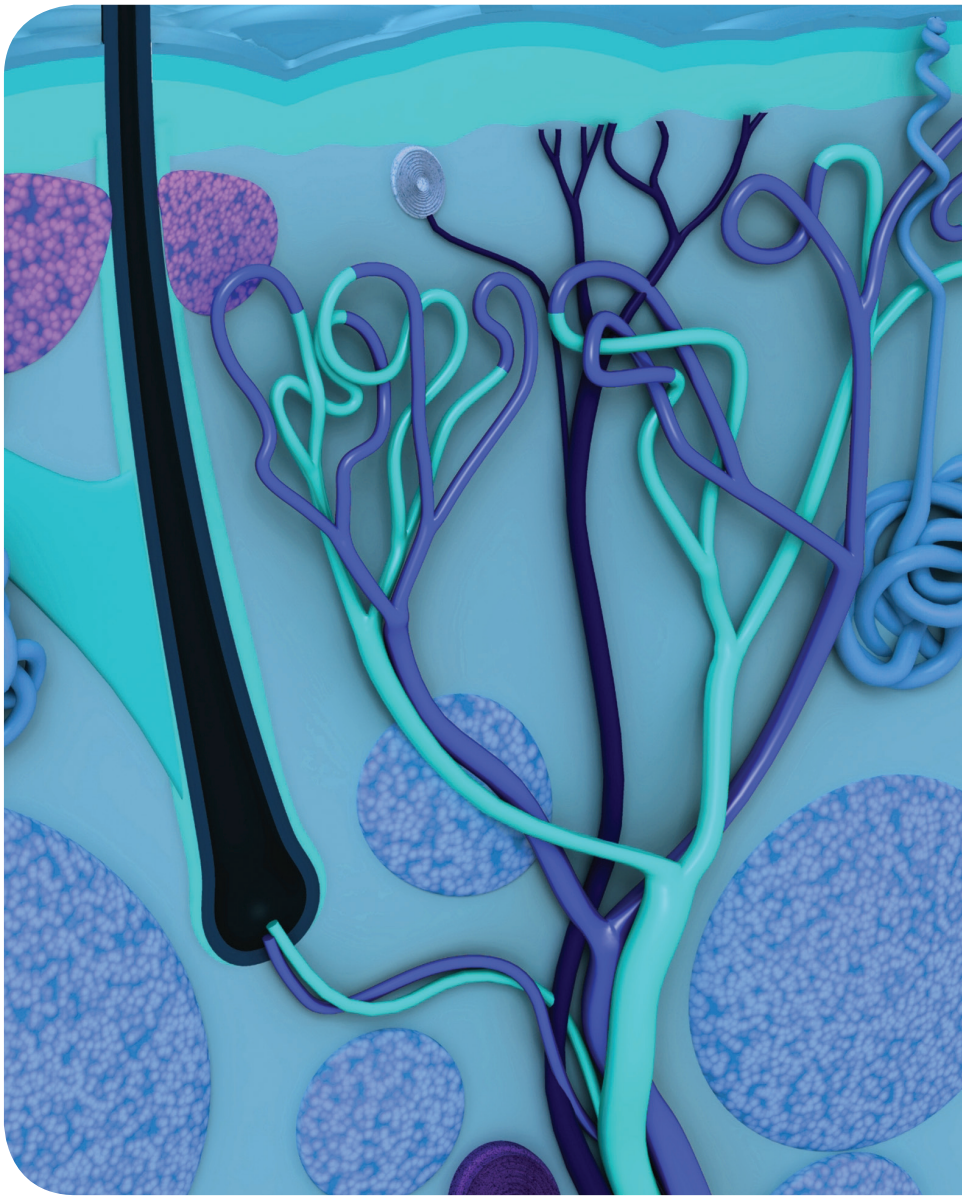
CRS Leading Delivery Science and Technology

Newsletter

A publication of the Controlled Release Society Volume 30 • Number 6 • 2013



What's Inside

18th Annual

DRUG DELIVERY PARTNERSHIPS™

The Only Event that Connects Senior Executives Through Best-In-Class Education and Innovative Technology

January 27-29, 2014
Boca Raton Resort & Club
Boca Raton, FL

Moving Innovation from Concept to Marketable Success

DDP14 is the roadmap to your share of the $224 billion drug delivery market. **Start here.**


2014 KEYNOTE

Driving True Innovation in Life Sciences by Defining and Meeting the Unmet Need

Alfred Mann
Chief Executive Officer and Chairman of the Board
MANNKIND CORPORATION


2014 KEYNOTE

The Future of Drug Delivery Technologies

Fernando Sallés, PhD, CLP
Executive Director, Strategic Licensing & Acquisitions Lead,
Ophthalmics and Drug Delivery Technologies
MERCK RESEARCH LABORATORIES

CRS Leading Delivery Science and Technology

CRS Members SAVE 20%* use code XP1978CRS

NOW EXCLUSIVELY AT DDP14

Jumpstart your next multi-million dollar deal with state-of-the-art one-to-one partnering

powered by partneringONE®

Plus! Human Factors • Connected Health • Informatics • and more!

Register at **www.DDPEvent.com** or call **(888) 670-8200**

*valid after November 15, 2013 and only applicable to the standard registration rate

Charles Frey
Editor

Steven Giannos
Editor

Arlene McDowell
Editor

Bozena Michniak-Kohn
Editor

Yvonne Perrie
Editor

Rod Walker
Editor

CRS Newsletter

Leading Delivery Science and Technology

Vol. 30 • No. 6 • 2013

Table of Contents

Advertisers' Index

Cover image ©SebastianKaulitzki / Shutterstock.com

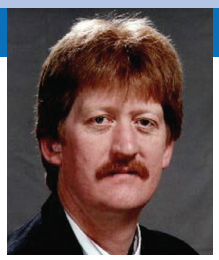
The CRS Newsletter is the official newsletter of the Controlled Release Society. The newsletter is published six times annually, providing scientific and technical information pertinent to the controlled release community and news about society and chapter activities. Members can receive the newsletter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

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

Telephone: +1.651.454.7250
Facsimile: +1.651.454.0766

Visit controlledreleasesociety.org or e-mail crs@scisoc.org on questions about membership, meetings, publications, and services.

Contact dwoodard@scisoc.org for information about exhibiting, advertising or other visibility opportunities.



Roderick B. Walker, Ph.D.
Rhodes University
South Africa

What Is Internationalization?

Like many CRS members, I have a strong personal interest in making CRS a truly international organization, which is vital to our future success.

On the facing page, CRS President Ian Tucker discusses the new International Committee and its initial brief to evaluate and establish how to make the local chapters more effective in terms of their mandate to the parent body and their members. This is in my view a narrow mandate; however, it is a starting point to finding a solution to the challenge of making CRS a truly global or international organization.

The establishment of a local chapter is not in itself internationalization, which should be a process of developing an international dimension to all aspects of the core business of the organization at all levels of that organization. In other words, it is how the local chapters and the broader CRS embrace and seek to share and develop all communities within the CRS umbrella with the common goal of ensuring we are the experts and the first port of call for finding solutions to healthcare and other challenges across the globe through delivery science.

There is a need to facilitate interaction with communities in the developing world that extends beyond an annual meeting and starting a local chapter. The question has been posed, and the answer needs to be found to ensure that CRS in its fifth decade becomes a truly global player that can truly be an international home for all researchers in the field of delivery science. Watch this space for developments in this area!

The content of the newsletter has once again brought some interesting topics to the members of the society, and I am sure that you will all learn something new as topics such as animal models for obsessive compulsive disorders, dissolution, response surface methodology, design of experiments, and subcutaneous delivery of proteins are reported. The feedback from the activities of the Young Scientist Committee makes for interesting reading, and they have certainly been busy. The success of the journal of *Drug Delivery and Translational Research* is unquestionable, and the updates in this issue of the newsletter are enlightening. The reflections of Tram Dang, the recipient of the Sung Wan Kim Postdoctoral Fellowship, provide insight into the value that creating such opportunities for up-and-coming scientists brings to their development.

All that remains is for me to wish you all well over the holiday season. Do enjoy the time with your friends and family, and come back refreshed in 2014 to advance delivery science further. ■

Ian Tucker
University of Otago
Dunedin, New Zealand

Creating the Future

In my previous letter, I said that I had asked chairs of CRS committees and the presidents of local chapters what questions are on the lips of CRS members. One question was: "What is my vision of where delivery science and technology will be heading in the next 10 years, and what will be the role of the CRS in supporting and encouraging these developments?" You might reasonably say that my crystal ball is as cloudy and fuzzy as any other CRS member's, and you would be right—so here is my philosophy rather than my vision.

To some degree at least, we can and do rationally create the future, but the complexity of possible interactions between scientific disciplines and collaborators means we don't have a road map. It is more a compass direction. Or, it is like Adam Smith's "invisible hand of the market," where the efforts and interplay of individuals, driven not necessarily by self-interest but by scientific curiosity, lead to the development of ever-better delivery technologies that benefit society. CRS is not an "invisible hand" in this but rather a highly visible and central influence in informing, supporting, and encouraging delivery science and technology.

Leading the Way in Delivery Science and Technology
The BSA is working hard on identifying current trends and research in the fundamental sciences that will underpin our science and technology. I look forward to sharing the BSA's report with the membership. In thinking about the fundamental science, I am reminded that October is Nobel Prize month, and it is readily apparent how the science of this year's laureates is informing our current delivery science and technology.

The Nobel Prize in Physiology or Medicine 2013 was awarded to James E. Rothman, Randy W. Schekman, and Thomas C. Südhof for their work on the molecular principles that govern how vesicles deliver their cargo to the right place at the right time in the cell. Schekman elucidated the set of genes required for vesicle trafficking; Rothman unravelled the protein machinery that enables vesicles to fuse with their specific targets; and Südhof elucidated signals to instruct vesicles to release the cargo when required. Using a phrase that could have come from CRS, one press release reported: "timing and location are everything." Since most of their work was published in the 1970s, 1980s, and 1990s, this material is now standard in cell-biology textbooks, but it is fundamental to the research of many of our members who seek to understand how to deliver bioactives using nanosystems.

The Nobel Prize in Chemistry 2013 was awarded to Martin Karplus, Michael Levitt, and Arieh Warshel for their work, which started in the 1970s, on modelling molecular processes using quantum physics calculations at reaction sites but classical physics approaches where possible, to reduce the prodigious computing time required even on supercomputers. Levitt writes about his dream to simulate a living organism on a molecular level. I know that some of our members are using molecular modelling to understand interaction of targeted nanoparticles with cell surface receptors. What is the fundamental research being done at present by the Nobel laureates of the 2020s?

Internationalisation
Recently, I had the privilege to visit one of the leading research universities in Malaysia, a country of 30 million people, which is making huge investments in education. Nearby countries include Indonesia, the fourth largest country in the world based on population (200 million), and Singapore (5.4 million). Other Southeast Asian countries include Vietnam (89 million), Thailand (66 million), Cambodia (15 million), Laos (6.6 million), and the Philippines (98 million), giving a combined population of about 500 million or 7% of the world's population. Perhaps surprisingly, CRS does not have a local chapter in this region, a region that is growing rapidly in terms of education and research and that has an eye to some knowledge-based industries. As an organisation, we have both an opportunity and a responsibility to serve delivery scientists in this region, as in other regions. In this regard, our International Committee is charged with making recommendations of how chapters should be linked to the parent body, the Finance Committee is doing a feasibility study for an annual meeting in a non-European non-U.S. venue, the Satellite Meeting (& workshop) Committee is investigating running a satellite meeting in Asia, and there are several other work programs on issues that underpin these potential developments. I look forward to being able to announce these developments in due course.

CRS is in its fifth decade and is an organisation that is going places. I expect people will want to join our organisation not only to access the member services and the opportunities for sharing and promoting their science and technology but also for the global networking opportunities CRS provides. Nowadays, people travel for health tourism. I think the CRS membership card can be a passport for knowledge-sharing tourism.

Ian Tucker ■

2014 CRS Annual Meeting Plenary Speakers Announced

This year's program, "Translation of Delivery Technology: Innovation to Commercialization," will offer an exceptional opportunity to connect with a diverse audience in the discovery, development, and delivery science continuum. The 2014 CRS Annual Meeting Program Committee has invited an impressive group of plenary speakers, all of whom are working on the cutting edge of science, translating scientific advances into novel innovations.

This year's meeting also offers an excellent opportunity for those interested in presenting their research to a diverse and expansive audience. The call for papers for the 2014 CRS Annual Meeting opens in November 2013 and runs through January 23, 2014.

David A. Edwards

David A. Edwards is a pioneer of healthcare innovations that are at the crossroads of delivery science and contemporary design. The Professor of the Practice of Idea Translation at Harvard University and founding faculty member of the Wyss Institute, David's early work in applied math and drug delivery led to advances in transdermal, cellular, and pulmonary drug and vaccine delivery innovations.

More recently, David has pursued his innovations at Le Laboratoire, a public cultural center in Paris. Innovations include WikiFoods, functionally nutritious food forms designed around natural fruit structures; AeroLife, a line of functional nutrition products delivered into the mouth for ingestion via the air; and the oPhone, a portable convenient system for delivering complex olfactory messaging via global information networks.

David has started the companies Advanced Inhalation Research, Pulmatrix, MEND, LabStore, Quantum Designs, and Vapor Communications and has won various awards including election to the U.S. and French National Academies of Engineering. For WikiFoods and AeroLife, David won separate international awards for best global innovation of the year at international food conferences in 2012 and 2013. He is also a three-time recipient of the Ebert Prize of the American Pharmaceutical Association (1996, 1997, 1999) and the winner of various national and international awards including the Theodor Herzl Award of the Jerusalem Fund and the Municipality of Jerusalem.

Chad Mirkin

Chad Mirkin is the director of the International Institute for Nanotechnology and the George B. Rathmann Professor of Chemistry, Chemical and Biological Engineering, Biomedical Engineering, Materials Science and Engineering, and Medicine at Northwestern University, U.S.A. He is a world-renowned nanoscience expert who is known for his development of nanoparticle-based biodetection schemes, the invention of dip-pen nanolithography, and contributions to supramolecular chemistry.

He has authored over 550 manuscripts, is an inventor on over 900 patent applications worldwide (242 issued), and has received over 80 awards. He is a member of the President's Council of Advisors on Science and Technology (Obama administration); one of only 12 scientists, engineers, and medical doctors to be elected to all three U.S. national academies; and the founder of four companies: Nanosphere, NanoInk, AuraSense, and AuraSense Therapeutics, which are commercializing nanotechnology applications in the life science and semiconductor industries.

David W. Grainger

David W. Grainger is a university distinguished professor and chair of the Department of Pharmaceutics and Pharmaceutical Chemistry and a professor of Bioengineering at the University of Utah, U.S.A. Grainger's research focuses on improving implanted medical device performance using drug delivery; methods to deliver therapeutic proteins, nucleic acids, and live vaccines; nanomaterials interactions with human tissues; low-infection biomaterials; and microarray-based diagnostic devices.

Grainger's expertise extends to surface analysis of biomedical interfaces and nanomaterials. He is an internationally recognized expert in perfluorinated thin films and biomaterials. Grainger has helped found three biomedical technology companies, sits on the scientific advisory boards for four biomedical companies, and actively consults with biomedical industries. ■

41st Annual Meeting & Exposition of the Controlled Release Society

July 13–16, 2014
The Hilton Chicago
Chicago, IL, U.S.A.

TRANSLATION
of Delivery Technology:
Innovation to Commercialization

Call for papers is open November 2013 through January 23, 2014.

Scientific Program Topics

Advances in Drug Delivery to the Eye
Advances in Drug Delivery to the Lung
Advances in Process Engineering—New Methods for the Production of Particles, Capsules, and Coatings
Advances in RNA and DNA Delivery
Breakthrough Technologies
Cells as Delivery Vehicles
Controlled Release Applications in Food, Feed, and Beverages
Controlled Release of Actives in Consumer Products
Evaluation and Characterization of Controlled Release Products and Production Processes
Innovations in Micro- and Nano-Based Delivery
Innovations in Oral Drug Delivery
Intracellular Delivery of Nucleic Acids and Proteins
Nanoparticle-Based Delivery to the Brain
Nanoparticles in Tumor Treatment
Novel Developments in Formulation, Analytical Chemistry, and Processing in Animal Health and Preclinical Sciences
Overcoming Barriers in the GI Tract
Overcoming Biological Barriers
Predictive Animal Models for Assessing Long-Acting Formulations for Human and Animal Health and Their Challenges
Proteins, Peptides, and Vaccines
Transdermal Delivery

Mini-Symposia Topics

Advancements to Develop and Deliver Biologics
Cancer Epigenetics, Epigenetic Drugs, and Delivery
Individualized Medicine and Theranostics
Interspecies Clinical Pharmacology Dosing Concepts
Micro- and Nano-Encapsulation: From Innovation to Commercialization

controlledreleasesociety.org/meetings/annual

CRS Webcasts – Access the Benefits of Membership in CRS

NOW AVAILABLE!

Webcasts of the 2013 CRS Annual Meeting in Hawaii—available online to CRS members and annual meeting attendees.

Access more than 120 webcasts, including presentations from the 2009–2012 CRS Annual Meetings, as a benefit of your membership in CRS. These multimedia presentations combine both audio and video via streaming media technology on a broad range of topics. Now you can draw on the vast knowledge of CRS members and experts in the field through this widely accessible platform whenever it's most convenient for you.

Online at controlledreleasesociety.org/Webcasts

Investigation of the Dissolution Behavior of Eudragit® RL/L-55 Blends Using a Response Surface Methodology

Robert Wulff and Claudia S. Leopold
University of Hamburg, Department of Chemistry, Division of Pharmaceutical Technology, Hamburg, Germany

Introduction

Getting perfect control over drug release from solid dosage forms is one of the major challenges in pharmaceutical sciences. Modified drug release from coated solid dosage forms may be achieved by taking advantage of electrostatic interactions between countercharged polymers. These interpolyelectrolyte complexes (IPECs) are a great tool for the design of new drug release profiles with well-known excipients.[1] For a pH-dependent drug release, a cationic polymer (Eudragit® RL) and an enteric polymer (Eudragit® L-55) may be combined.[1,2]

Response surface methods (RSMs) are design of experiment (DoE) techniques that have been widely used in the past to analyze and optimize pharmaceutical formulations.[3,4] RSMs attempt to model functional relationships between variables and responses. From the response surfaces, sweet spots and saddle points can be determined.

The objective of this work was to characterize the dissolution behavior of blends of Eudragit® RL and L-55.

Methods and Materials

Eudragit® RL and L-55 were dissolved at various ratios in an organic solvent. Triethyl citrate and talc were added. Theophylline pellets were coated in a fluidized bed coater (Solidlab 1, Bosch, Germany) and post-dried at 40°C for 24 h.

Four different RL/L-55 blends with RL fractions of 80.0, 88.9, 92.3, and 94.1%, respectively, were prepared. Three coating levels leading to 2.5, 5.0, and 10.0% weight gain, respectively, were applied.

Dissolution experiments were performed in phosphate buffer (pH 6.8) and hydrochloric acid (pH 1.2), respectively, using a paddle apparatus (n = 3). Dissolution profiles were recorded spectrophotometrically at 272 nm.

For DoE, the Design Expert® software version 8.0.7.1 (Stat-Ease, Minneapolis, MN, U.S.A.) was used.

An in-house written Microsoft Excel script served as a tool to fit the release profiles to the Weibull function.

Results and Discussion

Theophylline release from pellets coated with the different polymer blends (10% weight gain, referring to the polymer weight) is shown in Figure 1.

Addition of Eudragit® L-55 to the blend resulted in a prolonged release in comparison to the plain Eudragit® RL coating (dashed line) and in S-shaped release profiles. The effect was more pronounced in phosphate buffer. To get further information on the release mechanism, more dissolution tests were performed. Theophylline pellets with different coating thicknesses and

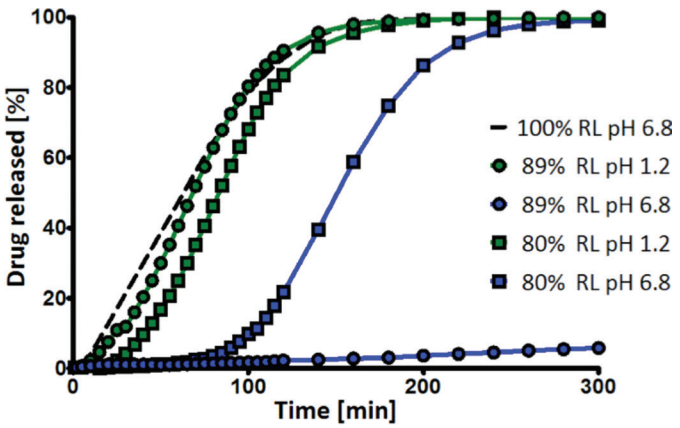


Figure 1. *Theophylline release from coated pellets in HCl, pH 1.2, and phosphate buffer, pH 6.8 (means ± SD, n = 3).*

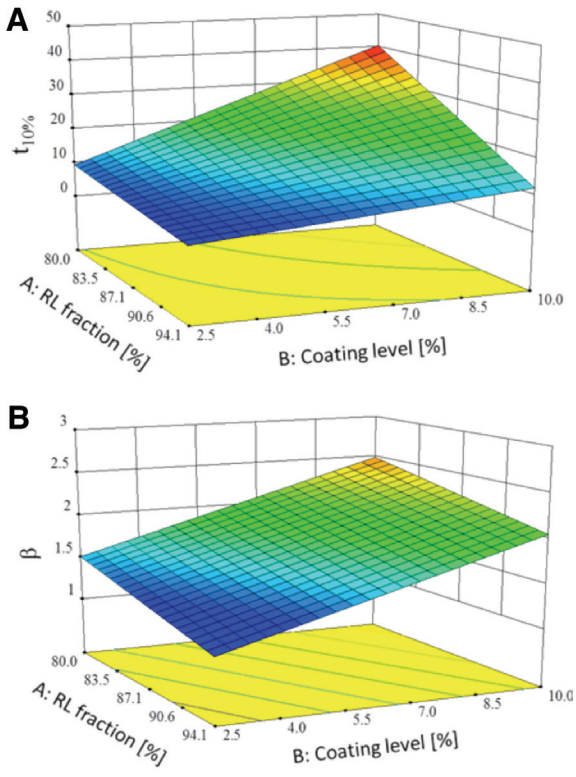


Figure 2. *Effects of RL fraction and coating level in hydrochloric acid pH 1.2 on $t_{10\%}$ (A) and on β (B).*

polymer ratios were tested. The results were fitted to the Weibull equation (equation 1) because of the sigmoidal shape of the release curves.

$$M_t = M_\infty \left[1 - \exp\left(\frac{t - t_0}{t_d} \right)^\beta \right] \qquad \text{(Eq. 1)}$$

M_t = theophylline released (%) at time point t
M_∞ = theophylline released (%) at infinite time
t_0 = lag time of dissolution (min)
β = shape parameter
t_d = time point of 63.2% drug release (min)

A two-factor historical data design was performed. The weight of the applied coating and the different polymer blends served as levels (Eudragit® RL fraction [A] and coating level [B]). Responses were the time point of 10% theophylline release ($t_{10\%}$) and the shape parameter β. The data corresponding to the different dissolution media were analyzed in separate experiments.

In general, theophylline release occurred faster in hydrochloric acid than in phosphate buffer. The shape parameter β varied between 1.02 and 4.21. For the $t_{10\%}$ value, time points between 3.5 and 473.7 min were determined. The effects of the Eudragit® RL fraction and the coating level on the $t_{10\%}$ value in hydrochloric acid are shown in Figure 2A.

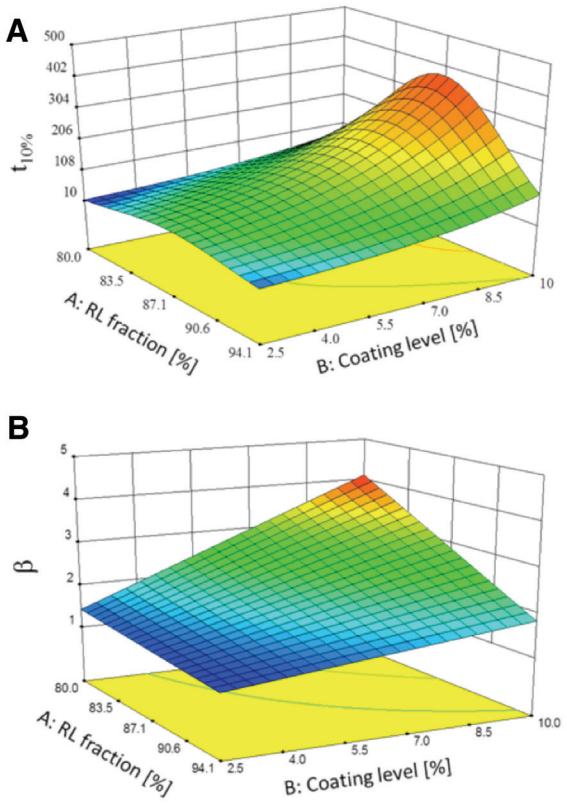


Figure 3. *Effects of RL fraction and coating level in phosphate buffer pH 6.8 on $t_{10\%}$ (A) and on β (B).*

An increase of the coating level and a simultaneous decrease of the Eudragit® RL fraction led to an increase of the $t_{10\%}$ value. In addition, an interaction of the two factors was observed, leading to an even greater increase of the $t_{10\%}$ values.

The shape parameter β also increased with increasing factor values, but in contrast to the $t_{10\%}$ value, the response surface of β did not show any factor interactions (Figure 2B).

In phosphate buffer, a significant change in drug release was observed (Figure 3A). Instead of an increase of $t_{10\%}$ with a maximum at 10% coating level and 80% Eudragit® RL fraction, the maximum of $t_{10\%}$ was located at a fraction of 88.9% RL. Thus, an increase in coating level led to a slower drug release. However, the effect was predominantly influenced by the RL fraction.

For the shape parameter β, a two-factor interaction led to maximum values at the highest coating level and the lowest RL fraction (Figure 3B). Here, in contrast to drug release in hydrochloric acid, the two-factor interaction resulted in an overproportional increase of β, with a maximum value of about 4.

The observed difference regarding the two dissolution media might be explained by the more pronounced dissociation of Eudragit® L-55 at pH 6.8 and therefore stronger electrostatic interactions between the polymers.

These interactions alter the shape of the drug release curves, resulting in a more sigmoidal profile, and decrease the drug release rate, probably by different mechanisms. The clarification of these mechanisms is currently under investigation.

Conclusion

The shape parameter β and the drug release rate are both influenced by the coating level and, even more predominantly, by the ratio of the cationic and the enteric polymer. This tendency is more pronounced at higher pH values and can be explained by a stronger dissociation of Eudragit® L-55 and thus resulting electrostatic interactions.

References

1. Moustafine, R. Interpolymer combinations of chemically complementary grades of Eudragit copolymers: A new direction in the design of peroral solid dosage forms of drug delivery systems with controlled release (review), Pharm. Chem. J. 45: 285-295 (2011).
2. Gallardo, D. Controlled release solid dosage forms using combinations of (meth)acrylate copolymers, Pharm. Dev. Technol. 13: 413-423 (2008).
3. Dawoodhai, S. Optimization of tablet formulations containing talc, Drug Dev. Ind. Pharm. 17: 1343-1371 (1991).
4. Bezerra, M. A. Response surface methodology (RSM) as a tool for optimization in analytical chemistry, Talanta 76: 965-977 (2008). ■

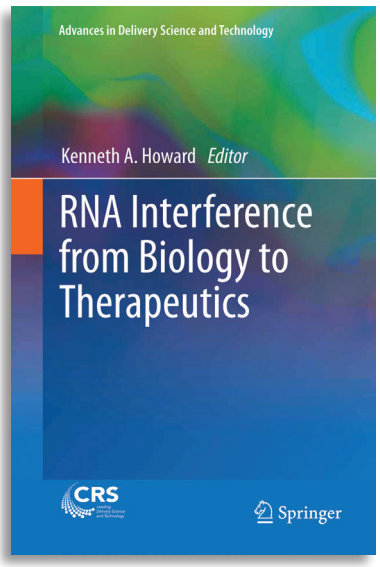
CRS Advances in Delivery Science and Technology Book Series

CRS Leading Delivery Science and Technology

FEATURED TITLE

RNA Interference from Biology to Therapeutics

Edited by Kenneth A. Howard



Key players and shapers in the fields of RNAi and delivery science have been assembled in a single volume to produce a truly unique interdisciplinary text, making it a "must read" for both students and experts in, and at the interface of, RNAi, pharmaceutical science, and medicine. An attractive feature is the "future perspectives" section within each chapter that allows global leaders the opportunity to express their views on the direction the field is moving.

2013, 1st Edition, XV, hardcover, 512 pages;
ISBN 978-1-4614-4743-6

CRS members save 25% on all purchases.

CRS members qualify for a 25% discount on all books in the *Advances in Delivery Science and Technology* series from CRS, along with all Springer book titles if you purchase through Springer's online site and use the exclusive CRS member discount token when ordering. CRS members must sign in to the CRS site to gain access to the discount token before ordering at the Springer site.

controlledreleasesociety.org

#8732-11/2013

Recombinant Human Hyaluronidase PH20 (rHuPH20) Facilitated Subcutaneous Delivery of Proteins in Nonclinical Models

David W. Kang,[1,2] Tara A. Nekoroski,[1] Marie A. Printz,[1] Carl K. Hoh,[3] David R. Vera,[3] James F. Skipper,[1] Adrian V. Radi,[1] Curtis B. Thompson,[1] Monica L. Zepeda,[1] and Daniel C. Maneval[1]

Introduction

Subcutaneous (SC) delivery of therapeutic proteins is an alternative to the traditional intravenous (IV) route of administration. It allows for less invasive delivery with key advantages, such as reduced incidence of systemic adverse effects and the ability to self-administer at home.[1,2] However, disadvantages of current SC administration include volume limitations, reduced flow rates, induration, and other potential adverse infusion site reactions. Recombinant human hyaluronidase PH20 (rHuPH20) has been shown to facilitate SC delivery of therapeutic proteins by improving local dispersion and systemic absorption. rHuPH20 allows for larger volumes to be delivered at a single site and shortens SC infusion times, while reducing the incidence of local and systemic adverse effects.[3,4]

rHuPH20 is a recombinant, soluble form of the naturally occurring human hyaluronidase enzyme that transiently and locally degrades the substrate, hyaluronan, in the extracellular matrix. The degradation of hyaluronan temporarily reduces the viscosity of the "gel-like" phase of the SC extracellular matrix, allowing enhanced dispersion and systemic absorption of drugs delivered subcutaneously.

A series of nonclinical studies was conducted to evaluate the effects of rHuPH20 facilitated delivery. Immunoglobulin G (IgG) was used as a representative therapeutic protein and delivered subcutaneously into miniature pigs (minipigs). The Yucatan minipig was selected as the nonclinical model because of its similarity in morphological and physiological skin characteristics when compared with humans,[5] including similarity in thickness and tight attachment to the subcutaneous tissue.[6] Quantitative endpoints of the studies included measurements of local infusion pressure, positron emission tomography (PET) imaging to measure volumetric dispersion and local clearance, and pharmacokinetic (PK) analysis to assess changes in systemic absorption.

Experimental Methods

Nonclinical studies were approved by institutional animal care and use committees, and animals were anesthetized with isoflurane gas prior to and during SC infusions.

Assessment of Local Infusion Pressures

Human IgG was reconstituted to a final 15% solution and mixed with vehicle or 2,000 U/mL of rHuPH20. IgG (20 mL) ± rHuPH20 was infused into the abdominal region of anesthetized minipigs (S&S Farms), at a flow rate of 2 mL/min via an 18-gauge infusion set. A large-bore infusion set was used to minimize the resistance from the hardware, allowing the measured pressure to reflect the tissue pressure at the local infusion site. Infusion pressure was measured using an in-line pressure transducer (Utah Medical Products) located between the syringe and needle. A syringe pump (KD Scientific) was used to deliver the 20 mL volume, while "real-time" pressure measurements were recorded using a data acquisition unit (AD Instruments).

Assessment of Local Subcutaneous Volumetric Dispersion and Clearance by PET Imaging

Ibritumomab tiuxetan (Zevalin®, Spectrum Pharmaceuticals) was radiolabeled by chelating radioactive gallium to the tiuxetan (DTPA) moieties of the antibody conjugate. Gallium-68 ($t_{½}$ = 68 min) was obtained by eluting a radio-isotopic generator (IGG100-10M, Eckert & Ziegler). Zevalin® (0.10 mL) was added to produce a stock solution of 0.32 mg/mL. A portion (0.10 mL) of this solution was combined with 1.0 mL of generator eluate and permitted to stand at room temperature for at least 10 min. Instant thin layer chromatography demonstrated radiochemical purity in excess of 97%. Human IgG was reconstituted (10% w/v) and mixed with vehicle or 2,000 U/mL of rHuPH20. IgG (15 mL) ± rHuPH20 was mixed with 1 mL of radio-labeled Zevalin®. The final control and test solutions (10 mL) were simultaneously injected (10 mL/min) subcutaneously into the abdomen of an anesthetized minipig that was positioned in a PET scanner (Exact HR+, Siemens). Emission scan in dynamic mode began at onset of injections in a 2D acquisition mode with the septa extended forward. A 12 min transmission scan was started immediately following the emission scan and used for quantitative attenuation correction with the scanner's OSEM iterative image reconstruction. The reconstructed transaxial images were analyzed using custom software (Exelis). Two rectangular box-shaped volumes of interest (VOIs), each of the same size and shape (32,708 voxels, 934 cm^3) were defined encompassing the two infusion sites. The size of the VOI was to include the initial injected radioactivity and subsequent distribution.

PK Analysis of Human IgG Absorption Following Subcutaneous Administration

Human IgG was reconstituted to a final 10% solution and mixed with vehicle or 2,000 U/mL of rHuPH20. Anesthetized minipigs were dosed subcutaneously in the abdominal region (10 mL of

[1] Halozyme Therapeutics, Inc., San Diego, CA, U.S.A.
[2] Corresponding author. Halozyme Therapeutics, Inc., 11388 Sorrento Valley Road, San Diego, CA 92121, U.S.A. Phone: 858-794-8889. E-mail: dkang@halozyme.com.
[3] University of California at San Diego, Department of Radiology, La Jolla, CA, U.S.A.

Scientifically Speaking Kang continued on page 10

Scientifically Speaking Kang continued from page 9

IgG ± rHuPH20) at a flow rate of 4 mL/min. Plasma specimens were collected predose and at defined intervals after dosing. A sandwich format ELISA was used to measure concentrations of human IgG. Standards, controls, and test samples were incubated with unlabeled AffiniPure F(ab′)$_2$ fragment goat anti-human IgG immobilized on a microtiter plate, and detected with a goat HRP-conjugated anti-human IgG + TMB. PK parameters were generated by analyses of time versus concentration data using ADAPT5 PK software (USC Biomedical Simulation Resource).

Results and Discussion

Assessment of Infusion Pressures

Control infusions of 15% IgG alone produced an overall mean local infusion pressure of 83.1 mmHg throughout the course of the 20 mL SC infusion, while the addition of rHuPH20 significantly reduced mean pressure to 23.3 mmHg (Figure 1; $p < 0.05$). This reduction in local tissue pressure suggests that rHuPH20 resulted in greater local dispersion and less local IgG retention at the infusion site.

Assessment of Local Subcutaneous Volumetric Dispersion and Clearance by PET Imaging

rHuPH20-facilitated SC infusions of 10% IgG resulted in a computed dispersion volume of 1,058 voxels at 25 min postinfusion, while SC infusions of IgG alone resulted in a slightly reduced dispersion volume (954 voxels) at the same time point. At 126 min postinfusion, SC infusions of IgG alone had minimal change in local dispersion or clearance (1,026 voxels). In contrast, SC infusions with rHuPH20 resulted in a nearly 50% reduction in volume (544 voxels) at the same time point (Figures 2–3). The PET results are consistent with the infusion pressure findings and indicate that rHuPH20 improves SC dispersion of IgG and facilitates greater clearance from the infusion site.

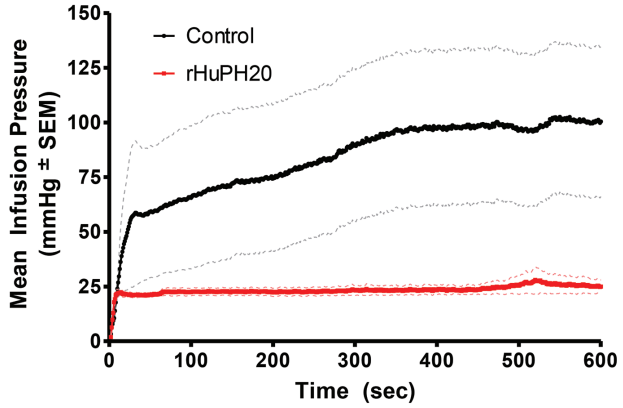


Figure 1. *rHuPH20 decreased infusion/interstitial pressure during SC administration of IgG (n = 8).*

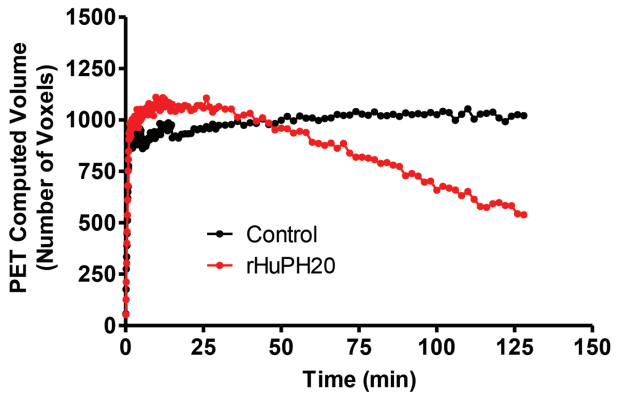


Figure 2. *rHuPH20 increased local volumetric dispersion and clearance after SC administration of IgG.*

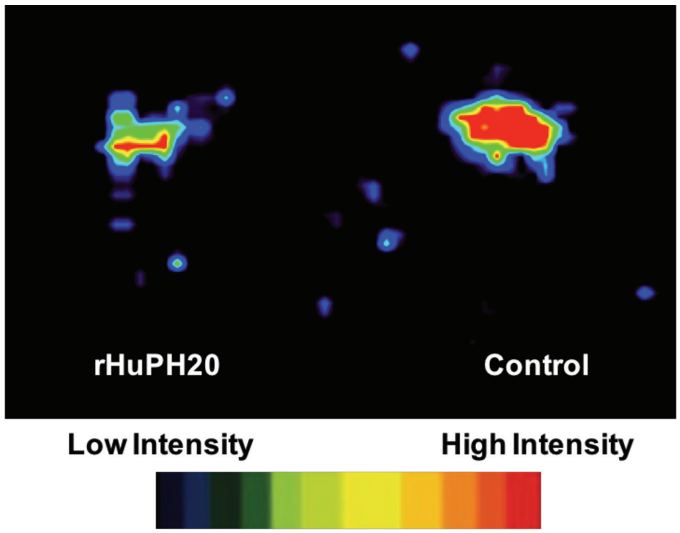


Figure 3. *Transaxial PET imaging demonstrated rHuPH20 effect on IgG dispersion and subsequent infusion site clearance 2 h postinfusion of IgG.*

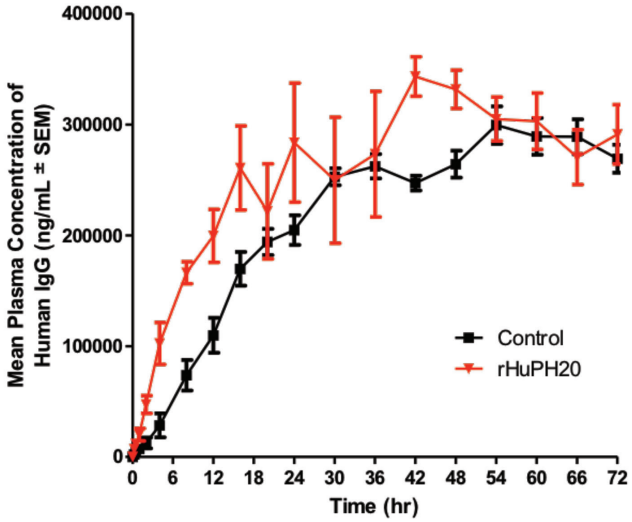


Figure 4. *rHuPH20 increased rate of systemic absorption of IgG following SC administration in pigs (n = 5).*

Table 1. Pharmacokinetic summary.

Parameter	Control	rHuPH20
t_{max} (h ± SD)	66 ± 9	43 ± 20
C_{max} (µg/mL ± SD)	310 ± 31	371 ± 36
K_a (h^{-1} ± SD)	0.028 ± 0.029	0.062 ± 0.060

PK Analysis of Human IgG Absorption Following Subcutaneous Administration

Plasma samples were collected at defined time intervals after SC dosing, and plasma was analyzed for human IgG via ELISA. PK analysis indicated the most significant changes in absorption were observed within the first 12 h. Infusions of 10% IgG alone resulted in a t_{max} of 66 h and a C_{max} of 310 µg/mL. In contrast, rHuPH20 facilitated infusions reduced the t_{max} to 43 h, while increasing C_{max} to 371 µg/mL (Figure 4 and Table 1).

Summary and Conclusion

The miniature swine was used as a preclinical model to assess the effect of rHuPH20 on SC infusions of human IgG. Multiple measurement techniques (local infusion pressure, PET imaging, and PK analysis) were used to provide quantitative endpoints that characterized the effects of the enzyme. rHuPH20 significantly reduced local infusion pressures, enabling a higher dose of IgG to be delivered in a shorter time. Additionally, rHuPH20 increased local volumetric dispersion and local infusion site clearance of 10% IgG as measured by quantitative PET imaging. Lastly, rHuPH20 improved systemic absorption of IgG, as measured by a reduction in t_{max} and increase in C_{max}.

Taken together, these results demonstrate that rHuPH20 facilitates rapid SC administration and improves the absorption of large volumes of therapeutic protein solutions at a single infusion site. These attributes provide a method of delivery that is an attractive alternative to IV administration.

Acknowledgement

The authors thank Ghia Bacani, Max Bersabe, Jacqueline Corbeil, Christopher Davis, Salman Farshchi-Heydari, Michael Jorge, Brad Lowery, Genaro Ronquillo, Xenometrics, and Intertek for their assistance with these studies.

References

1. Gardulf, A. Immunoglobulin treatment for primary antibody deficiencies, Biodrugs 21(2): 105-116 (2007).
2. Kittner, JM, Grimbacher, B, Wulff, W, Jäger, B, Schmidt, RE. Patients' attitude to subcutaneous immunoglobulin substitution as home therapy, J. Clin. Immunol. 26(4): 400-405 (2006).
3. Kang, DW, Jadin, LM, Nekoroski, TA, Drake, FH, Zepeda, ML. Recombinant human hyaluronidase PH20 (rHuPH20) facilitates subcutaneous infusions of large volumes of immunoglobulin in a swine model, J. Drug Del. Trans. Res. 2(4): 254-264 (2012).
4. Misbah, S, Sturzenegger, MH, Borte, M, Shapiro, RS, Wasserman, RL, Berger, M, Ochs, HD. Subcutaneous immunoglobulin: Opportunities and outlook, Clin. Exp. Immunol. 158(Suppl. 1): 51-59 (2009).
5. Mahl, JA, Vogel, BE, Court, M, Kolopp, M, Roman, D, Nogués, V. The minipig in dermatotoxicology: Methods and challenges, Exp. Toxicol. Pathol. 57(5-6): 341-345 (2006).
6. Nunoya, T, Shibuya, K, Saitoh, T, Yazawa, H, Nakamura, K, Baba, Y, Hirai, T. Use of miniature pig for biomedical research, with reference to toxicologic studies, J. Toxicol. Pathol. 20: 125-132 (2007). ■

The Application of Geoclock™ Technology to Address an Unmet Medical Need: The Management of Nocturnal Hypoglycemia

Hypoglycemia in Type 1 Diabetes Mellitus
For many patients with type 1 diabetes mellitus (T1DM), the immediate threat of sudden incapacitation and death as a result of hypoglycemia (low blood glucose) often leads them to slightly underdose their insulin, despite the fact that the consequential hyperglycemia (high blood glucose) can result in diabetic complications and a reduced longer-term quality of life.[1]

Hypoglycemia can manifest as lethargy, depression, or seizures but can be severe enough to lead to coma or even death. Nocturnal hypoglycemia (NH) is a particular concern, because when patients are sleeping they have reduced awareness, so the symptoms often go unrecognized. NH frequently occurs between 1 a.m. and 5 a.m.; up to 15% of diabetics with NH require intensive assistance, and 9% have to be hospitalized. Two to four percent of cases of "death in bed" in T1DM patients are attributed to NH. Currently, the only mitigation is a bedtime snack, self-monitoring of the blood glucose, or changes to the insulin regime, although the new longer-acting insulins do not seem to remove the risk of NH in T1DM.

The Management of NH: An Unmet Medical Need
The risk of NH is an important factor in the management of patients with T1DM. A simple means of reducing hypoglycemic risk without trade-offs on glycemic control, weight gain, cardiovascular risk, and adverse symptoms would be a major advance.

Skyepharma identified the unmet medical need for a treatment for NH that could be taken at bedtime and that would reliably raise blood glucose levels during the critical period from 1 a.m. to 5 a.m. without causing morning hyperglycemia or affecting overall metabolic control.

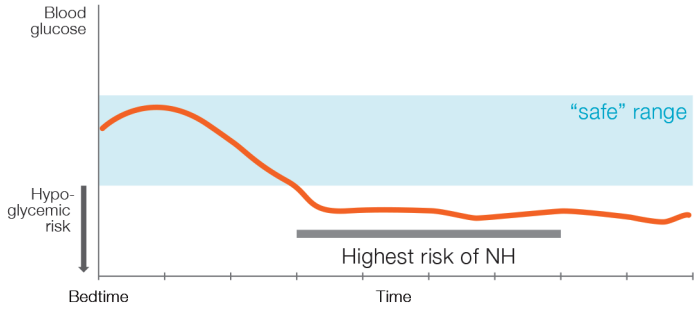
Skyepharma formulated SKP-1052 with an established active ingredient using its Geoclock™ chronotherapy (see box) so that the drug would be reliably released over several hours with a predictable lag time of 2 hours after bedtime dosing. The drug stimulates glycogenolysis (the breakdown of glycogen stores) and gluconeogenesis (synthesis of glucose from noncarbohydrate carbon substrates) and results in an increase of the blood glucose between 1 a.m. and 5 a.m. A comparable immediate release formulation given at bedtime would deliver the dose too early, leaving no protection during the critical period. Only a chrono technology like Geoclock™ is able to deliver the drug at the desired time.

[1] Green, L, Feher, M, Catalan, J. Fears and phobias in people with diabetes, Diabetes Metab. Res. 16: 287-293 (2000).

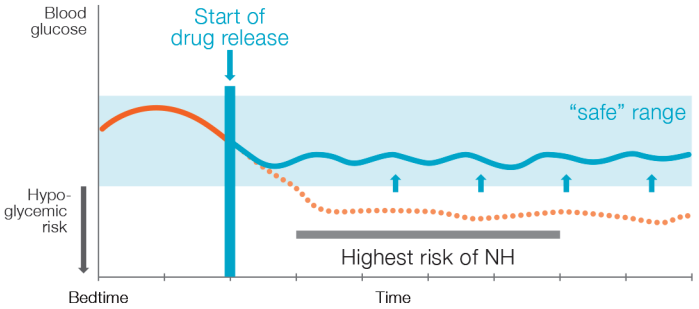
Proof of Concept Study
A proof of concept study in 30 patients with stable T1DM indicated that SKP-1052 is effective in releasing the drug with a 2-hour delay and confirmed that blood glucose concentrations follow the drug plasma concentrations. The study also demonstrated that the number of hypoglycemic events in the critical 1 a.m. to 5 a.m. period was reduced with SKP-1052 compared with placebo, without leading to morning hyperglycemia, and indicated that the treatment was well tolerated.

Further Development
SKP-1052 is an attractive candidate for further development. In addition to the core Geoclock™ patents, product-specific patents have been filed to provide a long period of protection, and advice has been obtained from FDA supporting a relatively short development program. Skyepharma is seeking a development and commercialisation partner for the product.

T1DM patient with Nocturnal Hypoglycemia
"Typical" blood glucose profile

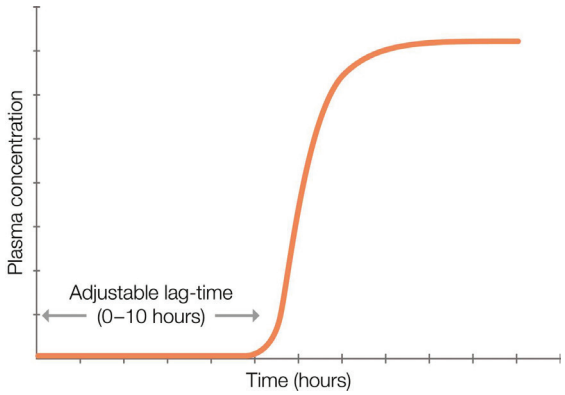


T1DM patient treated with SKP-1052
Expected blood glucose profile



Geoclock™: Customisable Chronotherapy

Skyepharma's Geoclock™ is a patented technology for dry-coated tablets. It is constructed with an active drug core surrounded by an outer tablet layer comprising a mixture of hydrophobic wax and brittle material. This configuration allows the production of a pH-independent and food-independent lag time prior to the release of the active drug. After the predefined, adjustable, and predictable lag time, the inner tablet can release the active drug, either immediately or with a controlled release. Geoclock™ has been incorporated into products that are approved and on the market in the United States and Europe and can be manufactured using standard tableting equipment. It is protected by issued patents.



Skyepharma is an expert drug delivery company and combines proven scientific expertise with validated proprietary drug delivery technologies to develop innovative oral and inhalation pharmaceutical products. Skyepharma currently has 14 approved products on the market in the areas of oral, inhalation, topical, and injectable drug delivery. The products developed by Skyepharma are marketed throughout the world by large pharmaceutical companies as well as specialty companies.

For more information, visit www.skyepharma.com or contact us:

Skyepharma AG
Eptingerstrasse 61
4132 Muttenz, Switzerland
Tel. +41 61 467 55 55
business.development@skyepharma.com ■

Animal Models of Obsessive Compulsive Disorders

Marilyn N. Martinez,[1] U.S. FDA Center for Veterinary Medicine

One of the missions of the Preclinical Sciences & Animal Health (PSAH) Division of the Controlled Release Society is to provide a platform to explore the use of animal models in preclinical studies, interspecies differences in drug absorption, pharmacokinetics, and target site drug delivery, and all matters relating to the animal health industry.

The division regularly invites experts who can develop articles for the *CRS Newsletter* in an effort to provide the CRS members with highlights of the current research being conducted in animal species when the goal of that research is to support the development of veterinary pharmaceuticals that address needs associated with animal health or to serve as a tool for identifying potential human drug targets or human product delivery systems.

With this goal in mind, we want to share interesting information on work recently conducted on obsessive compulsive disorders (OCD). This family of disorders occurs in both human and veterinary species. Although the exact etiology of the disease is still under investigation, there consistently appears to be an association with change in brain neural circuitry, with the brain alterations responsible for OCD best represented at the network level. While the origin, at least in humans, appears to focus around the frontal-based ganglia-thalamic circuits,[1] the characteristics of the circuitry changes appear to contribute to the heterogeneity of clinical manifestations and symptom severity of this disorder.[2] Similar structural disorders of the brain have been observed in affected Doberman pinschers,[3] a breed in which this disorder is characterized by extensive flank sucking. In fact, in dogs, the expression of the compulsion appears to be related to breed.[4]

OCD is a challenge to both humans and animals. In humans, both due to uncertainties as to its causality (what are the appropriate therapeutic targets) as well as the challenge of delivering therapeutic moieties to the brain, the use of animal models has taken on a high level of importance in efforts to identify pharmaceutical remedies. Two recent publications explore potential origins for this repetitive behavior disorder, one involving a canine model[5] and the other a mouse model.[6] For those of us with pets, OCD is not just a human problem but can also impact our canine companions.[7] Currently, researchers cannot identify individuals (humans or dogs) that will develop OCD.[8]

For those interested in animal model research into this disorder, Albelda and Joel[9] have written a review of current animal models for OCD.

We welcome suggestions for other topics of interest from the CRS community or articles of interest for inclusion on our website. You can contact us at:

PSAH Chair: marilyn.martinez@fda.hhs.gov
Deputy Chair: peter.cheifetz@merial.com

References

1. Zohar, J, Greenberg, B, Denys, D. Obsessive-compulsive disorder. Chapter 21 in: Handbook of Clinical Neurology, Vol. 106 (3rd series), Neurobiology of Psychiatric Disorders, TE Schlaepfer and CB Nemeroff, eds. Elsevier: Amsterdam, The Netherlands (2012).
2. Piras, F, Piras, F, Chiapponi, C, Girardi, P, Caltagirone, C, Spalletta, G. Widespread structural brain changes in OCD: A systematic review of voxel-based morphometry studies, Cortex (Feb 26, 2013).
3. Ogata, N, Gillis, TE, Liu, X, Cunningham, SM, Lowen, SB, Adams, BL, Sutherland-Smith, J, Mintzopoulos, D, Janes, AC, Dodman, NH, Kaufman, MJ. Brain structural abnormalities in Doberman pinschers with canine compulsive disorder, Prog. Neuro-Psychopharmacol. Biol. Psychiatry 45: 1-6 (2013).
4. Tiira, K, Hakosalo, O, Kareinen, L, Thomas, A, Hielm-Björkman, A, Escriou, C, Arnold, P, Lohi, H. Environmental effects on compulsive tail chasing in dogs, PLoS One 7(7): e41684 (2012).
5. Grace, CO. OCD: Dobermans to the rescue. Tufts J. (2010). Available at: http://tuftsjournal.tufts.edu/2010/03_1/features/03/
6. Columbia University. Mice give new clues to origins of OCD. (2013). Available at: http://www.labmanager.com/?articles.view/articleNo/35947/title/Mice-Give-New-Clues-to-Origins-of-OCD/
7. Dell'Amore, C. OCD dogs, people have similar brains; is your dog OCD? National Geographic Daily News. Available at: http://news.nationalgeographic.com/news/2013/06/130610-ocd-dogs-health-animals-science-brains
8. International OCD Foundation. Genetics Collaborative Board. Available at: http://ocfoundation.org/GCB.aspx
9. Albelda, N, Joel, D. Current animal models of obsessive compulsive disorder: An update, Neuroscience 211: 83-106 (2012). ■

[1] This article provides the perspective of the author and is not intended to reflect the opinion of the U.S. FDA.

Young Scientist Committee Update

Yewande Oni, University of Nottingham

Yewande Oni

This year's Young Scientist Committee held a variety of workshops, Get Up! Get Educated! sessions, a roundtable discussion, and the ever-popular networking event. As expected, all the events were a great success, but two stood out.

The topic of discussion for this year's roundtable was "Commercializing Ideas from Academia: Past Lessons and Current Challenges," an enlightening and inspiring topic. The discussion kicked off with a panel of successful entrepreneurs within the industry who were willing to share their ideas and experiences with aspiring scientists. The session chairs, Adam Bohr and Jorrit Water, posed a question to the panel before opening the discussion to the audience for a comprehensive interrogation. An in-depth discussion ranged from taking risks and pushing ideas forward to patenting and pulling the right team together to start your own business. At points, the discussion got so passionate that we saw some conflicting views between the panelists. This was an exciting part to the session and gave the audience a wide scope of information to encourage and motivate the entrepreneurs within the audience.

The second highlight and one of my favourite parts of the conference (aside from the amazing weather) was the Young Scientist Networking Evening. This year's event was a sellout, and everyone wanted to be there! Who wouldn't? It was a chance to meet, greet, and mingle with scientists from around the world.

We gathered at Jimmy Buffett's at the Beachcomber Restaurant and Honolulu Surfing Museum. Armed with drink vouchers and in great spirits, the night took off with human bingo. Human bingo is exactly as it sounds: instead of numbers, we had fact sheets about fellow attendees, and it was our job to find out who had done what! The first participant to name the persons who fit the facts wins. These "bingo cards" contained interesting, fascinating, and random facts collected prior to the meeting from those in attendance. To name a few, "Name someone who scuba dives" and "someone who owns purple pajamas." It was our job to mingle and jingle to find out who had done what and then validate it with their signature. Whoever filled their card with signatures first was deemed the winner. Simple. This gave people a chance to ask questions, start a conversation, and really get to know each other. It was great fun and certainly the highlight of the evening. The event provided a chance to make new international friends and really lived up to the name "networking."

I thoroughly enjoyed being a part of the YSC events at CRS Hawaii, and I cannot wait to get more involved next year. ■

CRS Hosts Workshop at AAPS

Knowledge of multiple encapsulation technologies and how they are applied is valuable information for developing new products or solving existing problems. Over 40 attendees from 12 countries attended the CRS Introduction to Microencapsulation Technologies Workshop preceding the 2013 AAPS Annual Meeting & Exposition in San Antonio, Texas, U.S.A. This workshop provided an introduction to common micro- and nanoencapsulation processes and their various applications. Speakers (left to right): Tom Tice, Evonik Degussa Corp.; James Oxley, Southwest Research Institute (SwRI), U.S.A.; David Dumbauld, Orbis Biosciences, Inc.; Irwin Jacobs, Jacobs Controlled Release Consulting, LLC; Chuck Frey, Coating Place Inc.; and Blair West, Formex LLC. ■

Connect with Your Colleagues Through the CRS Website

Membership in CRS has many privileges, and one of the most important ones is the opportunity to reach your colleagues in delivery science and technology around the world. The member directory search allows you to find colleagues by name and company. You can also search for delivery scientists within certain states or countries, others in academia or government, or look for scientists within certain tracks of interest. You must be a current member and logged in to fully access the member directory.

If you are looking for someone with the same interests as you, try looking for members in committees or chapters. The committee directory lists the active members of the committees, who are working to solve issues in delivery science and for the society. The "Chapters" page lists the officers of each local chapter, another excellent opportunity for you to connect locally.

The CRS website is your primary resource to connect with this unique community. Be sure to log in and click on the "Community" tab to take advantage of everything your membership gives you access to! Contact Cheryl Kruchten at ckruchten@scisoc.org if you need help with your password or follow the online link to reset it. ■

Welcome New CRS Members

Sree Haritha Chalasani
Danielle Clay
Rahul K. Keswani
Fang Liu
Mohd Cairul Iqbal Mohd Amin
Maria Paula G. Peixoto
David J. Sanders

CRS
Leading
Delivery Science
and Technology

Latest Tissue-Engineering Research Discussed at Rice University

Event sponsored by CRS features newest findings in medicine delivery systems, and biomaterials.

Leading experts in tissue engineering and regenerative medicine meet annually at Rice University's BioScience Research Collaborative to openly discuss techniques and biomedical technologies aimed at growing cells, tissues, and organs for transplantation. Featured research includes ongoing clinical trials and studies in growth factors and drug delivery systems, cellular and tissue therapeutics, imaging systems, and novel ideas in 3D printing and other microfabrication techniques.

The 21st annual Advances in Tissue Engineering short course was held August 14–17, 2013. Participants from the United States and many from around the globe heard experts talk about the latest knowledge and translation of technologies and therapeutics that range from the transplantation of cells and tissues to drug delivery systems to artificial organs.

The Controlled Release Society has endorsed this worthwhile course for over a decade.

The 2013 short course's four-day lecture-based format, which is designed for ample discussion, has been found to be ideal for advanced students and professionals in the field for continuing education purposes. The lecture series is designed for biomaterialists, biomedical engineers, pharmaceutical scientists, physicians, technical managers, advanced students, and researchers.

This year, 39 invited speakers from academia, medical research, and industry presented. Gordana Vunjak-Novakovic, the Mikati Foundation Professor of Biomedical Engineering and Medical Sciences at Columbia University, U.S.A., an expert in bioreactor technologies for tissue engineering and regenerative medicine, was keynote speaker.

The Advances in Tissue Engineering short course has been organized by Antonios Mikos, Rice's Louis Calder Professor of Bioengineering, Chemical and Biomolecular Engineering, since 1992. The conference is cosponsored by Rice's Center for Excellence in Tissue Engineering, the Cox Laboratory for Biomedical Engineering, the BioScience Research Collaborative, the Institute of Biosciences and Bioengineering, and the Rice University Department of Bioengineering.

The 22nd Advances in Tissue Engineering short course will be August 13–16, 2014. See http://tissue.rice.edu for updates and registration. ■

Clinical Studies in *Drug Delivery and Translational Research*

Vinod Labhasetwar, Editor-in-Chief

The focus of *DDTR* has been drug delivery and translational research, with particular emphasis on the treatment of diseases. Here, I wish to highlight two clinical studies that are most relevant to treatment of diseases. Prestidge's group described the results of phase I clinical studies with silica–lipid hybrid nanoparticles for poorly water-soluble drugs. Sorensen's group demonstrated the potential of serum miRNAs for diagnosing and staging of prostate cancer.

First in man bioavailability and tolerability studies of a silica–lipid hybrid (Lipoceramic) formulation: A phase I study with ibuprofen

Clive A. Prestidge

Angel Tan, Nasrin Ghouchi Eskandar, Shasha Rao, and Clive A. Prestidge

Ian Wark Research Institute, University of South Australia

Clinical trials addressing the viability of lipid and nanoparticle-based solid dosage forms for the oral delivery of poorly water-soluble drugs are limited to date. This phase I study aimed to assess the comparative tolerability and oral pharmacokinetics of a novel silica nanoparticle–lipid hybrid formulation encapsulating ibuprofen (i.e., Lipoceramic-IBU) with reference to a commercial tablet (i.e., Nurofen®). The test (Lipoceramic-IBU) and reference (Nurofen®) ibuprofen formulations were characterised for physicochemical properties and *in vitro* solubilisation performance prior to the clinical study. A randomised, double-blinded, one-period single oral dose (20 mg of ibuprofen) study was performed in 16 healthy male subjects under fasting conditions. Encapsulation of ibuprofen in a molecularly dispersed form in the Lipoceramic nanostructured silica–lipid matrices was shown to produce superior drug solubilisation in comparison to Nurofen® and the pure drug during a two-step dissolution (or solubilisation) study in aqueous buffers of pH 1.2 followed by pH 6.5. Pharmacokinetic profiles revealed an approximately 1.95-fold increased bioavailability (p = 0.02) and a 1.5-fold higher maximum plasma concentration (p = 0.14) for Lipoceramic-IBU with reference to Nurofen®. Review of the safety assessments, including physical examinations, clinical laboratory tests, and reports of adverse events, confirmed negligible acute side effects related to the administration of blank and ibuprofen-loaded Lipoceramic formulations. This first in man study of a dry lipid and nanoparticle-based formulation successfully demonstrated the safe use and effectiveness of the nanostructured Lipoceramic microparticles in mimicking the food effects for optimising the oral absorption of poorly water-soluble compounds.

Profiling of circulating microRNAs for prostate cancer biomarker discovery

Karina D. Sorensen

Christa Haldrup, Nobuyoshi Kosaka, Takahiro Ochiya, Michael Borre, Soren Høyer, Torben F. Orntoft, and Karina D. Sorensen

Department of Molecular Medicine, Aarhus University Hospital, Denmark

Prostate cancer (PC) is the most frequent cancer in men in the Western world. Currently, serum prostate-specific antigen levels and digital rectal examinations are used to indicate the need for diagnostic prostate biopsy, but they lack in specificity and sensitivity. Thus, many men undergo unnecessary biopsy, and better and less invasive tools for PC detection are needed. Furthermore, whereas aggressive PC should be treated immediately to prevent dissemination, indolent PC often does not progress, and overtreatment should be avoided. Currently, the best predictors of aggressiveness are Gleason score and T-stage of the primary PC. Better tools to assess PC aggressiveness could aid in treatment decisions. Recently, circulating miRNAs have been suggested as potential new biomarkers for PC with diagnostic and prognostic potential. Here, to identify new serum miRNA biomarker candidates for PC, they performed genome-wide miRNA profiling of serum samples from 13 benign prostatic hyperplasia (BPH) control patients and 31 PC patients. Furthermore, they carefully reviewed the literature on circulating miRNA biomarkers for PC. Their results confirmed the deregulation of miR-141 and miR-375, two of the most well-documented candidate miRNA markers for PC. Moreover, they identified several new potential serum miRNA markers for PC and developed three novel and highly specific (100%) miRNA candidate marker panels able to identify 84% of all PC patients (miR-562/miR-210/miR-501-3p/miR-375/miR-551b), 80% of patients with disseminated PC when compared with BPH patients (let-7a*/miR-210/miR-562/miR-616), and 75% of disseminated PC patients when compared with localized PC patients (miR-375/miR-708/miR-1203/miR-200a), demonstrating high potential of serum miRNAs for diagnosing and staging of PC.

CRS members have free access to these articles, and all articles published in *DDTR*, through the CRS website, controlledreleasesociety.org. ■

Impact Factor Continues to Rise for *Journal of Controlled Release*

The *Journal of Controlled Release*, an official journal of the Controlled Release Society, is proving to be one of the most influential journals in the pharmaceutics, biomaterials, and drug delivery fields. The five-year impact rating for *JCR* is 8.078, with a current Impact Factor of 7.633.

JCR publishes innovative, original research involving the controlled release and delivery of drugs and other biologically active agents. The terms "controlled release" and "delivery" are used in their broadest sense to include mechanisms such as diffusion, chemical and enzymatic reactions, dissolution, osmosis, targeting, and the utilization and manipulation of biological processes. A broad spectrum of studies dealing with all aspects of controlled release and delivery, including gene delivery, tissue engineering, and diagnostic agents, is encouraged. The use of prodrugs and carriers such as water-soluble polymers, micro- and nanoparticles, liposomes, and micelles is included in the scope.

These are the most-downloaded *JCR* articles during the past 90 days:

1. *PLGA-Based Nanoparticles: An Overview of Biomedical Applications*
   Fabienne Danhier, Eduardo Ansorena, Joana M. Silva, Regis Coco, Aude Le Breton, and Veronique Preat
   161(2): 505-522 (July 20, 2012)
2. *Biodegradable Polymeric Nanoparticles as Drug Delivery Devices*
   Kumaresh S. Soppimath, Tejraj M. Aminabhavi, Anandrao R. Kulkarni, and Walter E. Rudzinski
   70(1-2): 1-20 (January 29, 2001)
3. *Recent Advances on Chitosan-Based Micro and Nanoparticles in Drug Delivery*
   Sunil A. Agnihotri, Nadagouda N. Mallikarjuna, and Tejraj M. Aminabhavi
   100(1): 5-28 (November 5, 2004)
4. *Oral Delivery of Anticancer Drugs: Challenges and Opportunities*
   Kaushik Thanki, Rahul P. Gangwal, Abhay T. Sangamwar, and Sanyog Jain
   170(1): 15-40 (August 28, 2013)
5. *To Exploit the Tumor Microenvironment: Passive and Active Tumor Targeting of Nanocarriers for Anti-Cancer Drug Deliveries*
   Fabienne Danhier, Olivier Feron, and Veronique Preat
   148(2): 135-146 (December 1, 2010)
6. *Novel Glycidyl Methacrylated Dextran (Dex-GMA)/Gelatin Hydrogel Scaffolds Containing Microspheres Loaded with Bone Morphogenetic Proteins: Formulation and Characteristics*
   Fa-Ming Chen, Yi-Men Zhao, Hai-Hua Sun, Tao Jin, Qin-Tao Vang, Wei Zhou, Zhi-Fen Wu, and Yan Jin
   118(1): 65-77 (March 12, 2007)
7. *Biocompatibility of Engineered Nanoparticles for Drug Delivery*
   Sheva Naahidi, Mousa Jafari, Faramarz Edalat, Kevin Raymond, Ali Khademhosseini, and P. Chen
   166(2): 182-194 (March 10, 2013)
8. *Recent Expansions in an Emergent Novel Drug Delivery Technology: Emulgel*
   Ajazuddin, Amit Alexander, Ajita Khichariya, Saurabh Gupta, Ravish J. Patel, Tapan Kumar Giri, and Dulal Krishna Tripathi
   171(2): 122-132 (October 28, 2013)
9. *A Review of Stimuli-Responsive Nanocarriers for Drug and Gene Delivery*
   Srinivas Ganta, Harikrishna Devalapally, Aliasgar Shahiwala, and Mansoor Amiji
   126(3): 187-204 (March 20, 2008)
10. *Smart Ligand: Aptamer-Mediated Targeted Delivery of Chemotherapeutic Drugs and siRNA for Cancer Therapy*
    Xin Li, Qinghe Zhao, and Liyan Qiu
    171(2): 152-162 (October 28, 2013) ■

NEW! AudioSlides

JCR offers a new, free service called AudioSlides. These are brief, webcast-style presentations that are shown next to published articles on ScienceDirect. This format gives you the opportunity to explain your research in your own words and promote your work. For more information and examples, please visit www.elsevier.com/audioslides.

Open Access Options

JCR offers authors a choice in how they wish to disseminate their research—either by publishing it as a subscription article or as an open access article. All articles published open access will be immediately and permanently free for everyone to read and download from ScienceDirect. Authors publishing an open access article will need to pay a publication fee. There is no fee for publishing a subscription article.

CRS Member Discount

CRS members qualify for discounted subscription rates to the *Journal of Controlled Release*. New subscribers can find more information online at controlledreleasesociety.org/publications/Pages/JCR.

CRS member subscribers can access the *Journal of Controlled Release* at www.sciencedirect.com/jconrel/.

Fellowship Year Reflections

Tram Dang

Background
I completed my Ph.D. in chemical engineering in the laboratories of Prof. Robert Langer and Prof. Daniel Anderson at Massachusetts Institute of Technology, U.S.A. During my graduate training, I developed new noninvasive imaging techniques to investigate the effects of controlled release anti-inflammatory drugs on the immunological response to biomaterials and applied the findings to enhance cell-based therapeutics for diabetes therapy.

In September 2012, with the support of the Sung Wan Kim postdoctoral fellowship from the CRS Foundation, I joined the laboratory of Prof. Ali Khademhosseini at Brigham and Women's Hospital, Harvard Medical School. I was excited to play an important role in a multidisciplinary collaboration to develop new technologies for chronic wound management. The Sung Wan Kim Postdoctoral Fellowship gave me a wonderful opportunity to explore different aspects of a new medical challenge while capitalizing on my expertise in drug delivery to contribute to this emerging area of research.

Scientific Significance and Achievements
Chronic wounds are a major medical burden, imposing staggering costs on the health care systems in both developed and developing countries. For example, in the United States alone, chronic wounds affect about 6.5 million people, costing the country $20 billion annually in health care expenditure. These wounds are tissue injuries that fail to progress in an orderly and timely fashion, resulting in impaired healing. Underlying pathological conditions such as pressure ulcers, venous ulcers, diabetic foot ulcers, and their associated infection are often involved. Patients who are particularly vulnerable to chronic wounds include the elderly population and individuals suffering from diabetes or impaired mobility because of strokes and spinal cord injuries.

The wound microenvironment is biologically complex and dynamic, involving various cell types and a continuously changing level of cytokines and enzymes. Despite our growing understanding of wound healing biology, successes from different wound treatment therapies such as electrical stimulation, oxygenation, or delivery of cells and growth factors remain limited. A major shortcoming associated with such systems is their systemic and open-loop nature. There is no physical, chemical, or biological feedback mechanism to adjust the treatment in response to the changing microenvironment of the wounds.

Thanks to the generous support of the Sung Wan Kim Postdoctoral Fellowship, I had the opportunity to join a multidisciplinary team of scientists in Prof. Khademhosseini's laboratory at Harvard Medical School to address this pressing challenge in chronic wound therapy. Our project is a multiuniversity collaboration to combine the expertise in biomaterials, drug delivery, and microfabrication from our team at Harvard Medical School with the electrical engineering strengths in flexible electronics from our collaborators at Tufts and Purdue Universities. We aim to revolutionize chronic wound treatment by developing a flexible smart-dressing platform that integrates multiple sensing capabilities and treatment modalities for active intervention in the wound microenvironment. Specifically, we envision that this dressing can adjust therapeutic treatment in response to changing physical, chemical, and biological parameters in the wound microenvironment, such as temperature, mechanical stress, and oxygen and pH levels.

***Tram Dang** (pictured far left) receiving her fellowship from Sung Wan Kim and Foundation Chair Susan Cady at the 2012 CRS Annual Meeting & Exposition.*

I am particularly interested in the dynamic biological signals at the wound sites. During the different phases of the wound healing process, some inflammation is necessary for recruitment of various immune cells, which secrete cytokines and growth factors to modulate the progress of healing. However, excessive inflammation can impede healing or lead to extensive fibrotic deposition and scar formation. For example, overgranulation, a condition of excessive growth of collagen and new blood capillaries, often impedes the migration of epithelial cells, hinders wound closure, and increases the risk of infection.

To address this challenge, I proposed an innovative drug delivery system to be integrated into the smart-dressing platform and release anti-inflammatory therapeutics in response to the varying inflammatory signals at the wound sites. To achieve this goal, I synthesized and characterized a new inflammation-responsive hydrogel material conjugated with small-molecule anti-

inflammatory drugs via peptide linkers. The key advantage of this system is that the linkers can be cleaved by inflammatory proteases, which are secreted by inflammatory cells present at the wound sites. Therefore, the amount of drug released from this hydrogel material is dependent on the concentration of inflammatory proteases in the wound microenvironment. In the future, we plan to integrate this new material into our smart-dressing platform and evaluate its performance in an animal model of chronic wounds.

In addition to addressing exciting problems in chronic wound therapy, the Sung Wan Kim fellowship also allowed me the flexibility of working on many collaborative projects in other exciting research areas at Harvard Medical School. In the past year, these collaborations have resulted in one publication in the journal *Advanced Materials* on the topic of microengineered and mechanically tunable hydrogels and a book chapter on the subject of polymeric biomaterials for implantable prosthetics.

Professional Development

As the Sung Wan Kim fellow, I also had many opportunities for professional networking and for contributing to the controlled release community. During my fellowship year, I began to serve as an independent reviewer for the *Journal of Controlled Release* and an abstract reviewer for the 2013 CRS Annual Meeting. Currently, I am also excited to be involved in the launching of a new CRS Local Chapter for the Southeast Asia region.

I truly appreciate the CRS Foundation and its generous contributors who have given me a wonderful opportunity to broaden my scientific training and career development. I am honored to serve as the Sung Wan Kim fellow in the past year. In the future, I plan to remain an active member of the Controlled Release Society to contribute to the progress of the controlled delivery field. I am also grateful to Prof. Sung Wan Kim and my Ph.D. and postdoc advisors for their continuous support of my scientific endeavors. ■

2014 Alexander Florence Postdoctoral Fellowship

Alexander Florence

In 2014 the CRS Foundation will give a $30,000 postdoctoral fellowship named to honor CRS past president Alexander "Sandy" Florence, former dean and current emeritus professor of the School of Pharmacy, University of London. He is editor-in-chief (Europe) of the *International Journal of Pharmaceutics* and was founding coeditor of the *Journal of Drug Targeting*. Author of hundreds of papers and multiple books, and recipient of numerous awards, Prof. Florence's expertise in pharmaceutical nanotechnology, drug delivery systems, physical pharmaceutical chemistry, novel dendrimers, and surface chemistry has added greatly to drug delivery research.

Build the Endowment

The CRS Foundation Board is focusing its 2013 time and resources to build the endowment for future sustainability. Your contribution matters. Please help build the endowment and support the next postdoctoral fellowship by making a generous year-end donation on the CRS Foundation website, www.controlledreleasesociety.org/about/foundation.

Celebrate the Advances

Thanks to the generosity of CRS members and the delivery science community, the CRS Foundation has awarded postdoctoral fellowships of $30,000 each to four exceptional young delivery scientists since 2009. With each fellowship, CRS honors exemplary delivery scientists and supports the training of its future leaders.

2013 Membership Application

Personal Data

8061

Have you previously been a member of CRS? ❍ Yes ❍ No

Check the appropriate box: ❍ Mr. ❍ Mrs. ❍ Ms. ❍ Dr.

Name _____
First *M.I.* *Last*

Title _____

Degree _____

Company/Institution _____

Address _____

_____

City _____

State/Province _____

Zip/Postal Code _____

Country _____

Telephone _____

Fax _____

E-mail _____

Note: *The information you provide us below will remain confidential.*

Date of Birth _____/_____/_____ Gender: ❍ Male ❍ Female
Month Day Year

Select a category that best describes your work:
❍ Academia ❍ Industry ❍ Government ❍ Student

❍ Other _____

Primary track of interest:
❍ Bioactive Materials ❍ Consumer & Diversified Products
❍ Preclinical Sciences & Animal Health

How many years in this field? _____

I prefer to receive the *CRS Newsletter* by: *(check one)*
❍ E-mail ❍ Direct Mail
❍ Do not include my information in membership directories

Current Memberships

Please indicate the associations of which you are already a member:

❍ AAAS ❍ FIP ❍ RSC
❍ AAPS ❍ JSDDS ❍ Other
❍ ACS ❍ PDA _____

Divisions and Focus Groups

Optional – no charge. Choose as many as apply.

❍ Consumer & Diversified Products Division
❍ Preclinical Sciences & Animal Health Division
❍ Nanomedicine Focus Group
❍ Ocular Drug Delivery Focus Group
❍ Oral Drug Delivery Focus Group

Return form to:
Controlled Release Society,
3340 Pilot Knob Road, St. Paul, MN 55121 U.S.A.
Telephone: +1.651.454.7250 • Facsimile: +1.651.454.0766
E-mail: crs@scisoc.org • controlledreleasesociety.org

Membership Dues

Paid membership includes a complimentary online subscription to *Drug Delivery and Translational Research* and the *CRS Newsletter*.

❍ Individual $169
❍ Postdoc $62
❍ Student (*complete the student verification*) $52

Subtotal Membership Dues $_____

Student Status Verification
I attest that the named individual is a full-time, degree-seeking student.

_____
Signature of advisor or department chair

Printed Name _____
Expected Graduation Date _____
Telephone _____
E-mail _____

Journal Subscriptions *(check one or more)*

❍ *Drug Delivery and Translational Research*
Official Journal of CRS – Print $40

❍ *Journal of Controlled Release* (Vol. 165 – 172)
Official Journal of CRS – Print $193

❍ *Journal of Controlled Release* (Vol. 165 – 172)
Official Journal of CRS – Online $150

❍ *European Journal of Pharmaceutics and Biopharmaceutics*
(Vol. 83 – 85, 9 issues) $142

❍ *Biomaterials* (Vol. 34, 36 issues) $363
Includes ScienceDirect online access

Subtotal Journal Options $_____

Contribution

CRS Foundation Contribution *(optional)** **$_____**
For the 2014 Alexander "Sandy" Florence Postdoctoral Fellowship and Beyond.

40th Annual Meeting Student
Travel Grant Contribution (*optional*)* **$_____**

* *Your contribution may be tax deductible. CRS is a 501(c)(3) organization. Consult your tax advisor on how the current law applies to you.*

Contribution $_____

Grand Total $_____

Payment Method

Total payment must accompany completed application.

❍ Check enclosed made payable to Controlled Release Society
Must be in U.S. dollars drawn on a U.S. bank—When you provide a check as payment, you authorize us to use information from your check to make a one-time electronic fund transfer from your account or to process the payment as a check transaction. Funds may be withdrawn from your account the same day we deposit payment and you may not receive your check back from your financial institution.

❍ Charge Grand Total above to my:
❍ Visa ❍ MC ❍ Am. Express ❍ Discover

Credit Card Number _____

Expiration Date _____/_____
Month Year

Card Holder's Name _____

Agreement: I accept to receive information from CRS via e-mail and acknowledge that my contact information will appear on the CRS web-site in the online membership directory, unless I have stated otherwise.

_____ _____
Applicant Signature *Month/Year*

People in the News

Compiled by Steven Giannos, Independent Consultant

Centaur Animal Health Appoints New President and Chief Executive Officer

PRNewswire: August 27, 2013 – KANSAS CITY, KS, and PHILADELPHIA, PA, U.S.A. – Centaur Animal Health is pleased to announce the appointment of Jeffrey Boily as president, CEO, and director effective September 1, 2013.

Boily brings over 30 years of global life sciences experience in pharmaceuticals, biotechnology, drug delivery, and animal health and will be instrumental in accelerating plans toward Centaur becoming a major animal health company. Centaur has established a track record of successful execution on product initiatives and is aggressively looking to in-license additional products.

"I'm delighted to lead Centaur Animal Health as we embark on the next phase of growth," said Boily.

"Jeff's background as an entrepreneurial leader and his experience in fund-raising and partnering with large and small firms is a perfect fit for Centaur," said Mark Metrokotsas, board chair for Centaur Animal Health.

Jeffrey Boily is nonexecutive chairman of ProteaPex Therapeutics, a firm researching and developing innovative animal health therapeutics. Most recently he was president and CEO of the Center for Animal Health Innovation, which focused on identifying and funding breakthrough technologies. Previous to this, he was CEO of BioWizard, a VC-funded research and information firm for biomedical scientists. He gained large company executive experience at Abbott, Rogers and Wyeth including Fort Dodge Animal Health. He holds an M.B.A. from the John Molson School of Business, Concordia University, Montreal, Canada, and a B.S. in biology from the University of Ottawa. He also serves on the board of directors of various healthcare companies.

Centaur Animal Health is focused on developing innovative diagnostics, pharmaceuticals, and nutraceuticals that address significant therapeutic needs for companion and production animals. Centaur licenses patent-protected technologies acquired from animal health or human pharmaceutical and biotechnology companies. Contract manufacturing is available in their FDA-certified plant. For more information, please visit www.centauranimalhealth.com. ■

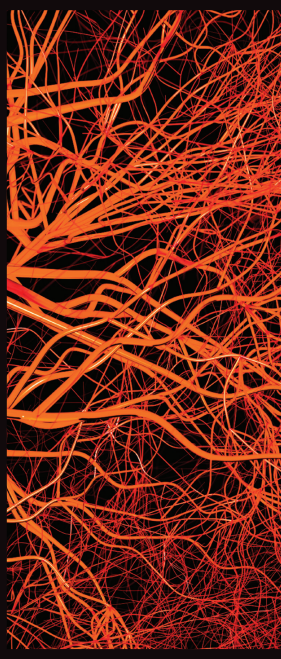
CRS Annual Meeting and Exposition

July 13–16, 2014 • Chicago, Illinois, U.S.A.

There's No Better Time or Place to Share Your Best Research

This year's program, "Translation of Delivery Technology: Innovation to Commercialization," offers an exceptional opportunity to reach a diverse audience in the discovery, development, and delivery continuum.

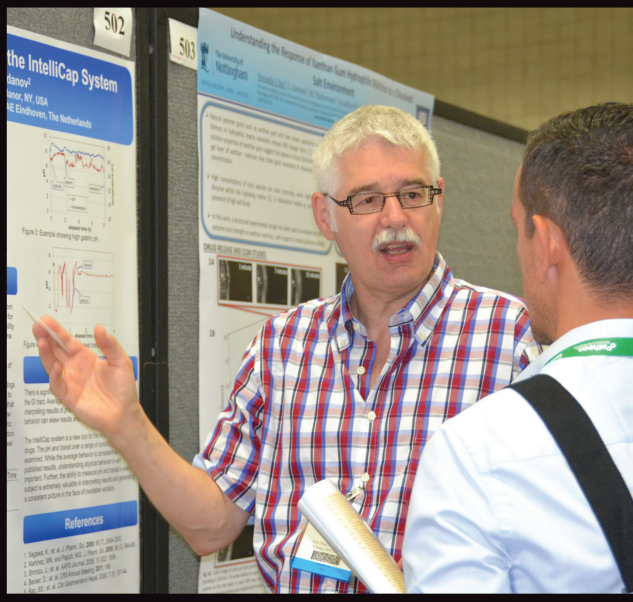
Share the passion. Submit your abstract online now at controlledreleasesociety.org



Call for Papers Open November 2013 Through January 23, 2014

TRANSLATION

of Delivery Technology: Innovation to Commercialization



CRS
Leading Delivery Science and Technology

controlledreleasesociety.org

Blood Vessels ©iStockphoto.com/Konstantin Inozemtsev

In the News

Compiled by Steven Giannos, Independent Consultant

October

Discovery Labs Announces IND Submission for AEROSURF®

PRNewswire: October 17, 2013 – WARRINGTON, PA, U.S.A. – Discovery Laboratories, Inc. (NASDAQ: DSCO), a specialty biotechnology company dedicated to advancing a new standard of respiratory critical care, today announced that it has submitted an investigational new drug (IND) application to the U.S. Food and Drug Administration (FDA) to initiate its AEROSURF® phase 2 clinical program. The FDA has confirmed receipt of the IND and has indicated that, unless otherwise notified during its review, the company may initiate the phase 2 clinical program after a 30-day period. Discovery Labs anticipates patient enrollment could begin in the fourth quarter of 2013. The company will host a conference call this morning at 10:00 AM ET to discuss the AEROSURF program. Conference call details are below.

"The filing of our AEROSURF IND with the FDA represents an important milestone for our company and a first step towards a potentially transformational medical advancement for the neonatology community and the infants they care for," said John G. Cooper, chief executive officer at Discovery Labs.

AEROSURF is a novel investigational drug-device combination product being developed to deliver Discovery Labs' KL4 surfactant in aerosolized form to premature infants with respiratory distress syndrome (RDS). AEROSURF could potentially allow for the administration of KL4 surfactant to premature infants without invasive endotracheal intubation and may enable the treatment of a significantly greater number of premature infants who could benefit from surfactant therapy but are currently not treated.

"The AEROSURF program is leveraging important advancements in our novel technology platform," said Russell Clayton, D.O., senior vice president, research and development, at Discovery Labs. "Our synthetic KL4 surfactant technology was recently validated with the FDA approval of SURFAXIN® for the prevention of RDS in infants at high risk for RDS. We are now combining our KL4 surfactant with our proprietary drug delivery technologies to potentially deliver aerosolized KL4 surfactant to patients with respiratory disease, with an initial focus on the unmet medical needs in premature infants with RDS."

Preclinical Results Show Alliqua's Investigational Lidocaine Transdermal Patch

PRNewswire: October 16, 2013 – LANGHORNE, PA, U.S.A. – A preclinical study commissioned by Alliqua, Inc. (OTCQB: ALQA) ("Alliqua" or "the company") concluded that the company's investigational lidocaine transdermal patch compares favorably to the Lidoderm® (lidocaine patch 5%) patch that is currently on the market. The overall study results indicate that Alliqua's patch is able to deliver in the pig a slightly higher amount of lidocaine than Lidoderm and to reach maximum delivery within a comparable period. No skin irritation occurred with either the Alliqua transdermal patch or Lidoderm patch. The study concludes that further development could result in Alliqua creating a commercial lidocaine patch that could be a generic version of the Lidoderm patch or provide better drug delivery resulting in a 505 (b)(2) approval.

David Johnson, chief executive officer of Alliqua, said, "As we continue to expand our suite of wound care products, building the value proposition of our hydrogel technology for topical and transdermal drug delivery remains one of our major goals. The results of this preclinical study serve as a significant motivation for us to continue our efforts to develop a core transdermal delivery technology platform to deliver lidocaine and other beneficial ingredients through the skin."

James Sapirstein, chief executive officer of Alliqua Biomedical, said, "The strong showing of our transdermal patch compared to Lidoderm, the leading product currently on the market, illustrates the potential of our technology. We are evaluating our strategic options to maximize these findings."

The primary objective of the study was to conduct a comparative pharmacokinetic (PK) analysis of lidocaine in Alliqua's transdermal patch compared to Lidoderm in the pig. The non-GLP *in vivo* crossover study was designed to evaluate the delivery of lidocaine over 24 hours in Alliqua's patch and Lidoderm with regard to feasible length of application.

The study found that Alliqua's patch offers a higher peak plasma concentration (Cmax) of lidocaine than Lidoderm (4.961.16 ng/mL versus 3.031.92 ng/mL) and higher mean total area under the curve (AUCtotal) than the competing product 66.5 ng/mL-h versus 48.9 ng/mL-h)). The mean period of peak concentration (Tmax) was 8.7 hours for Alliqua's patch versus 10.7 hours for Lidoderm.

In addition, Alliqua's patch was easier and cleaner to remove from the skin after application, with minimal or no patch impression (outline) remaining. The presence of adhesive in Lidoderm seemed to have a "peel-off effect" on the skin (similar

In the News continued on page 26

In the News continued from page 25

to a band-aid); in contrast, Alliqua patch hydrogel has self-adhering characteristics and is easily removed from the skin at the end of a patch application without residual skin markings.

NCKU Chemistry Professor Develops Application of Mesoporous Materials

Business Wire: October 15, 2013 – TAINAN, Taiwan – Dr. Hong-Ping Lin, who is a professor at the Department of Chemistry in National Cheng Kung University (NCKU), southern Taiwan, was invited by the *Chemical Society Review* to publish his research paper called "Synthesis of Mesoporous Silica Nanoparticle," and his research findings featured on the front cover in May.

Dr. Lin revealed in an interview that good control of mesoporous silica nanoparticles (MSNs) is of increasing importance to their use in catalyst, adsorption, polymer filler, optical devices, bioimaging, drug delivery, and biomedical applications.

Different synthesis methodologies to prepare well-dispersed MSNs and hollow silica nanoparticles with tunable dimensions ranging from a few to hundreds of nanometers of different mesostructures are discussed in his research paper.

In practical applications, Dr. Lin explained, "The materials demonstrate good potential for use in high-performance catalysis, antireflection coating, transparent polymer, drug-release, and theranostic systems."

Dr. Lin's study on mesoporous materials currently comes to a breakthrough in technology. "The materials can be used as the adsorbent for semiconductor exhaust and applied to the innovation of biomedical appliance," according to Lin, whose research interest is mainly in the synthesis and applications of the mesoporous materials.

Recently, he has applied mesoporous materials to develop an anti-hypersensitivity toothpaste and absorbents for removing toxic gas released from IC industry, which are about to enter the process of mass production.

"I think the application of research findings to benefit the industry and the general public is very important," said Dr. Lin, who put a great emphasis on the cooperation between the academia and the local industry.

He said that a material can be obtained through various synthetic methods, but it's always the simplest and most economic one that has the potential to be widely used; therefore, his research interest is in developing low-cost material with simple and economic synthesis methods.

Dr. Lin recently is busy in the laboratory experimenting to isolate bio-mesoporous materials from a variety of plants including rice husk, straw, and horsetail grass. He said the ashes after burning the plants is what he can recycle and reuse. Adding value to the recycled resources is one of his sought-after goals.

Rexahn Pharmaceuticals In-Licenses Novel Oligonucleotide Targeted Drug Delivery Platform from Ohio State University

Business Wire: October 10, 2013 – ROCKVILLE, MD, U.S.A. – Rexahn Pharmaceuticals, Inc. (NYSE MKT: RNN), a clinical-stage biopharmaceutical company, announced today that it has signed an exclusive license agreement with the Ohio State Innovation Foundation, an affiliate of The Ohio State University, for a novel oligonucleotide drug delivery platform, lipid-coated albumin nanoparticle (LCAN), developed at The Ohio State University College of Pharmacy. In preclinical studies, the LCAN platform has demonstrated the ability to deliver oligonucleotide compounds into cancer tumors, which can result in improved safety and efficacy. Rexahn's first preclinical candidate to be developed with this delivery platform will be RX-0201-nano.

"The LCAN platform allows Rexahn to specifically target cancer tumors with oligonucleotides in a way that increases potency and reduces side effects, and is a broad platform that has the ability to generate multiple therapeutic candidates going forward. We will initially move forward with RX-0201-nano as the first candidate from the LCAN platform, and we anticipate entering the clinic with the first candidate within two years," stated Peter D. Suzdak, Ph.D., Rexahn's chief executive officer. "Furthermore, the platform also offers Rexahn the ability to use this delivery platform to enhance and create additional next generation oligonucleotide therapies."

LCAN incorporates both cationic lipid and a cationized albumin that can form an electrostatic complex with oligonucleotides and be co-encapsulated by lipids. It also has a targeting moiety conjugated on the surface to direct the LCAN directly to the cancer tumors. RX-0201-nano is a nanoliposomal Akt1 inhibitor, similar to the company's Archexin®, which may be effective in solid tumors and hematological malignancies and has shown high efficiency and good stability in preclinical studies.

Robert J. Lee, Ph.D., researcher at the Ohio State University College of Pharmacy and the inventor of the LCAN technology, commented, "The LCAN platform represents a significant advancement in targeted delivery of oligonucleotides to cancer tumors. Other types of formulation approaches have been tried in the past, but none offered such potent activity for the targeted delivery of an oligonucleotide to the cancer tumor."

Particle Sciences Completes Manufacture of New Vaginal Ring for HIV Prevention

PRNewswire: October 10, 2013 – BETHLEHEM, PA, U.S.A. – Particle Sciences, a drug delivery contract development and manufacturing organization (CDMO), has completed the clinical trial manufacturing of vaginal rings with a unique architecture, essentially a powdered filled tube. Designed to deliver the prodrug tenofovir disoproxil fumarate for 30 days, the device is aimed at HIV prevention and joins several other microbicide delivery approaches under development. The ring provided complete protection in macaques against the related

virus SHIV in studies conducted at the Center for Disease Control. According to Mark Mitchnick, M.D., Particle Sciences' CEO, "Particle Sciences focuses on formulation design and manufacturing. Given the issues our clients face, the dosage forms we work with often require a high level of engineering, and reducing complex formulations to commercially viable products is something we frequently do. In this case, the product is a drug-eluting device funded under an NIH grant led by Betsy Herold, M.D., professor and director, Translational Prevention Research Center at Albert Einstein College of Medicine. The product itself was designed by Patrick Kiser, Ph.D., associate professor of biomedical engineering at Northwestern University." Mitchnick added, "We have worked very hard to make Particle Sciences the go-to resource for complex formulation and manufacturing. This year alone, in addition to this product, we have manufactured sterile nanodispersions, IV emulsions, IM sustained release suspensions, and a host of other products, the majority of which were developed at Particle Sciences. We have a long history with prevention technologies and were delighted to be able to work on this one."

GNT Biotech and Medicals Corporation Licenses Novel Cancer Molecule from Shenzhen Chipscreen Biosciences Ltd.

PRNewswire: October 10, 2013 – SHENZHEN, China – GNT Biotech and Medicals Corporation announces the grant of an exclusive license from Shenzhen Chipscreen Biosciences Ltd. for the development and commercialization of chidamide in Taiwan. Chidamide, an oral, selective histone deacetylase (HDAC) inhibitor, is currently being evaluated in phase II trials by Chipscreen Biosciences in peripheral T-cell lymphoma (PTCL), cutaneous T-cell lymphoma (CTCL), and non-small cell lung cancer (NSCLC) patients. GNTbm will develop and commercialize chidamide primarily in PTCL and NSCLC and will also retain the rights to develop and commercialize chidamide in other oncology indications in Taiwan.

Chidamide is a selective HDAC inhibitor against subtype 1, 2, 3, and 10 and is being studied in multiple clinical trials as a single agent or in combination with chemotherapeutic agents for the treatment of various hematological and solid cancers. Its anticancer effects are thought to be mediated through epigenetic modulation via multiple mechanisms of action, including the inhibition of cell proliferation and induction of apoptosis in blood derived cells, inhibition of epithelial to mesenchymal transition (EMT, a process that is highly relevant to tumor cell metastasis and drug resistance), induction of tumor specific antigen and antigen-specific T-cell cytotoxicity, enhancement of NK cell antitumor activity, induction of cancer stem cell differentiation, and resensitization of tumor cells that have become resistant to anticancer agents such as platinums, taxanes and topoisomerase II inhibitors. Chidamide has demonstrated clinical efficacy in pivotal phase II trials on cutaneous T-cell lymphoma (CTCL) and peripheral T-cell lymphoma (PTCL) conducted in China, and it is currently undergoing phase II trial in NSCLC together with first line PC therapeutic treatment. Due to its superior pharmacokinetic properties and selectivity, chidamide may offer a better clinical profile over the other HDAC inhibitors currently under development or being marketed.

GNTbm is a subsidiary of GNT Inc., a Taiwanese company focused on the manufacture of nanoscale metallic particles for food and medical purposes. Founded in 1992 by a team of electronic professionals, GNT has successfully developed the innovative technology of physical metal miniaturization based on the patent of molecular beam epitaxy (MBE). Further information about GNT Inc. is available at www.gnt.com.tw.

GNTbm was established in August 2013 and housed in the Nankang Biotech Incubation Center (NBIC) in Nankang, Taipei. Led by Dr. Chia-Nan Chen along with an experienced team of scientists, GNTbm will explore development and commercialization of novel drug delivery systems, and innovative biomedical and diagnostic tools based on gold nanoparticles.

MedPharm Aims High with New £0.5M U.K. GMP Facility

PRNewswire: October 8, 2013 – GUILDFORD, England – MedPharm Ltd. (www.medpharm.co.uk), the topical and transdermal formulation development specialist, today announced the opening of a new £0.5m GMP facility in Guildford as it strives to double turnover and increase market share over the next 5 years.

Dr. Andrew Muddle, CEO, commented: "The opening of the new site is a huge milestone for our business. We can now offer a true one stop shop for formulation development, all provided in house. From a commercial perspective, we are very much open for business and have already received significant interest from companies looking to use our manufacturing capabilities to assist with their clinical trial requirements. In particular, the bespoke clinical trials supplies production facility, regulated by state-of-the-art monitoring systems, will provide clinical manufacturing capabilities designed to handle a range of nonsterile dosage forms. These include liquids, semisolid gels, creams, and ointments, as well as inhaled products, sprays, and transdermal patches to name but a few."

The investment adds a new microbiology laboratory, clean room suites, a dedicated ICH stability testing area, and quality control and performance testing laboratories to support phase I and II clinical manufacture. The facility also allows for the manufacture of highly potent compounds up to OEB 4 level with a manufacturing batch scale of up to 50 kg and primary packaging, labelling, and randomisation services.

"This new capability allows MedPharm to ensure a smooth transfer from development and preclinical studies to clinical manufacturing by taking all the services in house on one site. This has the potential to significantly decrease project time lines and costs for clients," added MedPharm's CSO and COO, Prof. Marc Brown.

In the News continued on page 28

In the News continued from page 27

MedPharm's aim is to continue to build on its reputation as a specialist transdermal and topical pharmaceutical development company concentrating on the development and commercial exploitation of specialist products for dermatology and other topical and transdermal indications. More information can be found at www.medpharm.co.uk.

Experimental Therapeutics Centre and Debiopharm Group™ to Collaborate for the Development of an Epigenetic Innovative Oncology Target

PRNewswire: October 7, 2013 – SINGAPORE and LAUSANNE, Switzerland – The Agency for Science, Technology and Research (A*STAR)'s Experimental Therapeutics Centre (ETC), a center of excellence to advance and accelerate drug discovery in Singapore, and Debiopharm Group™ (Debiopharm), the Swiss-based global biopharmaceutical company that focuses on the development of prescription drugs that target unmet medical needs including oncology as well as companion diagnostics, today announced the signature of an exclusive research collaboration to develop oral small molecules targeting a new class of epigenetic modulators.

Under the terms of the agreement, Debiopharm and ETC will co-finance the discovery phase of the project, while Debiopharm will be in charge of development.

"This partnership aims to target tumors with genetic lesions. The use of epigenetic targets is emerging as an effective and valuable approach for personalized medicine strategies for cancer treatment," said Andres McAllister, chief scientific officer, research and evaluation, Debiopharm International SA. "ETC represents the perfect partner to develop this project, as they are experts in the field of oncology and possess the full range of drug discovery capabilities. Their situation within the Biopolis campus is a major asset for the development of new products."

ETC is directed by Prof. Alex Matter, who has a highly successful track record within the pharmaceutical industry. He was the global head of oncology research for Novartis Pharmaceuticals Corporation, and he played an important role in the success of several anticancer drugs, including Gleevec/Glivec® and more recently Tasigna®.

Prof. Matter was joined at ETC by a panel of seasoned industry colleagues and has put together a team of experts dedicated to the discovery and development of new medicines. According to Prof. Alex Matter, CEO, Experimental Therapeutics Centre, A*STAR: "This joint research collaboration will give both partners the opportunity to leverage on each other's strengths, with the objective of creating new and more effective treatments against cancer."

Rolland-Yves Mauvernay, president and founder of Debiopharm Group™, added: "We are very excited to be collaborating with ETC, top oncology and drug discovery experts. This partnership strengthens our presence in Asia in a highly dynamic area for innovation when it comes to the development of new drugs. Furthermore, this collaboration is in line with our strategy focusing on patients' outcomes by offering more targeted oncology therapies."

ETPL, the technology transfer arm of A*STAR, fosters strategic collaborations and deals between academia and industry. ETPL bridged the interests of ETC and Debiopharm and accelerated the research agreement and licensing deal between both parties in an effort to encourage more of such public-private partnerships.

September

Intersect ENT Announces Positive Results from a Pilot Study of Novel In-Office Implant for Chronic Sinusitis Patients

Business Wire: September 30, 2013 – MENLO PARK, CA, U.S.A., and VANCOUVER, BC, Canada – Intersect ENT, Inc., an innovator in treatment solutions for ear, nose, and throat clinicians and their patients, today reported findings from a prospective U.S. multicenter pilot study to evaluate the feasibility, safety, and efficacy of the company's newest steroid delivery implant for patients suffering from the debilitating symptoms of chronic sinusitis. Results were presented at the annual American Rhinologic Society Meeting in Vancouver, Canada, and were recognized by the society with the Cottle Award for Best Clinical Science Research.

Intersect ENT's new drug-eluting implant, which is placed during a routine physician office visit, is designed as a treatment alternative for patients with recurrent sinus obstruction. Like the company's PROPEL® and PROPEL® mini implants used in conjunction with sinus surgery to improve surgical outcomes, the product releases mometasone furoate, an advanced steroid with anti-inflammatory properties, directly into the sinus lining, then dissolves. The implant has more radial strength than the PROPEL products in order to dilate the obstructed sinus and releases the steroid over a longer period of time.

"The results from the pilot study are highly promising, demonstrating feasibility of this novel in-office solution for patients suffering from chronic sinusitis," said Francois Lavigne, M.D., FRCSC, adjunct professor of the University of Montreal and director of Institut ORL in Montréal, Quebec, Canada. "Patients experienced dramatic improvement in symptoms through the six-month follow-up period, and the vast majority of patients were able to avoid the need for costly revision surgery or oral steroids, which can have serious side effects."

Patients who had prior sinus surgery but experienced recurrent disease refractory to medical therapy were treated and then followed for six months. At three months, the mean ethmoid sinus obstruction was significantly reduced by 43%, from 66% obstruction at baseline to 21% obstruction ($p = 0.0002$). The reduction was sustained through six months ($p < 0.0001$). Statistically significant reductions in polyp grades and patient symptom scores were also observed, and the results were

sustained through six months. Use of the implant eliminated the need for revision surgery in 64% of patients.

"The results of the pilot study confirm the potential of our office-based product, which is designed to be a less-invasive, more cost-effective treatment alternative for chronic sinusitis patients facing another surgery," said Lisa Earnhardt, the company's president and CEO. "The larger randomized RESOLVE study, which is currently enrolling patients, will provide additional evidence regarding the clinical and economic benefits of the technology."

Intersect ENT Inc., located in Menlo Park, California, is an innovator in local drug delivery focused on advancing clinically proven therapy solutions that improve quality of life for patients with ear, nose and throat conditions. The company's initial products, the PROPEL and PROPEL mini dissolvable steroid-releasing implants, are the only products backed by level 1-A clinical evidence to improve sinus surgery outcomes for patients suffering from chronic sinusitis. Chronic sinusitis is a common condition that affects one out of seven adults in the United States and greatly impacts quality of life. The company holds 21 issued U.S. patents and more than 80 patents and pending applications worldwide. Intersect ENT is backed by Kleiner Perkins Caufield & Byers, U.S. Venture Partners, PTV Sciences, Norwest Venture Partners, and Medtronic. For more information, please visit www.intersectENT.com.

ProStrakan Launching SANCUSO (Granisetron Transdermal System) in European Union with 3M Drug Delivery Systems as Manufacturer

Business Wire: September 30, 2013 – ST. PAUL, MN, U.S.A. – The European Medicines Agency (EMA) has granted approval for ProStrakan Group plc to market SANCUSO® (Granisetron Transdermal System) in the European Union (EU), with 3M Drug Delivery Systems acting as the manufacturer. ProStrakan begins marketing the product this month in the United Kingdom, Germany, and the Netherlands. Additional European countries are expected to be added in 2014.

Initially introduced in the United States in 2008, SANCUSO is the first and only treatment for chemotherapy-induced nausea and vomiting that does not require pills or intravenous (IV) administration. The transdermal patch is applied to the upper arm and can be worn for seven days, providing continuous transdermal delivery and eliminating the need to take pills daily to control nausea and vomiting. This simple-to-use treatment has been proven effective in patients at risk for chemotherapy-induced nausea and vomiting.

"SANCUSO is a great illustration of the patient-friendly benefits of transdermal treatment," said Jim Ingebrand, president and general manager, 3M Drug Delivery Systems. "We look forward to a continued partnership with ProStrakan to bring SANCUSO to new markets."

3M Drug Delivery Systems is applying more than 30 years of transdermal experience and regulatory expertise to its manufacturing responsibilities for SANCUSO. The company's cGMP compliant manufacturing and strength in global supply chain management ensure reliability and a smooth process from start to finish for manufacturing partners.

"SANCUSO is already proving to be an important option for patients in the United States suffering from chemotherapy-induced nausea and vomiting," said Jamie Blackport, senior vice president of international marketing at ProStrakan. "We are excited about working together with 3M to bring this important treatment to patients in the EU." While ProStrakan has previously relied on a different manufacturer for the U.S. supply of SANCUSO, FDA approval is currently pending for the 3M Drug Delivery Systems manufactured product.

Aequus Pharmaceuticals Inc. Closes on C$1.2 Million in Equity Financings and In-Licenses Global Rights to Intellectual Property Enabling the Transdermal Delivery of Aripiprazole

Business Wire: September 26, 2013 – VANCOUVER, BC, Canada – Aequus Pharmaceuticals Inc., a life sciences company specializing in transdermal reformulations of existing and approved drugs that address the difficult clinical problems of side effects and patient compliance, announced today the closing of its first round of external financing.

"With this amount raised, we are excited to further the development of our proprietary long-acting, transdermal application of aripiprazole, the world's largest selling antipsychotic in its branded oral form. Over the coming months we expect to initiate human proof of concept studies and begin filing new intellectual property on additional pipeline projects," said Doug Janzen, president, director, and cofounder of Aequus Pharmaceuticals. "The amount raised was split equally between sophisticated investors from Canada and the United States, and we are pleased to welcome all of our new shareholders to this exciting new venture."

At the time of closing, Aequus finalized an exclusive, worldwide in-licensing deal of intellectual property enabling the transdermal application of aripiprazole from New York based laboratory Transdermal Research Pharm Laboratories, LLC.

Many widely used oral and injectable psychiatric and CNS medications have existing problems in convenience, side-effects, and compliance. A transdermal version has the potential to provide a well-tolerated long-acting alternative. Furthermore, a transdermal vehicle has the benefit of reversibility compared to long-acting injectables, which when given, adverse effects cannot be reversed.

"Our business model is centered upon identifying approved medications that could benefit from enhanced drug-delivery systems, including transdermal, thereby addressing currently unmet medical needs," said Mr. Janzen. "By reformulating approved products with known safety and efficacy profiles, we can pursue an accelerated regulatory pathway with the FDA and

In the News continued on page 30

In the News continued from page 29

other international regulatory bodies, minimizing the development costs, timelines, and risks. We anticipate that this will provide a more rapid and consistent return on investment compared to traditional drug development models."

Aequus's team has combined world-class expertise and know-how in drug development and transdermal delivery with clinical experience in treating patients with psychiatric and CNS disorders and management experience in financing and advancing growth companies.

Naloxone Nasal Spray on Development Fast Track as Emergency Treatment for Opioid Overdose

Business Wire: September 20, 2013 – LEXINGTON, KY, U.S.A. – AntiOp, Inc., a Kentucky company headed by a renowned expert in nasal delivery of medication, says its nasal spray could save the lives of thousands of narcotic pain medication and heroin overdose victims and that the Food and Drug Administration (FDA) has specified the final research requirements necessary for approval of the drug. With sufficient funding, AntiOp, Inc., says, its naloxone nasal spray could be on the market in about 18 months.

"The FDA has been very encouraging of our approach," said AntiOp founder and CEO Dr. Daniel Wermeling. "Once we file a new drug application, they plan to complete a priority review of our product, which usually takes about six months."

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

Overdosing of prescription pain medications known as opioids has reached epidemic proportions, according to the Centers for Disease Control and Prevention (CDC). The CDC's most recent data point to some 16,500 deaths in the United States each year from prescription opioids. Studies have shown that approximately 800,000 ambulance runs occur each year in the United States in response to suspected opioid overdoses, involving both prescription medications and heroin. Commonly prescribed opioid painkillers include hydrocodone, methadone, oxycodone, and oxymorphone.

Naloxone is already stocked in thousands of emergency rooms, ambulances, and postsurgery recovery rooms but in an injectable form. It must be administered intravenously or as a shot into muscle or under the skin. Because many heroin abusers carry hepatitis or the HIV virus, the risk of infection to medical personnel is high. Some emergency responders use atomizers to convert the injectable form of naloxone to a nasal spray. Wermeling and others believe a nasal spray version of naloxone will prove to be effective, safer, and easier to administer than the current injection-based approach.

In fact, the Substance Abuse and Mental Health Services Administration suggested in August that physicians should consider coprescribing naloxone to patients for whom they prescribe significant levels of opioids and have at least one risk factor for overdose.

AntiOp's solution is a single-dose, disposable naloxone nasal spray that combines a commercially marketed and proven nasal spray device with a stable, concentrated naloxone solution specifically formulated for nasal delivery. The company filed an investigational new drug (IND) application in 2012, and data were subsequently submitted to the FDA. In response, the FDA this year provided AntiOp with a clear regulatory path to approval.

Testing continues and the FDA will waive the usual $2 million new drug application fee. Efficacy and toxicology studies are not required since naloxone is already on the market. Wermeling said the company is seeking an additional $5 million–$7 million to accelerate the development of the spray and be the first on the U.S. market.

Karl Sporer, professor emeritus at the University of California, San Francisco, Department of Emergency Medicine, said he expects AntiOp's naloxone spray will perform better than the existing standard of care—an injection or nasal spray via atomizer device—for opioid overdoses. Sporer, a consultant to AntiOp, is an emergency physician who managed three emergency medical systems over 14 years in San Francisco and Northern California.

"We have strong support for our approach from a number of crucial stakeholders," Wermeling said. "We're very confident that our approach will prove to be highly effective and will soon become the standard of care in opioid overdose situations."

AntiOp, Inc., is a specialty pharmaceutical company working to develop naloxone nasal spray for the treatment of suspected opioid overdose. Founder and CEO Dr. Daniel Wermeling is a professor of pharmacy at the University of Kentucky and has published extensive research on nasal drug delivery. He holds patents on pharmaceutical products and delivery systems, many of which are in active clinical development as investigational new drugs.

Orexo Announces the Approval of Abstral® in Japan

Business Wire: September 20, 2013 – UPPSALA, Sweden – Orexo AB (STO: ORX) today announced the approval of Abstral® (fentanyl) sublingual tablets in Japan, where the product has been registered and will be sold by Kyowa Hakko Kirin Co., Ltd. Based on the agreement, the approval will trigger a milestone payment to Orexo.

Kyowa Hakko Kirin and its subsidiaries have the rights for Abstral in all markets except the United States, where the rights are held by Galena Biopharma, Inc. In Japan, Abstral will be distributed jointly by Kyowa Hakko Kirin and Hisamitsu

Pharmaceutical Co., Inc. The two companies are well established in the field of treatment of cancer pain. Kyowa Hakko Kirin and Hisamitsu Pharmaceutical are jointly selling Fentos® tape (fentanyl citrate transdermal absorption product) since June 2010.

"With this approval, Abstral has now successfully been developed in the three major pharmaceutical markets in the world. The approval in Japan demonstrates again the capability of our organization as well as the value recognized by the regulatory authorities from new and advanced pharmaceutical sublingual formulations that improve treatment of patients. The approval in Japan is an exciting opportunity for Abstral and for Orexo, and we are convinced that Kyowa Hakko Kirin is well positioned to successfully launch Abstral in Japan," said Nikolaj Sørensen, president and CEO of Orexo.

BioTime Signs Exclusive Agreement with Jade Therapeutics for Ophthalmic Drug Delivery Applications of HyStem® Technology

Business Wire: September 19, 2013 – ALAMEDA, CA, U.S.A. – BioTime, Inc. (NYSE MKT: BTX), a biotechnology company that develops and markets products in the field of regenerative medicine, today announced the signing of an exclusive sublicense agreement with Jade Therapeutics, Inc., a Salt Lake City-based developer of ophthalmic sustained-release drug delivery platforms. This new agreement supersedes the previously announced sublicense and supply agreements and expands the licensed "field of use" to include certain additional uses, such as the use of BioTime's HyStem® hydrogel technology for the delivery of all potential therapeutic molecules to the human eye. Excluded from the licensed field of use is the use of the HyStem® technology for the delivery of cells with or without any molecules necessary for the therapeutic benefit of those cells, for use in making punctal plugs, for diagnostic and research reagents, and for nonhuman applications. Jade's lead products in preclinical development utilize the licensed hydrogel technology to facilitate time-release, topical delivery of recombinant human growth hormone to help heal lesions on the ocular surface, as well as enable local delivery of antibiotics to treat ocular infections. Financial terms of the transaction were not disclosed.

William P. Tew, Ph.D., BioTime's chief commercial officer, stated that "we are pleased to have expanded our relationship with Jade Therapeutics and look forward to their efforts to develop novel ophthalmic drug delivery applications for our HyStem® hydrogel platform."

Said Jade CEO Arthur Klausner, "We have evaluated a variety of potential polymer-based drug delivery systems, and we believe that HyStem® hydrogels provide an excellent combination of the required physical properties to enable broad ocular use. We will also benefit significantly from the extensive preclinical work that BioTime has performed on its hydrogels outside the field of ophthalmology."

"Our HyStem® technology has potential utility in a wide array of human therapeutic products," said Michael West, Ph.D., BioTime's CEO. "Following up on the Jade agreement, we intend to seek additional industry partners for applications that are not core to our own therapeutic product development."

BioTime's HyStem® hydrogels are proprietary biocompatible hydrogels that can be used to deliver localized doses of small molecules, proteins, or cells. HyStem® hydrogels also can mimic the human extracellular matrix, a web of molecules surrounding cells that is essential to cellular growth. BioTime's HyStem® hydrogels are currently being used by researchers at a number of leading medical schools in studies of stem cell therapies for facilitating wound healing and for the treatment of ischemic stroke, brain cancer, vocal fold scarring, and cardiac infarct.

Mystic Pharmaceuticals Receives Multiple U.S. Patent Office Notices of Allowance on Drug Delivery Platform Technologies

Business Wire: September 17, 2013 – AUSTIN, TX, U.S.A. – Mystic Pharmaceuticals, Inc., an integrated specialty pharmaceutical company, announced today it has received two Notices of Allowance from the U.S. Patent Office for its "unit dose drug delivery platform" (serial number 12/851,524) and piercing device for drug delivery systems (serial number 13/149,584) patent applications. These patents expand Mystic's novel VersiDoser® and VRx2™ delivery platforms enabling the development of patient-centric pharmaceutical products. Mystic is applying its innovative delivery technology to develop therapeutics for the treatment of ocular, CNS, neurodegenerative, and infectious diseases affecting large global populations.

Mystic's president and CEO, Timothy Sullivan, stated that "there is a power shift in the pharmaceutical industry from product-oriented to patient-oriented products that deliver better health outcomes. Over the past decade Mystic has innovated packaging and delivery technologies that enable the development of patient-centric pharmaceutical products. These latest innovations further expand our capabilities to enhance the patient experience by making pharmaceutical products that are safer, easier, and more convenient to use."

The shift to patient-centric product development strategies by pharmaceutical manufacturers will benefit the consumer through improved compliance and health outcomes while building brand value for the manufacturer. Utilizing Mystic's delivery platform technologies, pharmaceutical and biotech manufacturers can extend or establish market exclusivity and competitive differentiation for new or existing drugs and biologics. Mystic's delivery platforms and products are designed to meet the diverse demands of consumers and pharma manufacturers in the globally competitive market.

Mystic Pharmaceuticals™ is an integrated specialty pharmaceutical company based in Austin, Texas. Mystic provides patient-centric pharmaceutical products and delivery technology and for pharmaceuticals, biopharmaceuticals, and biologics for

In the News continued on page 32

In the News continued from page 31

intranasal, ophthalmic, sublingual, and otic applications. Mystic combines its novel delivery systems with pharmaceuticals and biologics under development by Mystic and its partners, to meet the expanding global market demand for healthcare products that are safer, simpler to use, and cost effective. For more information, please visit the Mystic website: www.mysticpharmaceuticals.com.

Oramed's Platform Technology in Oral Delivery of Proteins Receives Patent in Russia

PRNewswire: September 17, 2013 – JERUSALEM, Israel – Oramed Pharmaceuticals Inc. (NASDAQCM: ORMP) (www.oramed.com), a developer of oral drug delivery systems, announced today that it has been granted a patent from Russia's Federal Service for Intellectual Property, Patents and Trademarks (ROSPATENT) for the company's invention, titled "Methods and Compositions for Oral Administrations of Proteins." The patent covers a core concept of the company's technology for the oral delivery of drugs currently delivered via injection. Oral delivery can greatly improve patient compliance and outcomes.

Access Pharmaceuticals Awarded Second European Patent for MuGard

PRNewswire: September 12, 2013 – DALLAS, TX, and NEW YORK, NY, U.S.A. – Access Pharmaceuticals, Inc. (OTCBB: ACCP), an emerging biopharmaceutical company, has received notification from the European Patent Office that an additional European patent for MuGard™ has been granted. The patent (EP1997478) protects a wide range of liquid formulations for the prevention and treatment of mucosal diseases and disorders. Notification of the grant was published in the European Patent Bulletin no. 13/36 earlier this month.

"This second patent for MuGard in the EU provides us with additional protection of the mucoadhesive liquid technology that forms the basis of MuGard," noted Dr. David Nowotnik, senior vice president research and development, Access Pharmaceuticals, Inc. "The new patent also provides us with additional protection of formulations that could form the basis of potential MuGard line extension products."

MuGard provides the oral mucosa with a thin protective hydrogel layer that has been demonstrated in several clinical studies of mucositis to benefit patients in terms of reduced pain and discomfort as well as a reduction in objective mucositis scores.

"Our new patent in Europe expands and strengthens our MuGard patent portfolio, and we anticipate that current and future formulations of MuGard might also benefit patients with various other ulcerative conditions with the oral cavity such as oral lichen planus," commented Jeffrey Davis, president and CEO of Access. "We continue to actively seek a European marketing partner for MuGard, where MuGard has achieved market clearance and is indicated for the prevention and management of oral mucositis."

MuGard™ mucoadhesive oral wound rinse is an oral mucoadhesive that is designed to manage oral mucositis by forming a protective hydrogel coating over the oral mucosa to shield the membranes of the mouth and tongue. In Europe, MuGard is indicated for the prevention of oral mucositis/stomatitis (that may be caused by radiotherapy and/or chemotherapy) and all types of oral wounds (mouth sores and injuries), including aphthous ulcers/canker sores and traumatic ulcers, such as those caused by oral surgery or ill-fitting dentures or braces.

Access Pharmaceuticals, Inc., is an emerging biopharmaceutical company that develops and commercializes proprietary products for the treatment and supportive care of cancer patients. Access developed MuGard, a prescription oral rinse for the management of mucositis and is developing multiple products, and recently licensed U.S. commercialization rights to AMAG Pharmaceuticals, Inc. Access also has other advanced drug delivery technologies including CobaCyte™-mediated targeted delivery and CobOral-oral drug delivery, its proprietary nanopolymer delivery technology based on the natural vitamin B12 uptake mechanism. For additional information on Access Pharmaceuticals, please visit our website at www.accesspharma.com.

HedgePath Pharmaceuticals Enters into Key Collaboration with Mayne Pharma

PRNewswire: September 10, 2013 – TAMPA, FL, and SAN DIEGO, CA, U.S.A. – HedgePath Pharmaceuticals, Inc. (OTCPink: HPPI) (HPPI), announced today that it has signed an exclusive supply and license agreement with Mayne Pharma International Pty. Ltd. (Mayne Pharma), a wholly owned subsidiary of Mayne Pharma Group Limited, an Australian ASX listed company, whereby HPPI will pursue clinical development of Mayne Pharma's patented formulation of the drug itraconazole, known as SUBA-Itraconazole, for treatment of a variety of cancers with a focus on seeking regulatory approvals and marketing in the United States.

The agreement represents a significant step forward for HPPI in the progression of its business plan of repurposing itraconazole as a potential treatment for cancer. Itraconazole, in other formulations now off-patent, is already approved by the U.S. Food and Drug Administration (FDA) for human use as a treatment for fungal infections.

The agreement provides for the supply to HPPI of specially formulated capsules of SUBA-Itraconazole, manufactured by Mayne Pharma under cGMP (current good manufacturing practice) standards, for use by HPPI in its anticipated clinical trials and for the future exclusive commercial supply following FDA approvals, if obtained. "SUBA technology" (which stands for "super bioavailability") is designed to improve the bioavailability of orally administered drugs that are poorly soluble. SUBA-Itraconazole is a patented formulation developed by Mayne Pharma, which has improved absorption and

significantly reduced variability compared to generic itraconazole. These benefits provide enhancements to patients and prescribers with reduced intra- and interpatient variability, enabling a more predictable clinical response and a reduction in the active drug quantity to deliver the required therapeutic blood levels.

HPPI and Mayne Pharma will collaborate through a joint development program for SUBA-Itraconazole for multiple oncology indications. Under the agreement, HPPI has been granted exclusive rights to SUBA-Itraconazole for treatment of cancer in the United States, and Mayne Pharma retains rights for use of the drug outside the United States, including a license from HPPI for current and future developments of anticancer therapies using SUBA-Itraconazole.

"This is a milestone event for HPPI, and we are very pleased to be collaborating with an innovative developer and manufacturer such as Mayne Pharma," stated Nicholas J. Virca, HPPI's president and chief executive officer.

"Our clinical strategy is to repurpose itraconazole as a potential treatment for cancer, and we believe that Mayne Pharma's patented formulation of itraconazole creates the potential to offer cancer patients the benefits of greater bioavailability of the active drug. In short, this agreement is more than just a supply agreement. It jumpstarts our business plan by giving us access to the key technology we need to progress our clinical development programs forward and, if ultimately approved by the FDA, market our anticancer therapies in the United States with exclusivity. We look forward to what we expect will be a long-term and mutually beneficial collaboration with Mayne Pharma," concluded Mr. Virca.

SUBA™ technology is proprietary technology that improves the oral bioavailability of poorly soluble drugs. It utilizes a solid dispersion of drug in a polymer to improve the absorption of drugs in the gastrointestinal tract to achieve "super bioavailability" compared to conventional formulations. In testing its use as an antifungal medication, clinical trials demonstrated that SUBA-Itraconazole had approximately double the bioavailability of the generic formulation and could be taken with or without meals. HPPI plans to administer SUBA-Itraconazole at doses lower than the generic itraconazole formulations previously tested in human cancer trials. This greater bioavailability at lower dosing is intended to improve product performance, while reducing the side-effects associated with the level of doses required for cancer therapy.

Oramed Granted Patent in China for Its Platform Technology in Oral Delivery of Proteins

PRNewswire: September 10, 2013 – JERUSALEM, Israel – Oramed Pharmaceuticals Inc. (NASDAQCM: ORMP) (www.oramed.com), a developer of oral drug delivery systems, announced today that it has received approval for a key patent from the State Intellectual Property Office of the People's Republic of China.

The patent, titled "Methods and Compositions for Oral Administrations of Proteins," covers a core concept of the company's technology. The patent has also been granted in New Zealand and South Africa. Oramed's portfolio now consists of eight issued patents and 27 patents pending.

According to a report by McKinsey & Company, China's healthcare sector is growing at an accelerated rate, with healthcare spending projected to grow from $357 billion in 2011 to $1 trillion by 2020.

"Our platform technology in the oral delivery of proteins applies to numerous treatment markets in geographies around the globe. China is a very important market for both our ORMD-0801 and ORMD-0901 technologies," stated Oramed CEO Nadav Kidron. "As an innovative company committed to discovery, we are pleased to see our IP portfolio expand."

Oramed Pharmaceuticals is a technology pioneer in the field of oral delivery solutions for drugs and vaccines currently delivered via injection. Established in 2006, Oramed's technology is based on over 30 years of research by top research scientists at Jerusalem's Hadassah Medical Center. Oramed is seeking to revolutionize the treatment of diabetes through its proprietary flagship product, an orally ingestible insulin capsule (ORMD-0801) currently initiating phase 2 clinical trials on patients with type 2 diabetes (T2DM) under an Investigational New Drug application with the U.S. Food and Drug Administration, and with its oral exenatide capsule (ORMD-0901; a GLP-1 analog), with trials on healthy volunteers (phase 1b) and T2DM patients (phase 2a) underway. Oramed is also moving forward with clinical trials of ORMD-0801 for the treatment of type 1 diabetes. The company's corporate and R&D headquarters are based in Jerusalem. For more information, please visit www.oramed.com.

Camurus Receives Option-Exercise Milestone for Octreotide FluidCrystal® Product CAM2029

PRNewswire: September 10, 2013 – LUND, Sweden – Camurus announced today that Novartis has exercised its option to acquire an exclusive license for the further development and worldwide commercialization of CAM2029 for treatment of patients with acromegaly and neuroendocrine tumors (NETs). The license also covers additional future products based on the Camurus FluidCrystal® injection depot technology.

The option exercise is the next stage in the collaboration, option, and license agreement between Novartis and Camurus executed in December 2011. It triggers an undisclosed milestone payment to Camurus from eligible potential payments of up to US$700 million, subject to achievement of predefined development, regulatory, and commercial milestones for the products included in the agreement. In addition, Camurus is entitled to royalties on global product sales.

In the News continued on page 34

In the News continued from page 33

CAM2029 is a novel, long-acting octreotide product that has been developed by Camurus with the goal of easy subcutaneous administration in the treatment of patients with acromegaly and NETs. CAM2029 has received orphan drug designation by EMA for the treatment of acromegaly and has been studied in three clinical phase I trials, assessing pharmacokinetics, pharmacodynamics, and safety after single and repeat dosing. Following the option exercise, Novartis will assume responsibility for further clinical development of CAM2029, including any phase III studies, product registration, and worldwide commercialization.

"We are very proud of the successful development of our collaboration and look forward to continue assisting Novartis in the clinical development and registration efforts for CAM2029," says Fredrik Tiberg, president and CEO of Camurus. "Novartis's decision to acquire full commercialization rights to CAM2029 and related products is a key milestone for Camurus that further validates our advanced delivery technologies and clinical product development capacity. Novartis's continued investment in this program strengthens our strategic relationship and enables Camurus to expand its proprietary pipeline of new and innovative therapies for serious diseases."

CAM2029 is a novel, ready-to-use, long-acting octreotide product for treatment of acromegaly and neuroendocrine tumors (NETs) based on Camurus's proprietary FluidCrystal® delivery system. Octreotide chloride, the active ingredient of CAM2029, is a synthetic, cyclic octapeptide, an eight amino acid analogue of the peptide hormone somatostatin. The CAM2029 product is designed for easy and patient-friendly drug administration. While traditional depot therapeutics frequently comprise complex microsphere technology for intramuscular injection, Camurus's FluidCrystal® depot allows for subcutaneous injection of a small volume liquid that transforms into a biodegradable liquid crystal gel at the site of injection. Thereby, the drug compound is effectively encapsulated, providing rapid onset and long-acting octreotide release.

Mylan Announces Completion of Transdermal Patch Facility Expansion Project in St. Albans, Vermont

PRNewswire: September 4, 2013 – ST. ALBANS, VT, U.S.A. – Mylan Inc. (Nasdaq: MYL) today announced the completion of an 85,000 square foot, three-story expansion project at its transdermal patch facility, operated by Mylan Technologies Inc. (MTI), in St. Albans, Vermont. Through Mylan's investment, including funding for expanded research and development (R&D) capabilities and additional manufacturing and laboratory space, the company is in the process of adding more than 160 new positions to its St. Albans-based workforce. MTI is a proven leader in transdermal drug delivery systems—patches that deliver medication through the skin—and related technologies.

In conjunction with the expansion project, Mylan today hosted a ribbon-cutting ceremony to commemorate the occasion. Vermont Governor Peter Shumlin as well as a number of local officials, community members, and employees attended the event.

Mylan CEO Heather Bresch said: "Mylan's investment in the ongoing growth of our transdermal franchise demonstrates our continued commitment to and confidence in our ability to provide complex generic and interchangeable products and innovative delivery alternatives, such as transdermals. Through this expansion, MTI will continue to play a critical role in the expansion and diversification of Mylan's global product portfolio, especially when it comes to difficult-to-develop and -manufacture products. I would like to thank Governor Shumlin as well as the city of St. Albans for their ongoing support of this project. Importantly, I would also like to recognize Mylan's more than 590 employees in Vermont for their hard work and dedication to our continued success."

The 14-month expansion project has increased MTI's total operating space to more than 391,000 square feet. Since becoming a part of the Mylan manufacturing network more than 20 years ago, MTI has developed a number of branded and generic transdermal products available to patients in markets around the world, including the United States, Canada, Europe, Japan, New Zealand, and Australia.

August

Imprimis Acquires Intellectual Property from Novel Drug Solutions and Eye Care Northwest

PRNewswire: August 28, 2013 – SAN DIEGO, CA, U.S.A. – Imprimis Pharmaceuticals, Inc. (NASDAQ: IMMY), which is focused on the commercialization of drug formulations through a growing proprietary network of compounding pharmacy relationships and by utilizing the FDA 505(b)(2) development pathway, has announced it has acquired intellectual property, including a provisional patent application, related to an ophthalmic compound for intraoperative ocular injection of anti-inflammatory and antibacterial agents. Imprimis believes this formulation has the potential to significantly impact the fast-growing $5 billion global cataract surgery drug market. The acquisition allows Imprimis to pursue the commercial development of certain proprietary innovations and also provides Imprimis with a preemptive right on additional Novel Drug Solutions and Eye Care Northwest intellectual property and drug development opportunities.

Imprimis CEO Mark L. Baum said, "This is an important acquisition of a novel drug formulation with an important clinical track record. It is gratifying to see our Asset Review Methodology (ARM™) at work. We believe that going forward our growing group of drug discovery and development relationships will bring additional clinically relevant formulations to our company, and these assets will drive additional value for our shareholders. We are in the process of conducting a feasibility assessment related to the development of this asset, together with a team that consists of leaders from the ophthalmic development and regulatory community. Imprimis will continue to develop partnerships with inventors and secure assets that will support our strategic objectives."

The target compound, referred to as IPI-140, is based on a novel combination of moxifloxacin and triamcinolone. IPI-140 was coinvented by Novel Drug Solutions of Randolph, New Jersey, and Dr. Jeffrey T. Liegner of Sparta, New Jersey. IPI-140 has been successfully administered by Dr. Liegner in more than 1,500 patients in his surgical practice.

Dr. Liegner stated, "The current treatment regimen for the prevention of post-cataract surgery complication is primarily a preoperative and postoperative self-administered eye drop regimen, which requires from the patient strict compliance and careful adherence to a prescribed dosing schedule. Individuals with physical limitations, impaired manual dexterity, or those who lack of a supportive caregiver, are particularly vulnerable to noncompliance and the subsequent complications of untreated postsurgical issues. This uniquely designed drug, utilizing a fourth generation quinolone therapy combined with potent inflammatory suppression, when placed as a depot inside the vitreous concurrent with cataract surgery, or any intraocular procedure, addresses the primary ocular complications of ophthalmic surgery: infection risk and postoperative inflammation."

Imprimis believes that IPI-140 may have broad application in ophthalmic surgery, including the $5 billion global cataract surgery drug market. According to Ocular Surgery News, the cataract surgery market continues to grow tremendously not only because of the expanding aging population, but because the age at which patients demand cataract surgery has lowered, portending a global market size of $7 billion to $9 billion in the next 5–7 years. Imprimis expects to continue to leverage its exclusive relationships with Novel Drug Solutions, Eye Care Northwest, and others to acquire assets with a proven clinical track record.

Emerging Animal Health Companies Pitch Today at KC Animal Health Investment Forum

PRNewswire: August 27, 2013 – KANSAS CITY, MO, U.S.A. – The world's only full-day investment forum exclusively for emerging animal health companies takes place today in Kansas City. Thirteen early and mid-stage companies from 11 states, Belgium, and Japan are presenting to investors at the KC Animal Health Investment Forum. Presenters are seeking to raise between $500,000 and $20 million in funds and have revenue projections of $20 million within 5–7 years.

"We have never had the opportunity to present this many good candidates to the audience," said Chris Ragland, CEO of Animalytix LLC, who served on the selection committee. "Presenting companies are in different segments and at varying development stages: venture, private equity, and traditional manufacturer opportunities are all included."

Presenting companies have developed a variety of innovative products for the animal health industry. These include protective and therapeutic gear for horses, lighting technology for production animal operations, and a detection strip for the diagnosis of periodontal disease in dogs.

"The most important shift we have seen in the animal health sector over the past decade is the increasing reliance on smaller firms for core innovations," continued Ragland. "Larger firms are best at commercializing existing technology, but smaller firms are increasingly important for driving innovation."

Forum attendees include representatives from venture capital funds, investment firms, corporate R&D, and business development professionals. Companies presenting at the KC Animal Health Investment Forum previously have raised more than $90 million.

Known as the KC Animal Health Corridor, the Greater Kansas City area boasts the world's largest concentration of animal health industry assets, and Kansas City area companies account for approximately one-third of total sales for the global animal health market. "Support for emerging animal health companies is a top priority for the KC Animal Health Corridor and key to our goal to become the global epicenter of animal health innovation," said Kimberly Young, vice president of bioscience development for the Kansas City Area Development Council.

Presenting companies are:

- DS Pharma Animal Health Co., Ltd. – Osaka, Japan: drug delivery system for animals, http://animal.ds-pharma.co.jp
- Fetch Pharma – Bellevue, WA: canine biopharmaceutical product developer, www.fetchpharma.com
- KAVB Farm – Bend, OR: therapeutic gear for horses, www.idealequinegear.com
- Mobile Assay Inc. – Boulder, CO: diagnostic platform for animal health applications, www.mobileassay.com
- Napo Animal Health, Inc. – San Francisco, CA: product controlling diarrhea in animals, www.napopharma.com
- Okapi Sciences NV – Leuven, Belgium: antiviral drugs for companion animals and livestock, www.okapi-sciences.com
- Once Innovations – Plymouth, MN: lighting technologies for production animal facilities, www.onceteam.com
- PDX BioTech – Lexington, KY: detection strip for canine periodontal disease diagnosis, www.periodx.com
- PonyUp Technologies, Inc. – Dallas, TX: equine boot for biological data collection, www.ponyuptechnologies.com
- Prairie AquaTech – Brookings, SD: utilizes enzyme-producing fungus to develop protein replacement, www.prairieaquatech.com
- Prommune, Inc. – Omaha, NE: develops immune stimulant for animals
- VaxLiant, LLC – Lincoln, NE: develops animal vaccines
- Vital Herd, Inc. – Falmouth, ME: disease detector in cattle, www.vitalherd.com

In the News continued on page 36

In the News continued from page 35

Exosome Research Set to Clean Up with New Technology

PRNewswire: August 22, 2013 – CAMBRIDGE, England – Once thought to be just part of the cell's waste disposal system, it is now clear that exosomes also act as microscopic delivery bags, protecting RNA and protein contents that can then be transported in the blood, influencing the activity of distant cells.

Exosomes may be useful in cancer diagnostics and for drug delivery, transporting therapeutic RNA and DNA, manufactured in cells *in vitro*, to specific diseased cells. In some cases, exosomes mediate the benefits of stem cell therapy.

One of the major technical hurdles facing the exosome field is the efficient purification of intact exosomes. The gold standard for their purification is currently ultracentrifugation, which is time-consuming and inefficient. Commercially available exosome precipitants, used in a small number of labs, yield exosome preparations of relatively low purity, in which the precipitant remains as a contaminant.

Exo-spin™ kits for exosome purification, launched today by Cell Guidance Systems, overcome all of these shortcomings. Exo-spin™ is based on technology licensed from A*STAR in Singapore. Exo-spin™ kits are suitable for the preparation of pure, functional exosomes from a variety of biological fluids including blood plasma/sera, cell culture media, urine, and saliva.

Dr Michael Jones, CEO of Cell Guidance Systems, commented, "Talking to exosome researchers, it is clear that the current options for exosome purification have significant shortcomings. Exo-spin™ is a breakthrough in reliable purification of exosomes that will enable the entire field to move forward more rapidly." Exo-spin™ provides a gentle purification process in which no organic phases are used, no ultracentrifugation is employed, and the exosomes are purified free of precipitants in as little as one hour.

Cell Guidance Systems provides reagents and tools for stem cell science and related fields. From its Cambridge, U.K., headquarters, the company manufactures and supplies growth factors, small molecules and the Pluripro® culture system for the confluent growth of human pluripotent cells. The company also recently introduced the SINEUP™ gene expression technology for knock-up of endogenous genes and offers quality karyotyping services. For more info, see www.cellgs.com/exosomes. ■

CRS Headquarters & Staff

3340 Pilot Knob Road, St. Paul, MN 55121 U.S.A.
Telephone +1.651.454.7250 • Facsimile +1.651.454.0766
controlledreleasesociety.org

Amy Hope
Executive Vice President
+1.651.994.3827
ahope@scisoc.org

Barbara Mock
Vice President of Finance
+1.651.994.3829
bmock@scisoc.org

Susan Kohn
Executive Director
+1.651.994.3812
skohn@scisoc.org

Megan Pagel
Program Manager
• **News Capsules**
• **Webcasts**
Chapter Coordinator
+1.651.994.3854
mpagel@scisoc.org

Leah Barna
Meeting Manager
+1.651.994.3867
lbarna@scisoc.org

Linda Schmitt
Program Supervisor
• **Annual Meeting Program**
• **Awards**
+1.651.994.3828
lschmitt@scisoc.org

Sue Casey
Registration and Abstracts Meeting Coordinator
+1.651.994.3846
scasey@scisoc.org

Debby Woodard
Director of Development
• **Exhibits, Sponsorship**
• **Advertising Sales**
• **CRS Foundation**
+1.651.994.3817
dwoodard@scisoc.org

Cheryl Kruchten
Member Relations Specialist
+1.651.994.3801
ckruchten@scisoc.org

Kayleen Larson
Marketing Manager
+1.651.994.3840
klarson@scisoc.org

Brian Simdars
Webmaster
+1.651.994.3849
bsimdars@scisoc.org

Greg Grahek
Publications Director
+1.651.994.3841
ggrahek@scisoc.org

Carol Duling
***CRS Newsletter* Technical Editor**
+1.651.994.3869
cduling@scisoc.org

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

Calendar of Events

2014

Drug Delivery Partnerships
January 27–29
Boca Raton, FL, U.S.A.
www.iirusa.com/ddp

6th Training School on Bioencapsulation
March 4–7
Nha Trang, Vietnam
http://bioencapsulation.net/2014_Nha_Trang/

5th FIP Pharmaceutical Sciences World Congress
April 13–16
Melbourne, Australia
www.fip.org/pswc2014

International Microneedles Conference
May 19–21
Baltimore, MD, U.S.A.
www.international-microneedles.org/about.html

IWPCPS-16
June 16–19
Prague, Czech Republic
www.assainternational.com/workshops/iwpcps-16

41st Annual Meeting & Exposition of the Controlled Release Society
July 13–16
Chicago, IL, U.S.A.
controlledreleasesociety.org