are approved for prevention of delayed CINV associated with HEC.

SUSTOL was the subject of a recently completed, multi-center, placebo-controlled, phase 3 clinical study in patients receiving HEC regimens known as MAGIC. The MAGIC study evaluated the efficacy and safety of SUSTOL as part of a three-drug regimen with the intravenous (IV) neurokinin-1 (NK1) receptor antagonist fosaprepitant and the IV/oral corticosteroid dexamethasone. The MAGIC study, which was conducted entirely in the United States using the 2011 ASCO guidelines for classification of emetogenic potential, is the only phase 3 CINV prophylaxis study in a HEC population performed to date to use the currently recommended, standard-of-care, three-drug regimen as a comparator: a 5-HT3 receptor antagonist,

fosaprepitant, and dexamethasone. The study’s primary endpoint was achieved. Specifically, the percentage of patients who achieved a complete response in the delayed phase was significantly higher in the SUSTOL arm compared with the comparator arm ($p = 0.014$). Heron resubmitted its New Drug Application (NDA) for SUSTOL to the U.S. Food and Drug Administration (FDA) in July 2015. SUSTOL is not approved by the FDA or any other regulatory authority.

Heron Therapeutics, Inc., is a biotechnology company focused on improving the lives of patients by developing best-in-class medicines that address major unmet medical needs. Heron is developing novel, patient-focused solutions that apply its innovative science and technologies to already-approved pharmacological agents. Heron’s goal is to build on therapeutics with well-known pharmacology by improving their tolerability and efficacy as well as broadening their potential field of use. Heron is currently developing four pharmaceutical products for patients suffering from cancer and pain. SUSTOL® is Heron’s injectable, extended-release formulation of granisetron that is being developed for the prevention of both acute and delayed chemotherapy-induced nausea and vomiting (CINV) associated with moderately emetogenic chemotherapy (MEC) or highly emetogenic chemotherapy (HEC). CINV is one of the most debilitating side effects of chemotherapy and is a leading cause of premature discontinuation of cancer treatment. Heron recently reported positive, top-line results from its phase 3 MAGIC study and resubmitted its New Drug Application (NDA) for SUSTOL to the U.S. Food and Drug Administration (FDA) in July 2015. HTX-019, also being developed for the prevention of CINV, has the potential to become the first polysorbate 80-free, intravenous formulation of aprepitant, a neurokinin-1 (NK1) receptor antagonist. Heron intends to file an NDA for HTX-019 using the 505(b)(2) regulatory pathway in the second half of 2016. HTX-011, Heron’s long-acting formulation of the local anesthetic bupivacaine in a fixed-dose combination with the anti-inflammatory meloxicam, is in a phase 2 trial for the prevention of postoperative pain. Heron expects to report results from this trial in the second half of 2015. HTX-003, a long-acting formulation of buprenorphine, is being developed for the potential management of chronic pain and opioid addiction. All of Heron’s product candidates utilize Heron’s innovative science and technology platforms, including its proprietary Biochronomer® drug delivery technology, which can deliver therapeutic levels of a wide range of otherwise short-acting pharmacological agents over a period of days to weeks with a single injection. For more information, visit www.heronx.com. ■

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Calendar of Events

2015

Drug Delivery Australia

Sponsored by CRS
November 19–20
Brisbane, Australia
www.crsaustalia.org

D4 – Devices for Diagnostics and Drug Delivery

Sponsored by CRS
November 25–26
Dunedin, New Zealand
www.nzcrs.org.nz

2016

XI Spanish-Portuguese Conference on Controlled Drug Delivery

Sponsored by CRS
January 21–23
Granada, Spain
www.splc-crs.org

Advances in Technology and Business Potential on New Drug Delivery Systems

Sponsored by CRS
February 23–24
Mumbai, India
www.crsic.org

2016 UKICRS Symposium

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

World Biomaterials Congress 2016

May 17–22
Montreal, Canada
www.wbc2016.org

11th International Symposium on Adjuvants for Agrochemicals (ISAA 2016)

June 20–24
Monterey, CA, U.S.A.
www.isaa2016.org