CRS Leading Delivery Science and Technology

Newsletter

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What's Inside

CRS Newsletter

Leading Delivery Science and Technology

Vol. 29 • No. 2 • 2012

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

Communication

Welcome to the 2012 *CRS Newsletter* No. 2. This year has been predicted to be one of great significance by several accounts extending well into human history. The greatest of these may be an impending catastrophic destruction on December 21. (I encourage you all to get your research in before this deadline because there may be little chance for a grace period.) At the end, what is done is done, with perhaps little to show for it, depending on the manifestation of the destruction.

Think for a moment about the cumulative human energy that will have been spent at such a point—the gains in knowledge of our physical world and the ways we have organized elements of it to accomplish our goals. If all were lost, would it ever have existed, or is it like the beauty of a flower that blooms in a desert but is never witnessed?

What is it all for? Some believe that a person's whole purpose is to communicate with others. Inadequate communication is commonly a cause of failure.

This *CRS Newsletter* issue, like every issue, is about communication. It communicates the news surrounding CRS to you. It features the science of our work, the contributors to our causes, the events of our smaller groups, and the interactions of our members. I encourage you not only to read it but also to mentally digest it to reap its full value:

Pages 4 to 7 contain information about the upcoming CRS Annual Meeting & Exposition, a wonderful communication vehicle. Take note of the Vet and C&DP programs, educational workshops, networking opportunities, and the exposition.

Take a look at the Michelson Grant & Prize communications on pages 12 and 17. One of our greatest communication challenges involves the merging of funding resources with research energy and knowledge.

Note communications about the new CRS Preclinical Sciences & Animal Health Division on page 14 and the CRS journal *Drug Delivery and Translational Research* on page 16.

Chapter activity in Australia, New Zealand, Italy, and Germany is shared on pages 18 to 22 and in CRS President Martyn Davies's message to the right.

Continued thanks to Steven Giannos for his "In the News" communication regarding people, company, and regulatory activity on pages 23 to 36.

That is it for my communication here, but you can find a bit more on pages 8 to 11, and I will leave you with a parting thought. The doomsday elements above could leave one feeling a bit empty. Doomsday predictions have come and gone and will likely continue to come and go. Regardless of any potential for prediction accuracy, move forth in your sphere of influence as if it all matters, and it all matters in a big way. In the grandest example, perhaps what falls in your path and what you do with it could help prevent a catastrophic event that we may be moving toward. Think big and approach life with a controlled, nondestructive passion and purpose.

Communicatively,

Chuck Frey ■

Martyn C. Davies
University of Nottingham
Nottingham, United Kingdom

Chapters Build the Future

Modern-day science is by its very nature collaborative. Biomedical research illustrates this point, as it embraces the chemical, biological, engineering, medical, and physical sciences. Such multidisciplinary research knows no international boundaries. Participation in the collaboration should not be constrained by race, religion, or gender, and rather like time, it waits for no one. It has long been recognised that scientific research can provide remarkable opportunities for social mobility.

At the centre of such collaborative activity is the sharing of information that informs, trains, and educates others in recent developments in current research. Within the CRS, chapters play a key role in fostering the advancement of our science across the globe. They provide a valuable network for scientists in our field to hear the latest breakthroughs in science and recent innovations in technology outside the CRS Annual Meeting & Exposition. For many young scientists just starting out on their careers, the local chapter is the first face-to-face interaction with the CRS and is one of their first chances to present their work at a scientific meeting.

The CRS Board recognises this importance of the role of chapters and has approved funding for the Australian, Canadian, Germany, India, Israeli, Italy, New Zealand, Nordic, Taiwan, and United Kingdom and Ireland (UKICRS) Chapters to host local meetings that will be held throughout the year. Funding was also provided to student chapters in Connecticut, Illinois, and New Jersey, U.S.A., to support their activities. There is so much to admire about the commitment and drive of the local volunteer leaders in running a successful chapter. I was involved with a great group of people in setting up the UKICRS Chapter, and I know that so much hard work goes into making their meetings a success.

In February, I was fortunate to see two such meetings at first hand. I attended the 12th International Symposium of the CRS Indian Chapter, held in a beautiful location at the J. W. Marriott Hotel in Juhu Beach, Mumbai, whose organisation was led by Dr. Amarjit Singh and Professor K. K. Singh (chairpersons of the Organising Committee and the Scientific Committee, respectively). It was my first time to India, and I must admit to being completely seduced by the wonderful vibrancy of Mumbai. With an attendance of over 250 scientists from across India, it was a superbly run two-day meeting with a blend of invited talks, excellent interactive poster sessions, and social events. Many of the attendees were young Ph.D. and postdoctoral scientists. I was very impressed by their passion for their work and their robust defence of their posters!

I travelled straight on to the joint workshop of the Australian and New Zealand Chapters at the University of Otago on New Zealand's beautiful South Island. Dunedin is rich in history, with some great coffee shops and a superb art gallery, but as a University town of just over a hundred thousand, it was quite a contrast to the bustling metropolis of Mumbai. The workshop was followed by the Formulation and Delivery of Bioactives Conference organised by Dr. Arlene McDowell and Prof. Thomas Rades and held in the impressive Otago Museum. One of our past CRS presidents, Randy Mrsny, gave a superb plenary lecture.

There was one remarkable event at both meetings that deserves special mention and commendation—a competition for the best poster. The prize? Funding toward the cost of attending the CRS Annual Meeting & Exposition. Preshita Desai and Medha Patel won the first and second prizes, respectively, at the Mumbai meeting, and Miriam Haaser won Best Presentation at the Otago meeting, with Sara Hanning as runner-up. Congratulations to these very talented young scientists!

This is a wonderful gesture by the chapters concerned. It will provide those students with a great opportunity to meet and befriend other young scientists from across the world. It will also allow them to see leading scientists at the top of their game present their pioneering research. I would encourage the young scientists to go up and introduce themselves to our invited speakers to talk about their work. You see, it's my view that collaborative research is really at the heart of our science, and I am grateful to the chapters for promoting that ethos and for giving their young scientists an opportunity that they hopefully will exploit and remember for the rest of their lives.

Martyn C. Davies ■

Make the Most of Your Time at the CRS Annual Meeting & Exposition

July 15–18, 2012 • Québec City, Canada

The CRS Annual Meeting & Exposition offers more than you might think, encompassing all areas of delivery science and technology. Beyond the traditional programming featuring premier scientists and the top research in delivery science, you are invited to arrive early or stay a little late to attend a workshop and to follow your track of interest. Do not forget to spend a few minutes exploring historic Québec City.

Registration is open—register now to join CRS in Québec!

Follow Your Track—Get Educated on Animal Health and Preclinical Sciences

Veterinary Program at the 2012 CRS Annual Meeting & Exposition

Program Cochairs: *Arlene McDowell, University of Otago, New Zealand, and Thierry Vandamme, University of Strasbourg, France*

Division Cochairs: *Marilyn Martinez, FDA Center for Veterinary Medicine, U.S.A., and Michael Rathbone, International Medical University, Malaysia*

The theme for the 2012 veterinary program is "Protein and Peptide Therapeutics for Animal Patients." Animals are administered a range of macromolecules, including vaccines, therapeutic drugs, and fertility-control agents, and these topics will be covered by our podium presenters.

Our invited speaker is Dr. Frank Aldwell, Chief Scientific Officer and Director of Immune Solutions Limited in New Zealand. Dr. Aldwell's expertise includes cell biology, vaccines, and novel delivery systems. Dr. Aldwell is the inventor of Liporale™, an oral lipid delivery matrix, and in his talk at the CRS Annual Meeting & Exposition, he will discuss development of the product for delivery of the tuberculosis vaccine, including delivery of vaccines to wildlife. Dosing therapeutics to wild animals extends the challenges of conventional veterinary delivery, as the compounds must often be remotely delivered to the often unseen animal. This situation poses fascinating challenges and requires unique solutions in delivery science.

The variety of animal species to be treated in the field of veterinary medicine often requires tailored delivery platforms. Understanding the anatomy and physiology of the target animal species is an important part of designing delivery systems for this group of patients. The contributed papers will cover aspects of delivery science in different animal species.

We have also planned a get-together for those interested in any aspect of animal health, so please come along—it would be great to meet you. This event will also provide a forum for you to meet new colleagues with similar interests.

What's Your Niche? Find the Latest Discoveries in Consumer & Diversified Products

Consumer & Diversified Products Program at the 2012 CRS Annual Meeting & Exposition

Program Cochairs: *Chris McDaniel, Fleet Laboratories Inc., U.S.A., and Teresa Virgallito, Microtek Laboratories Inc., U.S.A.*

Division Chair: *James Oxley, Southwest Research Institute, U.S.A.*

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The Consumer and Diversified Products (C&DP) Division will be providing insight into the broad range of controlled release applications by offering several dynamic sessions at the 2012 annual meeting in Québec City. Industrial and academic professionals from around the world will present their controlled release research in seven sessions.

Four unique scientific sessions are offered exclusively by the C&DP Division. Recent advances in submicron technologies will be presented and discussed in a session on "Consumer and Industrial Applications of Nanoparticles," focusing on nanoparticle technology that imparts controlled or delayed release properties to products for consumers and industrial applications. A session on "Hydrogel Delivery Systems in Consumer Products" will highlight recent advances in contact lenses and new hydrogel technologies that allow manufacturers to offer new innovative and useful products to the consumer. Participants attending the "Fragrances and Flavors" session will learn about the art of encapsulating flavors and fragrances into delivery systems, with emphasis on the scientific challenges imposed by the particular nature of these essentially volatile actives and the expected benefits of using fragrance and flavor delivery systems in consumer products. Finally, a session on "Nutraceuticals and Functional Foods" will explore controlled release technologies used to create new and innovative products in this rapidly growing market.

The C&DP Division has teamed up with the Bioactive Materials track to provide two joint sessions. "Nanofibers/Nanoparticles" will focus on nanofibers and nanoparticles used in consumer products and industrial applications and products. A session on

"Imaging Diagnostics for Material Characterization" will present recent research on the new products and methods used across a wide spectrum of industries and applications.

In addition to the scientific sessions, a mini-symposium on "Smart Textiles" is offered to present the latest advances on these specialty products engineered for specific end-uses. The focus of this mini-symposium will be the use of new delivery technologies that allow textile manufacturers to present new innovative and useful products to the consumer.

Finally, the C&DP Division will be hosting a lunch on Tuesday afternoon during the annual meeting. We welcome attendees to join us in uniting a multidisciplinary, international group of CRS members to advance science, technology, and education in the field of controlled release or delivery of nonpharmaceutical active ingredients.

Learn Even More with an Educational Workshop

The following pre- and post-meeting workshops will be offered at the 39th CRS Annual Meeting & Exposition. These workshops offer focused presentations on specific topics by noted speakers and are open to a limited number of participants for an additional fee. The educational workshops will be held on Saturday, July 14–Sunday, July 15 and the afternoon of Wednesday, July 18. All educational workshops must be registered for in advance. You do not need to attend the entire meeting to attend a workshop. See the website for more complete workshop details.

Mitigating Risks for Patients When Developing Oral Controlled Release Dosage Forms

Saturday, July 14, 08:00 – 17:00
Sunday, July 15, 08:00 – 12:00

Chaired by Ali Rajabi-Siahboomi, Colorcon Inc., U.S.A.

The focus will be to understand the possible risks to patients and approaches to manage them when developing oral extended-release (ER) dosage forms. The discussion will relate to the design, development, and manufacture of commonly used ER systems. Industry leaders and subject-matter experts will provide scientific basis to the material science, formulation, and process attributes that will help to mitigate risks, under the umbrella of quality by design (QbD). The overall goals of such approaches are to improve quality and reduce costs but maintain patient safety and treatment.

Critical Appraisal of EPR Effect and Intratumoral Distribution of Nanomedicine

Saturday, July 14, 08:00 – 17:00

Chaired by Khaled Gerish, University of Otago, New Zealand, and You Han Bae, University of Utah, U.S.A.

Enhanced permeability and retention (EPR) effect is the most popular strategy for the delivery of nano-size anticancer drugs to solid tumor tissues. Workshop attendees will gain in-depth understanding of the phenomenon and how it can be influenced by variables such as tumor diversity, animal models, biodistribution, intracellular interaction, and release rate of active agents from their nanocarriers. The workshop will identify and explicate the critical factors that are essential for the success of EPR-based nanomedicine.

Formulation and Process Considerations in the Development and Scale-up of Osmotic Dosage Forms

Saturday, July 14, 08:00 – 12:00

Chaired by Don Barbieri, Patheon, U.S.A., and Karen Coppens, Dow Wolff Cellulosics, U.S.A.

Participants will be provided a practical overview of formulation and process considerations involved in the successful development and scale-up of osmotic dosage forms. Participants will gain a greater understanding of the theory behind osmotic dosage forms and how they could offer an advantage over other types of controlled released formulations. The speakers will involve the participants in practical discussions on formulation development, membrane coating considerations, and the use of specialized laser drilling and vision system inspection equipment.

Setting Release Specifications for *In Vitro* Testing of Controlled Release Dosage Forms

Saturday, July 14, 13:00 – 17:00

Chaired by Bob Stagner, Patheon, U.S.A.

This workshop will educate formulators, analytical scientists, QA/QC professionals, regulatory professionals, and nonclinical statisticians about approaches and relevant issues in the evolutions of setting *in vitro* specifications from early development, scale-up, and registration scale manufacture and corresponding phase-appropriate limits for controlled release products. The attendees will gain insight into how phase and manufacturing-scale appropriate limits are applied and specifications are set and verified for controlled/modified release products.

Preserving and Enhancing Vision via Ophthalmic Drug Delivery

Sunday, July 15, 12:30 – 17:30

Chaired by Charles Doillon, University of Laval, Canada, and Todd Hoare, McMaster University, Canada

Whether you are actively involved in developing ophthalmic drug delivery vehicles or are interested to learn more about the unique complexities presented by the eye in controlled release applications, this workshop will bring together industrial researchers, clinicians, and research scientists to discuss the current state-of-the-art technology in ophthalmic drug delivery (at both the front and the back of the eye) and the opportunities and challenges for future developments.

CRS Annual Meeting continued

Considerations for Future Regulatory Submissions of Transdermal Products

Wednesday, July 18, 12:00 – 16:00

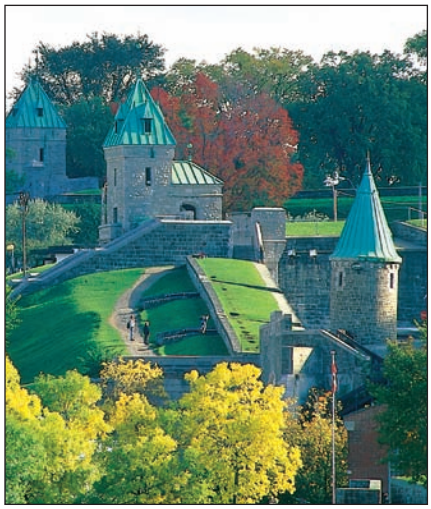
Chaired by Tapash Ghosh, FDA, U.S.A.

This workshop will bring a sound understanding of transdermal drug delivery system (TDDS) across multiple disciplines and multiple sectors with the goal of meeting the challenges of 21st-century TDDS and discuss considerations for future regulatory submissions from an FDA perspective as a whole with emphasis on new drug quality assessment.

Discover the Old World Charm of Québec City

Aerial View of Old Québec. Jean-François Bergeron, Enviro Foto.

Be sure to steal a few minutes away at the end of the programming or stay an extra day or two to explore beautiful and historic Québec City. Considered to be the birthplace of French North America, it is the only walled city north of Mexico. Québec City is walkable and is full of beautiful architecture, culture, and history. Its European background and modern, North American character are combined with 400 years of history, traditional and contemporary art, and culture to make Québec City a destination like no other.



Gates to the Old Québec. Brigitte Ostiguy

Old Québec is a UNESCO World Heritage site. Be sure to visit Old Québec (Vieux-Québec) to enjoy this fortified part of the city, which exudes old-world charm with winding cobblestoned streets, European architecture, museums, attractions, shops, and restaurants.

Build Your Networks for Success: CRS Innovation Sunday

Sunday, July 15

Sponsored by Pfizer

Science • Connections • Development • Commercialization

Build your networks for success during the third annual CRS Innovation Sunday! Designed to connect you with people, companies, novel technologies, and research that address challenges in delivery, come to Sunday's interactive program open to asking questions and finding answers.

Releasing Technology Workshops

Are you interested in learning more about a company's research and products? Interested in a new technology from the company that developed it? The Releasing Technology Workshops (RTWs) give you the opportunity to gain in-depth information presented by the hosting company. Participants as of press time:

Agilent Technologies
Ashland Chemical
Catalent Pharma Solutions
Colorcon Inc.
Gattefossé
Grunenthal GmbH
OctoPlus
SOTAX Corporation
Team Consulting Ltd.

Soapbox Sessions

What's new in delivery science? Come to the program where presenters "get up on their soapbox" to give you a quick glimpse of some of the most innovative technologies and products in development today. Linger to network and exchange business cards with the presenters as you enjoy refreshments sponsored by Catalent Pharma Solutions.

Industry Roundtable: Game-Changing Innovation

Invited Speakers: *Julia Rashba-Step, Pfizer, U.S.A., and Ronald L. Smith, Merck & Co., Inc., U.S.A.*

Game Changer

Definition: A visionary. A person or idea that transforms the accepted rules, processes, strategies, and management of business functions.

From Incremental to Exponential Innovation: Game Changing!

If most innovation is incremental and game changers spark exponential innovation, how do you find a game changer? How do you identify one, or a dozen, game changers for your organization? Who has the skills to put the new rules into play? How do you recognize, integrate, and fully benefit from a game changer arriving from an entirely different discipline? Through panels, presentations, and audience participation, gain insight for *game-changing* Strategies • Communication • Nontraditional partners • Relationships

Exposition Grand Opening & Welcome Reception

CRS Innovation Sunday culminates in the Exposition Hall, where thousands of products, services, and still-to-be-developed innovations can be discussed one-on-one.

Connect with Top Companies in the Industry

Exposition

Come to the Exposition Hall for discovery, solutions, opportunities, and refreshments! Kicking off with the Sunday evening Exposition Opening and Welcome Reception, the Exposition/Poster Hall will also be open Monday and Tuesday as the central hub for poster viewing, program breaks, and refreshments. Be sure to thank the CRS Café Sponsors (noted by *) for providing complimentary beverages.

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Theoretical Coat Assessment: Influence of Size, Size Distribution, Coat Thickness, and Density on Particle Encapsulation

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

Encapsulation is a common strategy for controlling release or delivery of an active material. This typically involves an active material within or on a core particle and an outer coat layer that encapsulates the particle and controls active material release or delivery. Release or delivery is dependent on the chemical and physical properties of the core materials, of the coat formulation, and of the environment(s) in which the release or delivery will take place.

The properties of the coat material are the means of controlling release or delivery. In addition to factors such as coat solubility and porosity, proper coat layer thickness is often the key to meeting release or delivery goals. Required layer thickness is not often known or measured but is built into a successful formulation through the use of consistent raw materials and processing parameters and formulating to a performance goal. Nevertheless, knowledge of the required coat thickness can be used to estimate coat requirements for a new or reformulated product. This article assesses the theoretical aspects of coat thickness in relation to core particle size, core and coat densities, and particle size distribution.

Coat Volume Fractions for Spherical Particles of a Given Size

The volume of a sphere can be calculated using the following formula:

$$V = \frac{4}{3}\pi R^3$$

where V is volume and R is radius.

The thickness of a coat on a particle can be translated to a coat volume fraction (VF_{coat}) using the following base equation:

$$VF_{coat} = \frac{\text{coated particle volume} - \text{core particle volume}}{\text{coated particle volume}}$$

For a core particle radius of R_1 and a coat thickness of T (Figure 1),

$$VF_{coat} = \frac{\frac{4}{3}\pi(R_1+T)^3 - \frac{4}{3}\pi R_1^{\,3}}{\frac{4}{3}\pi(R_1+T)^3}$$

Simplifying provides the following:

$$VF_{coat} = 1 - \frac{R_1^{\,3}}{(R_1+T)^3}$$

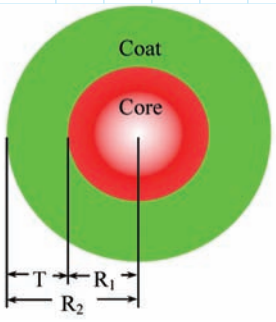


Figure 1. *Schematic representation of a spherical particle.*

Substituting R_2 for $R_1 + T$, we arrive at the following:

$$VF_{coat} = 1 - \frac{R_1^{\,3}}{R_2^{\,3}} \quad (1)$$

Equation 1 can be used to determine the VF_{coat} at a given coat thickness T on a spherical core particle of radius R_1.

Coat Weight Fractions for Spherical Particles of a Given Size

VF_{coat} values are useful; however, they are not easily translated into a useful specification without sophisticated measurement devices. This difficulty is overcome by translating the VF_{coat} to a coat weight fraction (WF_{coat}). The weight fraction can be measured with an appropriate balance or scale. Provided the core and coat have the same absolute density, the VF_{coat} will equal the WF_{coat}; however, if the absolute density of the coat differs from the absolute density of the core, WF_{coat} can be determined by incorporating the absolute density of the core (d_{core}) and the absolute density of the coat (d_{coat}) into a WF_{coat} equation:

$$WF_{coat} = \frac{d_{coat}(\text{coated part. vol.} - \text{core part. vol.})}{d_{coat}(\text{coated part. vol.} - \text{core part. vol.}) + d_{core}(\text{core part. vol.})}$$

where part. vol. is particle volume.

This translates to the following, using the references shown in Figure 1:

$$WF_{coat} = \frac{d_{coat}\left[\frac{4}{3}\pi(R_1+T)^3 - \frac{4}{3}\pi R_1^{\,3}\right]}{d_{coat}\left[\frac{4}{3}\pi(R_1+T)^3 - \frac{4}{3}\pi R_1^{\,3}\right] + d_{core}\frac{4}{3}\pi R_1^{\,3}}$$

$$WF_{coat} = \frac{d_{coat}\left[(R_1 + T)^3 - R_1^{\,3}\right]}{d_{coat}\left[(R_1 + T)^3 - R_1^{\,3}\right] + d_{core}R_1^{\,3}} \quad (2)$$

Replacing $R_1 + T$ with R_2, we have the following:

$$WF_{coat} = \frac{d_{coat}\left(R_2^{\,3} - R_1^{\,3}\right)}{d_{coat}\left(R_2^{\,3} - R_1^{\,3}\right) + d_{core}R_1^{\,3}} \quad (3)$$

Equations 2 or 3 can be used to determine the theoretical WF_{coat} required to achieve a given coat thickness on a given particle size. These WF_{coat} equations can be rearranged to solve for the coat thickness that would be achieved with a given weight fraction on a given particle size. From equation 3, we have the following:

$$WF_{coat}d_{coat}R_2^{\,3} - WF_{coat}d_{coat}R_1^{\,3} + WF_{coat}d_{core}R_1^{\,3} = d_{coat}R_2^{\,3} - d_{coat}R_1^{\,3}$$

$$WF_{coat}d_{coat}R_2^{\,3} - d_{coat}R_2^{\,3} = WF_{coat}d_{coat}R_1^{\,3} - d_{coat}R_1^{\,3} - WF_{coat}d_{core}R_1^{\,3}$$

$$R_2^{\,3} = \frac{WF_{coat}\,d_{coat}\,R_1^{\,3} - d_{coat}\,R_1^{\,3} - WF_{coat}\,d_{core}\,R_1^{\,3}}{WF_{coat}\,d_{coat} - d_{coat}}$$

$$R_2^{\,3} = R_1^{\,3}\left(1 - \frac{WF_{coat}\,d_{core}}{WF_{coat}\,d_{coat} - d_{coat}}\right)$$

$$R_2 = R_1\sqrt[3]{\left(1 - \frac{WF_{coat}\,d_{core}}{WF_{coat}\,d_{coat} - d_{coat}}\right)}$$

Substituting $R_1 + T$ for R_2, we arrive at the following:

$$T = R_1\left[\sqrt[3]{\left(1 - \frac{WF_{coat}\,d_{core}}{WF_{coat}\,d_{coat} - d_{coat}}\right)} - 1\right] \quad (4)$$

Equations 3 and 4 were applied to a range of nominal spherical particle sizes to indicate the dependence of WF_{coat} on particle size and densities for a fixed 10 µm coat thickness (Table 1) and the dependence of coat thickness on particle size and densities for a fixed 0.20 coat weight fraction (20% coat level) (Table 2). Some practical considerations for coating become apparent when studying these data. As smaller particle sizes are engineered for applications, coat requirements may become economically prohibitive or impractical. From the upper portion of Table 1, a 10 µm coat could be achieved on a 500 µm core particle with a 0.069 coat weight fraction (6.9% coat, 93.1% core). That same 10 µm coat thickness on a 10 µm core particle would be achieved at a product composition of 0.9392 coat weight fraction (93.92% coat, 6.08% core). Both a low active load and potentially challenging process hurdles to achieving a high coat level (depending on the coating technique being used) become significant considerations as particle size decreases.

Influence of Particle Size Distribution

This simple assessment works well for a mono-disperse particle size distribution of a given size; however, in reality, particle size distributions are broad. Although the same principles hold,

Table 1. Fixed Coat Thickness

Core Diameter (µm)	Coat Thickness (µm)	Coat Volume Fraction	Core Absolute Density	Coat Absolute Density	Coat Weight Fraction
1	10	0.9999	1.6	0.95	0.9998
5	10	0.9920	1.6	0.95	0.9866
10	10	0.9630	1.6	0.95	0.9392
50	10	0.6356	1.6	0.95	0.5087
100	10	0.4213	1.6	0.95	0.3018
200	10	0.2487	1.6	0.95	0.1643
500	10	0.1110	1.6	0.95	0.0690
700	10	0.0810	1.6	0.95	0.0498
1,000	10	0.0577	1.6	0.95	0.0351
1	10	0.9999	0.95	1.6	0.9999
5	10	0.9920	0.95	1.6	0.9952
10	10	0.9630	0.95	1.6	0.9777
50	10	0.6356	0.95	1.6	0.7460
100	10	0.4213	0.95	1.6	0.5508
200	10	0.2487	0.95	1.6	0.3579
500	10	0.1110	0.95	1.6	0.1738
700	10	0.0810	0.95	1.6	0.1293
1,000	10	0.0577	0.95	1.6	0.0935

Table 2. Fixed Coat Weight Fraction

Core Diameter (µm)	Coat Thickness (µm)	Coat Volume Fraction	Core Absolute Density	Coat Absolute Density	Coat Weight Fraction
1	0.0621	0.2963	1.6	0.95	0.20
5	0.3107	0.2963	1.6	0.95	0.20
10	0.6213	0.2963	1.6	0.95	0.20
50	3.1067	0.2963	1.6	0.95	0.20
100	6.2134	0.2963	1.6	0.95	0.20
200	12.4269	0.2963	1.6	0.95	0.20
500	31.0671	0.2963	1.6	0.95	0.20
700	43.4940	0.2963	1.6	0.95	0.20
1,000	62.1343	0.2963	1.6	0.95	0.20
1	0.0236	0.1293	0.95	1.6	0.20
5	0.1180	0.1293	0.95	1.6	0.20
10	0.2361	0.1293	0.95	1.6	0.20
50	1.1804	0.1293	0.95	1.6	0.20
100	2.3607	0.1293	0.95	1.6	0.20
200	4.7215	0.1293	0.95	1.6	0.20
500	11.8037	0.1293	0.95	1.6	0.20
700	16.5252	0.1293	0.95	1.6	0.20
1,000	23.6074	0.1293	0.95	1.6	0.20

Scientifically Speaking continued on page 10

Scientifically Speaking continued from page 9

characteristics of the coating process may influence the thickness outcome for the various size fractions in the distribution. For coating processes such as coacervation, solvent extraction, or parylene polymerization, which provide a relatively consistent layer thickness independent of particle size, data such as those shown in Table 1 provide an estimate of the actual coat weight fractions that might be realized on specific particle size cuts of the overall distribution. The coat thickness is the same on all particles, but the coat weight fraction at each size is dependent on particle size owing to surface-to-volume differences.

For processes such as fluid bed coating, in which coat layer thickness is also dependent on the surface-to-volume ratios within the core particle size distribution, layer thickness may vary with particle size. A theoretical assessment for application of 20% coat level (0.20 coat weight fraction) to a hypothetical size distribution is summarized in Table 3. The number, volume, and area distributions for the core particle population are shown in the left half of the table. Data in the right half of the table were based on the assumption that every particle passes through the spray zone of the coater the same number of times during the process, regardless of size. Under this assumption, the amount of coat that reaches each particle is dependent on the percentage of the overall surface area for that size in the core material; thus, the Area % column, which is a measure of the percentage of the overall area at that particle size fraction, is equal to the percentage of the applied coat that reaches that size fraction of the core. Assuming that 20 g of coat is applied to 80 g of core particles (0.20 coat weight fraction, 20% coat level), the Coat column indicates the amount of that 20 g that would be coated on the particles in that size fraction. The Core column indicates the weight in grams of particles at each particle size within the distribution. The Coat Weight Fraction column was determined from the coat and core weights for each size, using the following equation: coat weight/(coat weight + core weight) = WF_{coat}. Coat thickness was determined from the WF_{coat} and density values using equation 4. Note that the coat weight fraction increases with decreasing particle size within the core particle size distribution, as would be expected, since smaller particles have a larger surface-to-volume ratio. Also, note that coat thickness varies; larger particles have thicker coats.

This theoretical assessment likely shows an extreme of the influence of the size distribution on the coat weight fraction and coat thickness for a process such as fluid bed coating. In actual practice, smaller particles in a distribution are believed to follow a broader circulatory path in the coater and may ride higher in the process; both of these conditions would lead to potentially less time in the coat zone compared with larger particles in the distribution. It is also possible that particle trajectory through the spray zone of the process may be influenced by size.

Influence of Particle Shape

Although this assessment has been made using a spherical particle model, a similar assessment can be made with other shapes as well with similar outcomes. For a cube with sides of a length D and coat applied to a thickness T, the coat volume fraction can be calculated from the following:

$$VF_{coat} = \frac{(D+2T)^3 - D^3}{(D+2T)^3}$$

Table 3. Theoretical Assessment of Coat Parameters for a Particle Size Distribution at 20% Applied Coat Level

Size (µm)	Number %	Cumulative Number %	Volume %	Cumulative Volume %	Area %	Cumulative Area %	Share of the Applied Coating (%)	Coat (g)	Core (g)	Core Absolute Density	Coat Absolute Density	Coat Weight Fraction	Coat Thickness (µm)
418.60	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.0000	0.0000	1.6	0.95		
383.90	0.50	0.50	4.00	4.00	2.18	2.18	2.18	0.4366	3.1994	1.6	0.95	0.1201	14.3217
352.00	0.75	1.25	4.63	8.62	2.75	4.94	2.75	0.5507	3.7003	1.6	0.95	0.1295	14.2396
322.80	1.25	2.50	5.94	14.57	3.86	8.79	3.86	0.7717	4.7556	1.6	0.95	0.1396	14.1484
296.00	2.00	4.50	7.33	21.90	5.19	13.99	5.19	1.0383	5.8660	1.6	0.95	0.1504	14.0562
271.40	3.00	7.50	8.48	30.38	6.55	20.53	6.55	1.3094	6.7847	1.6	0.95	0.1618	13.9520
248.90	4.25	11.75	9.26	39.65	7.80	28.33	7.80	1.5598	7.4108	1.6	0.95	0.1739	13.8445
228.20	5.75	17.50	9.66	49.31	8.87	37.20	8.87	1.7745	7.7312	1.6	0.95	0.1867	13.7282
209.30	7.00	24.50	9.07	58.38	9.08	46.29	9.08	1.8165	7.2582	1.6	0.95	0.2002	13.6049
191.90	10.00	34.50	9.99	68.38	10.91	57.20	10.91	2.1822	7.9953	1.6	0.95	0.2144	13.4769
176.00	15.50	50.00	11.95	80.33	14.22	71.42	14.22	2.8443	9.5590	1.6	0.95	0.2293	13.3366
161.40	15.50	65.50	9.21	89.54	11.96	83.38	11.96	2.3922	7.3712	1.6	0.95	0.2450	13.1961
148.00	10.00	75.50	4.58	94.12	6.49	89.87	6.49	1.2978	3.6663	1.6	0.95	0.2614	13.0474
135.70	7.00	82.50	2.48	96.60	3.82	93.69	3.82	0.7638	1.9800	1.6	0.95	0.2784	12.8799
124.50	5.75	88.25	1.57	98.17	2.64	96.33	2.64	0.5278	1.2541	1.6	0.95	0.2962	12.7200
114.10	4.25	92.50	0.89	99.06	1.64	97.97	1.64	0.3280	0.7148	1.6	0.95	0.3146	12.5448
104.70	3.00	95.50	0.49	99.55	0.97	98.94	0.97	0.1947	0.3892	1.6	0.95	0.3335	12.3606
95.96	2.00	97.50	0.25	99.80	0.55	99.49	0.55	0.1092	0.1999	1.6	0.95	0.3532	12.1823
88.00	1.25	98.75	0.12	99.92	0.29	99.77	0.29	0.0574	0.0964	1.6	0.95	0.3731	11.9767
80.70	0.75	99.50	0.06	99.97	0.14	99.92	0.14	0.0289	0.0446	1.6	0.95	0.3936	11.7748
74.00	0.50	100.00	0.03	100.00	0.08	100.00	0.08	0.0162	0.0229	1.6	0.95	0.4145	11.5655
Totals:	100.00		100.00		100.00		100.00	20.0000	80.0000				

$$VF_{coat} = 1 - \frac{D^3}{(D+2T)^3} \quad (5)$$

As expected for a volume measurement, equation 5 is similar to equation 1.

As particle shape becomes more irregular and crevices or holes are introduced into the surface, it becomes more difficult to theorize these parameters because of the irregularity of the particle surface. Surface area increases or decreases may occur in such systems as coat is applied and crevices or holes are filled or bridged.

Other Considerations

An underlying assumption in these theoretical assessments is that the core and coat border one another but are completely isolated from one another. More commonly, there is a porosity to the core that will likely allow some coat to penetrate. Depending on the process, core could also bleed into the coat. Also, core particles might be fragile and break during the coating process, or they could agglomerate; both situations create an unpredictable outcome and deviations from theory.

Summary

The theoretical assessment of particle coat parameters discussed in this article provides a tool for estimating size characteristics of coat systems. Knowledge of coat requirements in the areas of coat thickness or coat weight fraction can be translated into tangible formulation parameters. These parameters can help predict coat formulation needs for a range of core particle sizes and size distributions. ■

Foundation Seeks Cutting-Edge Controlled Release Technology: The Michelson Prize & Grants in Reproductive Biology

Katy Palfrey, B.A., and Shirley D. Johnston, DVM, Ph.D., DACT

The Michelson Prize & Grants seeks scientists to bring the latest controlled release technologies to bear in development of a permanent non-surgical sterilant for cats and dogs. The first entity to provide to Found Animals Foundation a safe and effective, single-dose, permanent non-surgical sterilant for male and female cats and dogs will be awarded the $25 million Michelson Prize, and grants of up to US$250,000 per year for up to three years are available from the foundation to fund research in pursuit of this product.

Background

In 2008, the Michelson Prize & Grants was established by Found Animals Foundation, a privately funded non-profit operating foundation with the mission of minimizing shelter euthanasia of dogs and cats. Currently, three to four million animals are euthanized each year in U.S. shelters, and the majority of these animals are healthy, adoptable pets, put down for no reason other than the lack of a home. The availability of a non-surgical sterilant to address populations of animals not currently served by surgical approaches would have a game-changing effect on shelter intake and euthanasia of cats and dogs. Though it is not the mission of the foundation, a non-surgical sterilant for cats and dogs would also significantly impact the (approximately 55,000) human rabies deaths in the world annually, most of which are caused by infected feral dogs. The Michelson Prize & Grants are funded by Dr. Gary Michelson, a Los Angeles orthopedic surgeon and the billionaire founder of Found Animals.

To date, 19 projects totaling $8.5 million have been approved for Michelson Grant funding. Three funded projects are for the silencing of genes in the central nervous system that code for proteins essential to reproduction. Six funded projects are for immunization against gonadotropin releasing hormone (GnRH) and permanently breaking tolerance to that peptide. Ten projects involve targeted delivery of cytotoxins to specific cells in the brain or gonad to induce permanent sterility.

Beverly L. Davidson, Ph.D., at the University of Iowa Medical School, U.S.A., received a Michelson Grant to research inducing stable infertility by RNA interference.

Seeking Controlled Release Technologies

Could your controlled release technology win you $25 million? It just might. The major limitation of one of the most popular approaches, immunization against GnRH, is the need for booster vaccination to maintain the effect. The foundation is optimistic that this limitation could be overcome by utilizing an innovative controlled release technology and is interested in considering proposals from scientists to use slow-releasing drug delivery to maintain the duration of effect of a single dose for the 10–20 year lifetime of the animal. Information about the advantages and limitations of current approaches to long-term fertility control for cats and dogs can be found at http://michelson.foundanimals.org/resources.

Winning the $25 Million Michelson Prize

Found Animals will award the Michelson Prize to the first entity to provide the foundation with a product that has, at minimum, the following characteristics:

- Single-dose, non-surgical sterilant
- Safe and effective in male and female cats and dogs
- Suitable for administration in a field setting
- Viable pathway to regulatory approval
- Reasonable manufacturing process and cost

Found Animals plans to take the successful product through regulatory approval, manufacturing processes, and commercializa-

tion for provision at a low cost to shelters and will award the $25 million prize in exchange for commercialization rights.

Applying for Michelson Grant Funding

Investigators wishing to be considered for Michelson Grant funding to test their hypotheses are required to submit a brief letter of intent (LOI) containing: (1) proposed approach for developing a single-dose non-surgical sterilant; (2) the rationale for proposing this approach; and (3) an overview of proposed research. If the LOI is approved, a full proposal will be invited and will be reviewed by the Scientific Advisory Board. Upon approval of a project, funding is released after negotiation of grant contract details that include agreement on progress reporting, animal welfare oversight (including institutional IACUC approval), and provision of first right of refusal to the foundation for a license to products arising from foundation-funded research. To learn more about submitting an LOI for Michelson Grant funding, visit http://michelson.foundanimals.org/michelson-grants/grant-application-process.

William W. Ja, Ph.D., at Scripps Research Institute in Jupiter, FL, U.S.A., received a Michelson Grant to research follicle-stimulating hormone receptor ligand-cytotoxin conjugates for permanent chemosterilization.

Proposals for the Michelson Grants are considered for research on a product that is administered by any route (oral; intranasal; topical; intradermal, subcutaneous [SQ], intramuscular [IM], or intravenous injection; or other). However, the foundation's advisors indicate that it is unlikely that an oral sterilant product in a bait formulation would be approved by the FDA because of safety concerns in humans and wildlife; SQ or IM administration is considered the most effective route of administration in shelters.

Investigators are encouraged to submit for "proof of concept" studies in target species, cell culture, and/or laboratory animals. The foundation will consider proposals for grants on a mechanism or product that applies to only one species (cats, dogs) or one gender, but the $25 million Michelson Prize will be awarded only for a product that is safe and effective in both species and genders.

The Michelson Prize & Grants in Reproductive Biology is an international program open to any entity. Found Animals welcomes letters of intent from academic institutions and commercial entities, as well as qualified individuals or groups.

Questions about applying? Visit our website at http://michelson.foundanimals.org/ or contact Program Manager Katy Palfrey at k.palfrey@foundanimals.org. ■

Preclinical Sciences & Animal Health: Merging Topics of Interest to Animal and Human Health

The CRS is excited to announce the **Preclinical Sciences & Animal Health Division,** which will be based upon a wider scope of topics than the previous Veterinary Products Division and will foster an opportunity for collaboration between CRS members interested in animal and human health. The division aims to provide a platform to explore 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.

Thus, the Preclinical Sciences & Animal Health Division is intended to meet not only the needs of scientists involved in the development and regulation of drugs and biologics intended for veterinary use but also the interests of pharmaceutical scientists working in preclinical drug development. Under the leadership of Michael Rathbone (michael_rathbone@imu.edu.my) and Marilyn Martinez (marilyn.martinez@fda.hhs.gov), the division will promote involvement and participation of its membership through webinars, workshops, conference tracks, and *CRS Newsletter* articles that benefit the scientists working in these areas. Another division membership benefit is a division webpage that serves as an information resource by providing articles in areas of interest, updates on the area, and notices of upcoming events of interest.

Our vision will be supported by the following initiatives and activities:

1. Rather than having veterinary-specific sessions, the goal will be to unite scientists working in the areas of animal health and animal models and to integrate these two topics into a joint annual meeting track.
2. The division website will have a list of citations focusing on interspecies differences that may influence interspecies extrapolations. Members will be encouraged to contribute to this resource.
3. This new initiative will be highly focused on engagement of CRS members interested in 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. This will be accomplished by the scheduling of focused discussions on scientific issues and challenges, controversial publications, important initiatives, and *in silico* tools to facilitate the development of novel drugs and delivery platforms. The engagement initiative will be organized as follows:
    a. Placement of discussion materials on the CRS portal (in the Preclinical Sciences & Animal Health Division webpage).
    b. The CRS will set up a blog where folks can place thoughts prior to the discussion. Although, in the past, blogs have not been successful, our hope is that, over time, this will become a mechanism for member exchange.
    c. Conference calls in which the article and any blog discussions can be shared. Membership conference calls will occur every other month.
4. All CRS members can participate in these discussions by signing up to for the call-in information.
5. The highlights of the division webpage and discussions will be published in the *CRS Newsletter*. This regularly scheduled write-up will also showcase the next scheduled discussion topic. In addition, members will be given the opportunity to share highlights of their recent publications.
6. Members will have the opportunity to recommend webinar speakers on interspecies differences. We will also plan workshops at annual meetings on such topics as use of simulation and modeling of animal species to support drug development in human and veterinary species.

To support these goals, subcommittees will be formed before the next CRS Annual Meeting & Exposition, providing members with leadership opportunities and ensuring that the Preclinical Sciences & Animal Health Division will address the needs and opinions of all its membership.

If you would like to join the Preclinical Sciences & Animal Health Division (at no cost but a current CRS membership) and would like to be placed on our listserv, please provide your name, affiliation, area of specialization, and e-mail address to michael_rathbone@imu.edu.my.

We hope that you share our excitement on the beginning of an initiative that will be of great benefit to all of our members. We welcome your input and contributions. Please sign up to be a part of this division by contacting Cheryl Kruchten, ckruchten@scisoc.org, or on your membership renewal invoice.

We look forward to working with each of you in the coming months!

Many thanks,

Mike Rathbone and Marilyn Martinez ■

Erratum

On page 19 of volume 29, number 1, the editors for *Long Acting Injections and Implants* were incorrectly listed. The editors are Jeremy C. Wright and Diane J. Burgess.

Are You Linked In? Nearly 2,800 Delivery Scientists Are!

The CRS LinkedIn group, launched in September 2009, has seen steady growth over the past two years and now has close to 2,800 members. The CRS LinkedIn group has quickly become a place to share information and find answers to challenging delivery science issues from your peers. Andy Lewis, manager of the LinkedIn group, shared, "It's been brilliant to see the group grow so rapidly and being used by the CRS community to share interesting news items, papers, and publications and get help on their projects, often from leaders in the field who are happy to help out. It's an indication of the vibrancy of the field and the CRS community."

By the Numbers
This is an influential and intelligent group—nearly 39% are senior level, with 13% managers, 8% directors, and 3% vice presidents. Thirty-seven percent are in research, with 10% in education. A majority of group members are in pharmaceuticals, with other members in research, biotechnology, chemicals, and medical devices. At times, the group will grow by more than 70 members per week, and the numbers of discussions and comments have grown exponentially.

By the Topic
Members are invited to post their breakthroughs, issues, announcements, and more. Here is a look at some of the most popular discussions over the past few months—and an idea of what you are able to discuss on this forum.

- Does anyone know of a CRO [contract research organization] that can provide services for microcrystal formulation development?
- Does anyone have any advice about how to calculate the required nominal dose size per unit to obtain a 24-hour controlled release profile from a hydrophilic matrix system?
- Does anyone have any experience on using roller compaction for formulating MR [modified release] matrix tablets?
- I am carrying out some research into comparisons between multi-particulate systems and monolithic tablets. Does anyone have any information on this area?
- There is something I want to ask: A hydrophilic matrices such as chitosan nano-hydrogels can achieve a sustained release (3 weeks) of an anticancer drug (logP = 5)?
- Critical factors in the release of drugs from sustained release hydrophilic matrices [discussion of an article in the *Journal of Controlled Release*].

The CRS LinkedIn group is an excellent complement to your CRS membership, keeping you connected to the delivery science and technology community all year long. ■

Drug Delivery and Translational Research (*DDTR*) Updates

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

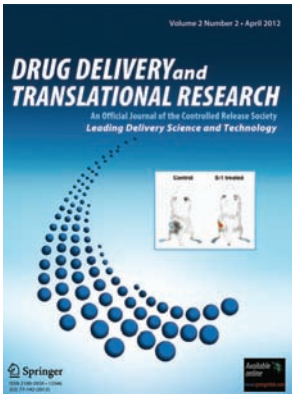
Editor's Pick (Vol. 2, Issue 1)

Bispecific antibody complex pre-targeted delivery of polymer–drug conjugates for cancer therapy

Keyur S. Gada, Vishwesh Patil, Rajiv Panwar, Arash Hatefi, and Ban-An Khaw

From a special focus issue on "Advances in Image-Guided Drug Delivery."

In this paper, the authors have studied the approach of pre-targeting using bispecific affibody-antibody complex and targeting of chemotherapeutic agents using drug-loaded polymers in breast cancer cells. It is suggested that such a pre-targeting and targeting approach may allow development of very efficient, lower non-target toxicity, and image-guided targeted therapy since these polymers can also be labeled with radioisotopes. View this article on the *DDTR* website.



Upcoming *New* Special Issues

We have published two well-received theme issues: "Advances in Vaginal Drug Delivery," edited by David R. Friend of CONRAD, Arlington, VA, U.S.A., and "Advances in Image-Guided Drug Delivery," edited by Prof. Arash Hatefi and Tamara Minko from Rutgers, The State University of New Jersey, U.S.A. We are developing several theme issues on delivery science and technology with a translational focus. The upcoming special issues are described below. The primary focus of *DDTR* is to advance delivery science and technology and to provide a unique forum for publication of high-quality translational drug delivery research. If you are interested in developing a theme issue, please contact Editor-in-Chief Vinod Labhasetwar (labhasv@ccf.org) with a brief summary and list of potential contributors.

A *DDTR* Special Focus Issue on "Cancer Stem Cells," with Jayanth Panyam, University of Minnesota, U.S.A., as Guest Editor

There is growing evidence that cancers contain a small subset of stem-like cells (cancer stem cells, CSCs) that can self-renew. CSCs may play a critical role in cancer treatment outcomes, because they are resistant to conventional chemotherapy and can initiate tumor recurrence following treatment. The goal of this theme issue is to review the role that CSCs may play in tumor response to therapy and the strategies to inhibit CSCs.

A *DDTR* Special Focus Issue on "CNS Drug Delivery of Biologics," with Pericles Calias, Shire HGT, U.S.A., as Guest Editor

Strategies for treating the Central Nervous System (CNS) manifestations of diseases have evolved well beyond the traditional size/lipophilicity paradigm. This special issue describes the challenges of developing therapies targeted to the CNS, from bench to clinical development. A review of the biological hurdles and current strategies for overcoming them will set the stage for discussions on the assessment of the product's pharmacologic effect within the CNS and regulatory considerations for the incorporation of biomarkers into product development programs.

***DDTR* Outstanding Paper Award**

DDTR is an official member journal of CRS, providing a unique forum for publication of high-quality research that focuses exclusively on translational aspects of delivery science and technology. Submit your best translational drug delivery research to be published in *DDTR* and become eligible to compete for the 2012 *DDTR* Outstanding Research Paper Award. The first such award will be given during the 2012 CRS Annual Meeting & Exposition in Québec City, Canada. The awardee will be selected from the research articles published in *DDTR* during 2011. ■

DDTR Top Article Downloads in 2012

(as of March 12, 2012)

Chitosan-coated solid lipid nanoparticles enhance the oral absorption of insulin
Pedro Fonte, Tiago Nogueira, Christiane Gehm, Domingos Ferreira, and Bruno Sarmento

Comparative oral bioavailability advantage from curcumin formulations
Bhushan Munjal, Yogesh Bapurao Pawar, Sarsvatkumar Babulal Patel, and Arvind Kumar Bansal

Drug delivery to the testis: Current status and potential pathways for the development of novel therapeutics
Devon C. Snow-Lisy, Mary K. Samplaski, Vinod Labhasetwar, and Edmund S. Sabanegh, Jr.

Enhanced dermal delivery of acyclovir using solid lipid nanoparticles
Sanyog Jain, Meghal A. Mistry, and Nitin K. Swarnakar

Paclitaxel- and lapatinib-loaded lipopolymer micelles overcome multidrug resistance in prostate cancer
Feng Li, Michael Danquah, Saurabh Singh, Hao Wu, and Ram I. Mahato

MICHELSON
PRIZE & GRANTS

Could Your Controlled Release Technology WIN YOU $25 MILLION?

Found Animals Foundation seeks controlled release technologies to lengthen the duration of contraceptives for cats and dogs. The Foundation will offer the **$25 million Michelson Prize** to the first entity to provide the Foundation with a permanent, non-surgical method of sterilizing cats and dogs.*

Grants of up to **$250,000 per year** per grant for up to three years of funding are available through the Michelson Grants to fund research in pursuit of this product.

For more information, visit **michelson.foundanimals.org**

**Must meet all criteria for the Michelson Prize as stated at michelson.foundanimals.org*

FoundAnimals®

Success for NZCRS with Back-to-Back Events

The Joint New Zealand and Australian Local Chapters of the Controlled Release Society Workshop on "Polymers in Drug Delivery"

By Travis Badenhorst, School of Pharmacy, University of Auckland, New Zealand

On February 15, 2012, the combined workshop of the New Zealand and Australian local chapters of the CRS was held at the School of Pharmacy, University of Otago, Dunedin, New Zealand. This workshop focussed on the topic of "Polymers in Drug Delivery." The workshop was free for students and provided a broad perspective into the use of polymers in many differing fields. Unfortunately, the keynote speaker, Dr. Sebastian Koltzenburg (BASF, Germany), could not make it at short notice; however, he was able to deliver a very interesting talk via a recorded audio presentation. It was a shame that Dr. Koltzenburg could not be there in person, but his talk was still very valuable and provided an excellent foundation for the following talks. The title of his talk was "Polymer Chemistry and Polymers Used for Pharmaceutical Purposes," and it gave an excellent introduction to the structure of polymers and their use for a variety of applications. Other speakers also presented on interesting aspects of polymers when used to deliver therapeutic agents: Assoc. Prof. Ben Boyd (Monash University, Australia) gave an excellent talk on dendrimers and their use in cancer therapies. Prof. Thomas Rades (University of Otago, New Zealand) spoke on the formation and utilization of polymeric nanoparticle structures for drug delivery. This talk was followed by Dr. Arlene McDowell (University of Otago, New Zealand), who discussed the interactions of peptide therapeutics with polymeric dosage forms and the *in vivo* implications. Dr. Darren Svirskis (University of Auckland, New Zealand) spoke about the ability to manipulate drug release using electrochemically controlled polymers. Also discussing modulation of drug release, Dr. Ilva Rupenthal (University of Auckland, New Zealand) focused on *in situ* gelling polymers. The final speaker of the workshop was Dr. Hywell Williams (Monash University, Australia). Dr. Williams covered altering release profiles by modifying polymer composition.

Lunchtime discussions at the workshop. Photo by Arlene McDowell.

A roundtable discussion at the end of the day enabled lively discussion of some key aspects of the future of polymers in delivering therapeutic agents.

The workshop was closed by Dr. McDowell and Assoc. Prof. Boyd thanking everybody for their participation. The contribution made by Prof. Rades on the organising committee was also acknowledged. At the conclusion of the day's events, the majority of the workshop's attendees met at a local restaurant to network and reflect on the day's proceedings.

Immediately following the workshop, on February 16 and 17, the NZCRS co-sponsored the 14th Annual Formulation and Delivery of Bioactives (FDB) Conference, also held in Dunedin.

Many thanks go to the organising committee, Dr. Arlene McDowell (President of NZCRS), Assoc. Prof. Ben Boyd (President of AUS-CRS), and Prof. Thomas Rades for their valuable time spent organising both of the highly successful events. ■

Protein and Peptide Delivery in Focus at the Joint FDB/NZCRS Conference, 2012

By Ms. Petra Priemel and Ms. Miriam Haaser
School of Pharmacy, University of Otago, Dunedin, New Zealand

Using the opportunity for interaction and knowledge exchange, international attendees from academia and industry came together at the joint conference of the Formulation and Delivery of Bioactives (FDB) research theme of the University of Otago and the New Zealand Local Chapter of the Controlled Release Society (NZCRS). The focus this year was on protein and peptide delivery, based on the increasing number of newly approved medicines coming from this group.

With a very warm welcome from Prof. Thomas Rades, convenor of the FDB research theme, the two-day conference was opened. The first day was devoted to the use of proteins and endogenous peptides as therapeutics as well as the enhancement of their oral delivery. After the introductory presentation given by Assoc. Prof. Natalie Medlicott (University of Otago, New Zealand) on the use of proteins as therapeutic agents, keynote speaker Prof. Randy Mrsny (University of Bath, U.K.) engaged the audience talking about the potential delivery mechanism used by exotoxin A from *Pseudomonas aeruginosa* for efficient protein delivery through polarized epithelial cells without their intoxication. Nasal delivery as another administration target for protein formulations was presented by Dr. Regina Scherliess (University of Kiel, Germany), who focussed in particular on vaccine formulations and their stabilisation.

The second session of the day was a rapid-fire oral presentation of posters, giving postgraduate students from New Zealand as well as visiting students from Thailand and Denmark the opportunity to briefly introduce their work and draw the attention of the audience to the posters exhibited. This session was immediately followed by the annual general meeting of the NZCRS.

Session three opened with Prof. Martyn Davies (University of Nottingham, U.K.) talking about modern analytical tools and their suitability to probe the surface chemistry, morphology, and topography of biomedical systems. Further, Prof. Thomas Rades

Presidents three. Associate Professor Ben Boyd (AUS-CRS President), Dr. Arlene McDowell (NZCRS President), and Prof. Martyn Davies (CRS President) at the FDB Conference in Dunedin. Photo by Len Stevenson.

Conference attendees during one of the talks as part of the FDB Conference, Dunedin. Photo by Len Stevenson.

(University of Otago, New Zealand) talked about oral delivery, focussing on the use of polymeric nanoparticles. Assoc. Prof. Ben Boyd (Monash University, Australia) closed the session with a talk about the potential use of proteins or peptides as stabilisers for cubosomes, using β-casein as a promising example. This very successful first day closed with the conference dinner at the University of Otago Staff Club, giving participants a great opportunity for informal discussion and interaction.

Day two of the conference was opened by the CRS keynote speaker, Prof. Mike Pikal (University of Connecticut, U.S.A.). Prof. Pikal gave a brief overview of the freeze-drying process from an engineering perspective and then moved on to storage stability in amorphous pharmaceutical systems, in particular chemical degradation and aggregation in proteins. He highlighted the glass dynamics being the critical factor that determines the stability of proteins and small molecules in the amorphous state. Following the keynote speaker, Dr. Chris Pemberton (University of Otago, New Zealand) introduced the audience to endogenous peptides that can be used as cardiovascular and anti-inflammatory therapeutic agents.

The second session of the day was opened by Prof. Margaret Baird (University of Otago, New Zealand), who gave a very interesting overview of vaccine delivery, vehicles, and adjuvants. Furthermore, she focussed on nanoparticular systems and the role of adjuvants in effective immune response. Dr. Ilva Rupenthal (University of Auckland, New Zealand) talked about her recent research on ocular delivery of gap junction modulators, in which she emphasised the importance of controlled delivery systems to protect drug molecules from degeneration. Finally, in this session, Prof. Randy Mrsny (University of Bath, U.K.) talked about a case study for the development process of a protein drug (Dornase alpha). Prof. Mrsny addressed the pros and cons of developing two protein therapeutics to improve lung function in cystic fibrosis patients.

The afternoon session of day two mainly consisted of oral presentations covering a wide range of topics given by postgraduate

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The FDB conference prize winners. Left to right: Linda Grøn Jensen, Miriam Haaser, and Sara Hanning.

students from New Zealand and a visiting student from Belgium. The final speaker of the conference was Dr. Hywel Williams (Monash University, Australia). In his talk, he pointed out the importance of polymer properties, in particular hydration behaviour, in an environment similar to the human body.

Before the 14th FDB conference came to an end, the awarding of prizes and final formalities were initiated. The FDB poster prize was announced by Prof. Thomas Rades as Linda Grøn Jensen (University of Copenhagen, Denmark). The NZCRS student prizes were then announced by NZCRS President Dr. Arlene McDowell. The first prize in this year's speaking competition was awarded to Miriam Haaser (University of Otago, New Zealand), with Sara Hanning (University of Otago, New Zealand) being announced as the runner up. This year, we are also very grateful to Molecular Profiles Ltd. for providing additional funding for the NZCRS prizes.

As with prior years, this year's meeting was great success that brought together a mix of local and international presenters covering a wide range of research areas in the field of formulation and drug delivery. With another successful FDB and NZCRS conference hosted in Dunedin, the outlook for the 15th joint conference can only be promising. ■

Outcomes from the CRS Italy Local Chapter Workshop Roundtable: "Translation of Controlled Release Platforms from Bench to Bedside up to Marketed Products"

Paolo Blasi,[1] Paolo Caliceti,[2] Giuseppe De Rosa,[3] Heinrich Haas,[4] Mario Maio,[5] Pietro Matricardi,[6] and Stefano Salmaso[2]

The CRS Italy Local Chapter annual workshop, "Nanostructured Devices for Drug Delivery: From Small Molecules to Biotech Drugs," held in Rome on November 17–19, 2011, dedicated a thematic roundtable to a critical issue for the drug delivery community: translation of controlled release platforms from bench to bedside up to marketed products. The attendees of the roundtable participated enthusiastically in the attempt to spread light over the difficulties of translational science. In particular, the technical requirements that should be taken into account in the development of new products from the academic research as well as feasible pathways that can value the efforts of those working in the drug delivery and controlled release fields were deeply discussed.

One of the points highlighted during the roundtable was the relevance of patenting systems at the very early stages of the investigation, when potential clinical evaluation and marketing development are envisaged. Even though patented systems are not required for clinical-phase investigations, they are mandatory for the market launch of the product if it is successful. Patentability was remarked to be a prerequisite to interest private investors in research projects, to ensure a rapid technological development of the system from the bench to the clinical investigation step. In this respect, comments from the audience highlighted how the attraction of venture capital can only take place when the early design of the drug delivery platform is business oriented. Moreover, it was highlighted that, for development of a product for the clinical trials and for the market, issues related to chemistry, manufacturing, and control (CMC) play an important role. Several constraints need to be considered during scale-up (for example, batch-to-batch repeatability, knowledge and control of each production step, costs of the starting materials and production process, and choice of materials approved for pharmaceutical use). In particular, for innovative, complex pharmaceutical formulations, cost of goods and shipment (COGS) may be the limiting factor for a marketable product. These coherencies should be considered ideally already at early stages of development with respect to engineering of the pharmaceutical formulations and manufacturing processes.

The discussion analysed the role of the university technology transfer offices (TTOs) in supporting the translation of a controlled release platform from the bench toward its biomedical application. The TTO should be the institution, namely university, component in charge of valuing new ideas that are generated. To this aim, this office should actively scout their research groups and research centres to find out where new potentially marketable platforms are in the process of being created and deserve further development, beyond the mere scientific publication of the outcome in a journal. Once a

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[2] University of Padua, Italy.
[3] University Federico II, Naples, Italy.
[4] Ribological GmbH, Mainz, Germany.
[5] Merck-Serono, Darmstadt, Germany.
[6] University La Sapienza, Rome, Italy.

potential commercialization value of the product has been identified, the patent office should support the researcher to carry out the patent-filing process. Finally, the TTO should drive the commercialization of patented platforms, searching for companies to licence the patent or for potential funds to support further developments. These tasks of the university TTO hardly need to be pursued by researchers, who usually are not acquainted with marketing skills. Overall, during the discussion, the relevance of the TTO was considered crucial to setting under the market light the intellectual properties of the university. This can conceivably lead the prototype's development toward an advanced stage in the clinic and to the market.

Another bottleneck identified and stressed during the roundtable was the need to produce the aforementioned devices while complying with good laboratory practice (GLP) and good manufacturing practice (GMP) requirements. One option is that the GMP requirements are kept in mind but not applied from the early stage of the investigation for a pharmaceutical formulation, even though GMP certification of a product is mandatory to guarantee the batch-to-batch production repeatability that certifies the safety and efficacy of products that will be tested in a clinical phase. In particular, attendees highlighted how some universities have recently established GMP facilities to produce their own drug product batches for clinical trials. However, concerns have been raised about the costs of maintaining such facilities in-house. In a global scenario of budget restriction that is striking the university system, academia might not be able to bear the costs for setting up such facilities. Alternatively and cheaply, when the translation of a product into a clinical phase is foreseen, a contract manufacturing organisation (CMO) can be involved in the production of GMP-certified batches. This allows obtaining products with required quality and reduced costs instead of maintaining GMP facilities in-house.

The last point discussed was the importance of a multidisciplinary team for the success of a research project in the field of drug delivery. In fact, owing to the commonly occurring elevated complexity of a drug delivery system, the presence of investigators with diverse scientific backgrounds can provide a relevant support to the whole development of the system. The team multidisciplinarity was underlined to be paramount from the very beginning, especially when the platform is going to be designed. In fact, having such diversified scientists collaborating in the research team, ranging from pharmaceutical technologists to chemists, material science engineers, physicists, biologists, toxicologists, and obviously clinicians, can be very helpful to meet both the physicochemical requirements of the device and the disease physiopathologic features. Indeed, it was observed how the lack of a multidisciplinary team hinders bypassing the many pitfalls along the path of investigations, which may grind to a halt in the advanced stage of the project, with a consequent waste of resources. Thus, good interdisciplinary collaboration with effective communication among individuals is required along the whole life of the project.

In conclusion, patentability, GMP mindset, team multidisciplinarity, and the pivotal role of the TTO all contribute to the final goal of translating innovation into industrially feasible drug delivery systems, particularly in times when pharmaceutical companies' budgets are limited and internal research is synergistically linked to external collaborations with universities. Therefore, this article is intended to stimulate attention for those in charge of TTOs on how to proactively capture more opportunities for academia–industry collaborations. ■

Germany Local Chapter of the Controlled Release Society Report on the Annual Meeting and Activities in 2011

Dagmar Fischer,[1] President

The most important event in 2011 of the Germany Local Chapter of the Controlled Release Society was the annual meeting, which was held in Jena, Germany, in the famous historical ambience of Rosensaele on March 15–16, 2011. The traditional city of Jena, located in the valley of the Saale River, is brought to life by a fascinating combination of a historic, intellectual past; a delightful countryside; and innovative, international research and industry, as well as a youthful student life at the Friedrich-Schiller University with about 21,000 students. Therefore, it was a perfect place for an event like the CRS local chapter meeting focusing on the scientific education and collaboration of young scientists.

[1] Institute of Pharmacy, Department of Pharmaceutical Technology, Friedrich-Schiller-University of Jena, Otto-Schott-Strasse 41, 07745 Jena, Germany.

The meeting, organized by Prof. Dagmar Fischer, was a highly successful event: 153 scientists from academia, clinics, and industry took part, with 72 peer-reviewed posters and oral presentations. The meeting was hosted together with the international symposium of the Thuringian ProExcellence Initiative

Attendees enjoy the poster session.

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The Germany Local Chapter annual meeting, 2011.

NanoConSens, headed by Prof. Ulrich S. Schubert, University of Jena, to strengthen the collaborations between researchers of different disciplines. This collaboration was an excellent opportunity to attract more chemists and physicists to CRS and the needs of controlled release of drugs.

On day one, the program was given by five internationally renowned speakers. Prof. Katharina Landfester, Max Planck Institute for Polymer Research in Mainz, talked about stimuli-responsive nanocapsules for drug release. Dr. Hildegard Büning, Center for Molecular Medicine in Cologne, gave an overview about the status quo of tailored adeno-associated viruses for gene transfer and gene therapy. Prof. Pierre Lutz from the Centre National de la Recherche Scientifique (CNRS) Strasbourg introduced poly(ethylene oxide) based materials from the synthesis to biomedical applications. The importance of lipid membrane coatings for siRNA, silica nanoparticles, and single-cell micro-arrays was highlighted by Prof. Joachim Raedler, University of Munich. Prof. Eric Goethals from Ghent University presented his research as "playing with polymeric amines and ammonium salts."

The program on day two consisted of two keynote speakers—Prof. Michaela Schulz-Siegmund (University of Leipzig) and Prof. Klaus Langer (University of Münster), who were invited to share their latest research with the young scientists—as well as many oral presentations given by students. Prof. Schulz-Siegmund highlighted the application of active substances in adipose and bone tissue engineering. Prof. Langer gave a comprehensive overview of nanoparticulate systems for cell-specific drug delivery, with a special focus on antibody-targeted nanoparticles in tumor therapy. The student presentations covered a wide range of pharmaceutical topics such as formulation of novel drugs (for example, proteins and nucleic acids), controlled release aspects, stimuli-induced drug release, and biological and pharmacokinetic models for testing of the systems. The standard of the contributed talks was outstanding, and we thank all of our speakers for their participation.

During coffee breaks and lunch, the meeting offered the opportunity for young researchers to showcase their recent results in several poster sessions. In a relaxed atmosphere, students discussed their latest work and took the chance to network, build up collaborations, and exchange their experiences. This was also possible at one of the traditional events of the Germany Local Chapter, the gala dinner on the first evening. This year's dinner was held at the Ricarda Huch house with good food, good music, wine and beer, and many interesting discussions.

During the membership meeting, which took place during lunchtime, all members of the Germany Local Chapter were invited to elect a new chapter executive committee. Former vice president Prof. Dagmar Fischer, University of Jena, was elected as president, and Prof. Lorenz Meinel, University of Würzburg, was elected as vice president. Prof. Meinel was entrusted with organizing the 2012 annual meeting of the Germany Local Chapter in Würzburg. Dr. Michael Hacker, University of Leipzig, was re-elected as treasurer and Dr. Martin Bultmann, Abbott GmbH & Co. KG, as secretary in chief. To check finances, Prof. Dr. Michaela Schulz-Siegmund, University of Leipzig, and Dr. Eva-Maria Collnot, Saarland University, were chosen.

The studemt speakers at the CRS Germany Local Chapter annual meeting, March 2011.

A special thanks goes to our sponsors for making this highly successful symposium possible: Controlled Release Society, Sanofi Aventis, Abbott GmbH & Co. KG, Landesapothekerkammer Thüringen, Schering GmbH & Co. Produktions KG, Capsugel, Dr. Willmar Schwabe GmbH & Co. KG, Spektrum Akademischer Verlag, Scienova GmbH, and University of Jena. We gratefully acknowledge this support, especially as it enabled the participation of students at a low cost.

A second highlight of the Germany Local Chapter in 2011 was the announcement of three travel grants to support participation at the 38th CRS Annual Meeting & Exposition in National Harbor, Maryland, U.S.A. Many applications were received and reviewed by the executive board, and the following awardees were announced:

Dr. Belal Al Zaitone, University of Bonn
Lutz Asmus, University of Geneva and Lausanne
Dr. Ratnesh Jain, Helmholtz Centre for Infection Research and Saarland University

For further information, please visit our new website (www.controlledreleasesociety.de). ■

People in the News

Compiled by Steven Giannos, Chrono Therapeutics Inc.
Industrial Editor

Koch Institute, Dana-Farber/Harvard Cancer Center Announce Launch of "Bridge Project" to Attack Most Lethal Forms of Cancer

Business Wire: March 6, 2012 – CAMBRIDGE, MA, U.S.A. – The David H. Koch Institute for Integrative Cancer Research at MIT and Dana-Farber/Harvard Cancer Center (DF/HCC) announced today that they have funded several research teams in a joint collaboration aimed at solving the most intractable challenges in cancer.

"We have made tremendous advances in many cancers in recent decades, but pancreatic cancer and glioblastoma remain exceedingly difficult to treat." The Bridge Project—an unprecedented clinical research collaboration between MIT and DF/HCC—has awarded grants to four interdisciplinary teams made up of biologists, bioengineers, and clinical researchers representing both cancer centers. Each joint team is focused on improving the prognosis facing patients affected by two of the most lethal cancers today: pancreatic cancer and a form of brain cancer, glioblastoma.

The Bridge Project grants represent the most extensive collaboration of its kind between Boston's two National Cancer Institute (NCI)-designated cancer centers. In addition to individual philanthropists Arthur Gelb and Thomas Peterson, key support for the initiative comes from two leading innovative non-profit cancer research organizations—The Lustgarten Foundation, the nation's largest private foundation dedicated solely to funding pancreatic cancer research, and the National Brain Tumor Society.

"We have made tremendous advances in many cancers in recent decades, but pancreatic cancer and glioblastoma remain exceedingly difficult to treat," said David Livingston, Deputy Director of Dana-Farber/Harvard Cancer Center. "From a clinical perspective, we are eager to gain a more sophisticated understanding of the underlying biology that's driving these diseases, and to work with leading scientists and engineers to design fresh approaches for how we might intervene."

"We believe that success against cancer will come if we apply the same creativity and innovation to the research enterprise that we do to the research itself," said Tyler Jacks, Director, Koch Institute at MIT. "New kinds of interdisciplinary collaboration are absolutely essential in order to rapidly translate research discoveries into clinical strategies that will benefit patients in the near-term. We are very excited to work with Dana-Farber/Harvard Cancer Center, with the help of visionary philanthropists and support of two leading research organizations, to make this program a reality."

The initial grant recipients were selected by an external advisory team that provided rigorous, expert review of more than a dozen proposals submitted by faculty from both institutions for consideration in this round of funding. The external advisors selected those projects that they believe have the greatest potential of generating high-impact clinical outcomes in the future.

The Bridge Project aims to raise and deploy $50M over the next three to five years into additional research teams focused on potentially transformative initiatives.

The teams receiving grant funding in this first round include:

Keith L. Ligon (Dana-Farber), J. Christopher Love (Koch Institute at MIT), Matthew Meyerson (Dana-Farber and Broad Institute) working on single-cell functional, genomic, and transcriptonic analysis in glioblastoma;

Rakesh K. Jain (Massachusetts General Hospital) and Robert S. Langer (Koch Institute at MIT) working on angiotensin receptor blockers (ARBs) as a novel approach to improve drug delivery in the treatment of pancreatic cancer;

Jeffrey W. Clark (MGH), Robert S. Langer (Koch Institute at MIT), Elazer Edelman (Harvard:MIT HST Program) working on the development of a pancreatobiliary chemotherapy eluting stent for pancreatic ductal adenocarcinomas;

Hidde Ploegh (Whitehead and Koch Institutes), Kai W. Wucherpfennig (Dana-Farber), and J. Christopher Love (Koch Institute at MIT) working on novel immunotherapies against pancreatic cancer.

Georgia Research Alliance Names First Eminent Scholar in Nanomedicine

Business Wire: February 28, 2012 – ATLANTA, GA, U.S.A. – Younan Xia, Ph.D., an internationally recognized leader in the field of nanotechnology, recently joined the Georgia Institute of Technology as the first Georgia Research Alliance (GRA) Eminent Scholar in Nanomedicine.

Dr. Xia is the Brock Family Chair and GRA Eminent Scholar in Nanomedicine in the Wallace H. Coulter Department of Biomedical Engineering at Georgia Tech and Emory University, with a joint appointment in the School of Chemistry and Biochemistry. His research focuses on nanocrystals—a novel class of materials with features smaller than 100 nanometers—as well as the development of innovative technologies enabled by nanocrystals. One nanometer is equal to one billionth of a meter.

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These technologies span the fields of molecular imaging, early cancer diagnosis, targeted drug delivery, biomaterials, regenerative medicine, and catalysis.

"The possible applications of nanotechnology in medicine have only begun to be explored," said Michael Cassidy, president and CEO of the Georgia Research Alliance. "Dr. Xia's expertise and collaborative vision will lead to vital new scientific discoveries that can be transformed into new tools to help people live healthier lives."

Dr. Xia is an international leader in the synthesis of nanomaterials designed to improve the way we live. He has been ranked as one of the top 10 chemists in the world, as well as the second most cited scientist in the fields of nanomedicine and materials science.

"Dr. Xia is a world-renowned teacher and leader at the forefront of nanomedicine and materials science," said Larry McIntire, the Wallace H. Coulter Chair of Biomedical Engineering. "His reputation and innovative research in these areas will clearly strengthen our expanding efforts in nanomedicine and biomaterials. We are honored to welcome him to the Department and to the Institute."

Regents' Professor and Chair of Chemistry and Biochemistry Charles Liotta said, "Dr. Xia is an outstanding addition to our faculty in the School of Chemistry and Biochemistry. His research in nanomedicine and biomaterials lies at the interface between chemistry and engineering and fits in so well with the interdisciplinary culture at Georgia Tech. Dr. Xia's presence will clearly enhance our efforts in these critical research areas."

Dr. Xia received his Ph.D. in physical chemistry from Harvard University (with Professor George M. Whitesides) in 1996, his M.S. in inorganic chemistry from the University of Pennsylvania (with the late Professor Alan G. MacDiarmid, a Nobel Laureate in Chemistry, 2000) in 1993. He has received a number of prestigious awards, including AIMBE Fellow (2011), MRS Fellow (2009), NIH Director's Pioneer Award (2006), Leo Hendrik Baekeland Award (2005), Camille Dreyfus Teacher Scholar (2002), David and Lucile Packard Fellowship in Science and Engineering (2000), Alfred P. Sloan Research Fellow (2000), NSF Early Career Development Award (2000), and the ACS Victor K. LaMer Award (1999).

Zicam® Maker, Matrixx Initiatives, Names Personal Care Products Pioneer M'lou Arnett as CEO

PRNewswire: February 1, 2012 – SKILLMAN, NJ, U.S.A. – Matrixx Initiatives, Inc., the maker of the Zicam® cold, sinus, and allergy line of products, is proud to announce the appointment of pioneering personal healthcare products executive M'lou Arnett, 47, as Chief Executive Officer, effective immediately. Ms. Arnett has more than 20 years of management and healthcare marketing experience and was a principal architect of the highly successful marketing campaign for the Mucinex® cold remedy products. Immediately prior to joining Matrixx, Ms. Arnett was Chief Operating Officer of Scerene Healthcare Inc. of Peapack, NJ, a company she co-founded in 2009 to develop the Puristics™ brand of personal care products.

"Matrixx is an opportunity I couldn't pass up," Ms. Arnett said. "Matrixx's Zicam cold remedy line of products has strong brand equity and a great history, and I feel that I have been given a fantastic opportunity to write the next chapter. Matrixx has great people, a tremendous heritage and all the pieces in place to create some magic."

Previously, Ms. Arnett was Senior Vice President, Marketing and Advertising for Adams Respiratory Therapeutics, the marketer of Mucinex and Delsym®. She is renowned in the OTC industry for overseeing the development of the award-winning "Mr. Mucus" advertising campaign, which not only increased sales of Mucinex but also increased awareness of the entire category of mucus relieving products. From 2004, when she joined Adams, to 2008 Ms. Arnett played a key role in growing the Adams business from $60 million to nearly $500 million. Adams was sold to Reckitt Benckiser in 2008.

Prior to joining Adams, Ms. Arnett managed a broad spectrum of healthcare businesses at Pfizer Consumer Healthcare and its predecessor Warner Lambert Consumer Healthcare, including Listerine®, Lubriderm®, and Benadryl®. She was named one of the top 50 marketers of the year by Advertising Age in 2006 and one of the top 20 marketers of the year by OTC Perspectives in 2008.

Ms. Arnett says she believes Zicam is well-positioned to take advantage of consumers' increasing interest in self-care. "We have a solution for consumers that can change the way they take care of themselves, and Matrixx is well-positioned to be a major player in this space."

"I have a long history of growing brands through developing strong strategies for consumer brands based on insights into the needs and daily lives of consumers," she continued. "We have the opportunity to make Zicam a household name, something everyone has in their medicine cabinet."

Ms. Arnett began her career in commercial banking with Chase Manhattan Bank. She received an MBA from Columbia University Graduate School of Business and a B.A. from Yale University. She is proud to be a working mother of four teenagers, and is passionate about maintaining a healthy lifestyle.

Tris Pharma Announces Appointment of Dr. Mahdi Fawzi as Top R&D Executive

PRNewswire: January 25, 2012 – MONMOUTH JUNCTION, NJ, U.S.A. – Tris Pharma, an emerging specialty pharmaceutical company, announced joining of a highly regarded Big Pharma executive Dr. Mahdi Fawzi to its leadership position as the Chief Scientific Officer and Executive Vice President of R&D including Regulatory Affairs.

Throughout his career Dr. Fawzi has helped create a huge value, as exemplified by having many blockbuster drugs developed under his leadership, such as Lipitor®, Enbrel®, Protoni®, Effexor X®, Rapamune®, and Pristiq®, among others. Most recently Dr. Fawzi was President, Global Research & Development at Warner Chilcott, where he led approval of Atelvia™ and Loestrin 24Fe and managed integration of P&G's Pharmaceutical R&D operation. From 1995 to 2009, Dr. Fawzi was part of the senior leadership team at Wyeth, including the last five years as Executive Vice President of Preclinical Development. Under his leadership Wyeth advanced 91 new molecules, filed 70 INDs, and 10 NDAs over the last seven years prior to the Pfizer merger. He oversaw 1,300 scientists worldwide and managed a budget of over a quarter of a billion dollars. While at Wyeth, he won several prestigious industry awards and was one of the four finalists in 2004 for the Pharmaceutical Executive of the Year Award. He also held senior management positions at Warner Lambert and P&G. He is an author or co-author of over 50 publications and awarded more than 80 patents. He is a pharmacist by education and earned his M.S. and Ph.D. in Pharmaceutical Chemistry at the University of Michigan.

"We are fortunate to have someone of Dr. Fawzi's caliber lead Tris R&D. Mahdi will lead our development, strengthen the research base of various technology initiatives that are underway, direct clinical and regulatory disciplines," said Ketan Mehta, Tris's President and CEO. "Dr. Yu-Hsing Tu, who has led R&D for the last ten years, will focus on product development and report to Mahdi."

"I am truly excited to be part of Tris's pioneering work involving new technologies, especially the OralXR+ platform and its application in liquid and other unique dosage forms," stated Dr. Mahdi Fawzi. "Tris has accomplished a great deal in its relatively short history, and I look forward to building upon the successes Dr. Tu and the R&D team have had to date." ■

In the News

Compiled by Steven Giannos, Chrono Therapeutics Inc.
Industrial Editor

March 2012

Moberg Derma AB: Moberg Derma Receives Approval to Initiate Clinical Trial for Limtop

Business Wire: March 9, 2012 – STOCKHOLM, Sweden – The German Federal Institute for Drugs and Medical Devices (BfArM) has granted Moberg Derma (STO: MOB) approval to initiate a clinical phase I trial for Limtop. Limtop is an innovative formulation of an immunomodulatory compound with potential to treat actinic keratosis, genital warts, and basal cell carcinoma. The objective is a product with short treatment duration, an improved safety profile, and an efficacy similar to or better than that of competing preparations.

"Limtop has the potential to make a real difference for many patients who currently suffer significant side effects, and we are now looking forward to testing the formulation clinically. The results from the Phase I study are expected in the second quarter of 2012," said Peter Wolpert, CEO and founder of Moberg Derma.

Orexo AB Focuses Its Business and Reduces Costs

Business Wire: March 6, 2012 – UPPSALA, Sweden – Orexo AB is focusing its development activities to the three proprietary programs OX219, OX51, and OX27. The total requirement for resources will thereby be reduced with up to 35 full-time employees.

The personnel reduction, which will have full effect in 2013, is expected to lower the costs by a total of SEK 30 million annually. Negotiations with trade union representatives will commence immediately. The reduction in personnel is expected to be completed during the second quarter of 2012.

"The focus of our business activities will now be fully in line with Orexo's strategy, and we shall exclusively invest in further development and commercialization of our proprietary products. This means that we are directing all our resources towards our key later stage development programs," says CEO Anders Lundström.

The three programs, OX219, OX51, and OX27 are based on proprietary drug delivery technologies applied to well-known substances with licensed uses. This results in programs with significantly lower development risk, lower cost, and shorter development time than traditional drug development programs. This approach was used to successfully develop Orexo's pain product Abstral® and the insomnia product Edluar™.

Orexo develops and markets pharmaceuticals based on proprietary drug delivery technologies applied to well-known substances. The company's largest product is Abstral, a treatment of breakthrough cancer pain. Orexo has today 110 employees, of which approximately 80 work in research and development. Orexo's shares are listed on the Stockholm Stock Exchange, and Danish Novo A/S and Swedish HealthCap are the largest shareholders. More information can be found at www.orexo.com

Columbia Laboratories Announces 42% Workforce Reduction, Projected Annual Savings of over $1.5 Million

Business Wire: March 1, 2012 – LIVINGSTON, NJ, U.S.A. – Columbia Laboratories Inc. (Nasdaq: CBRX) today announced a 42% workforce reduction from 24 employees at December 31, 2011, to 14 employees. The Company will record a severance charge of approximately $0.5 million in the first quarter of 2012, and expects to realize annual savings of over $1.5 million.

The reduction primarily impacts research and development and general administrative positions. Columbia's remaining staff will continue to focus on the future course of Columbia's business, executing its public reporting obligations, management of its supply chain, and its role on the Joint Development Committee with Watson Pharmaceuticals, Inc. (NYSE: WPI) for progesterone vaginal gel 8% for use in the reduction of risk of preterm birth in women with premature cervical shortening.

"Our action today is difficult, particularly because we greatly appreciate the contributions of those we must let go," said Frank Condella, Columbia's president and chief executive officer. "However, it is a step we must take to streamline operations and secure the Company's positive financial position. The workforce reduction will lower our costs and better align operating expense with revenues. Our remaining employees will remain focused on the future course of our business."

The Company is evaluating all strategic options moving forward and will update investors on its 2011 Earnings Conference Call scheduled for Thursday, March 8, 2012.

APR Applied Pharma Research (APR) and Labtec GmbH (Labtec) Announce the European Approval of Zolmitriptan Oral Dispersible Film (ODF)

Business Wire: March 1, 2012 – BALERNA, Switzerland & LANGENFELD, Germany & WARREN, NJ, U.S.A. – APR and Labtec announce to have received on February 8, 2012, the marketing authorization through a decentralized procedure (DCP) in 15 European countries of Zolmitriptan ODF, a film strip formulation containing 2.5 mg and 5 mg Zolmitriptan. It is their second prescription drug product, after SetoFilm® (Ondansetron ODF), approved in Europe in a dosage form based on a film strip technology. The product is developed in collaboration with Warren, New Jersey, based company Monosol Rx.

The DCP had Germany as Reference Member State and 14 Concerned Member States (Austria, Belgium, Denmark, Finland, France, Ireland, Italy, The Netherlands, Norway, Poland, Portugal, Spain, Sweden, and Ukraine). The product will be manufactured at Labtec's production site in Hamburg, Germany. APR and Labtec are now proceeding with the national procedures to complete the registration process. The team of companies that developed Zolmitriptan ODF is now entering discussions with other pharmaceutical companies to find the best marketing and distribution partner for the product.

Concurrently, MonoSol Rx and APR are reviewing their options in the Unites States to complete the required steps to obtain Marketing Approval by the FDA under a 505(b) 2 procedure.

Zolmitriptan Oral Dispersible Film ("ODF") is a unique formulation of Zolmitriptan based on the RapidFilm® technology, APR and Labtec's novel and proprietary oral drug delivery technology platform. The product consists of a very thin polymeric film strip containing the active ingredient. It has a size of 3 cm^2 and 6 cm^2 for the 2.5 mg and 5 mg dosage strengths, respectively. Once placed in the mouth, it dissolves in a few seconds and is swallowed with the saliva without the need of water. The Zolmitriptan ODF not only avoids the risk of aspiration but also improves patient compliance by reducing swallowing difficulties experienced by many patients taking other oral Zolmitriptan formulations currently available.

"The approval of the ODF form of Zolmitriptan proves once more that our technology performs well. The Oral Film Strip dosage form is a less invasive way to administer Zolmitriptan than regular tablets and does not require water, thus avoiding potential triggers of nausea and vomiting, which are symptoms frequently accompanying migraines," said Paolo Galfetti, CEO of APR.

"This is the next step in the success story of our Orally Dispersible Film (ODF) based products; Zolmitriptan ODF is intended to be a more user friendly form of Zolmitriptan and provides significant advantages to patients," said Ingo Lehrke, Managing Director of Labtec.

Asked about the market rationales of the Orally Dispersible Film based products, Mark Schobel, CEO of Monosol RX said: "One of the key features of Orally Dispersible Film products is to bring innovation to the market at a very competitive cost, and this is the key for any pharmaceutical company that strives to differentiate from others."

Zolmitriptan is the top selling anti-migraine drug in the combined top five European markets, with total sales in excess of $130 million and an approx. 18% market share (Datamonitor, Aug. 2010) and one of the leading triptans in the U.S., with sales in excess of $200 million. According to independent studies and researches, nausea occurs in more than 90% of all migraine sufferers; nearly one-third of these experienced nausea during every attack. Vomiting occurs in almost 70% of all migraine sufferers.

February 2012

OPKO Invests in BioZone Pharmaceuticals, Inc., Acquires Rights to Proprietary Technology to Enhance Solubility of Drugs

Business Wire: February 27, 2012 – MIAMI, FL, U.S.A. – OPKO Health, Inc. (NYSE: OPK) announced today it made an investment in BioZone Pharmaceuticals, Inc., (OTCBB: BZNE) and acquired rights to BioZone's novel drug delivery platforms, including its QuSome® technology. With BioZone's proprietary chemical and formulation technology, the solubility of many drugs can be enhanced to provide superior final dosage forms. BioZone's technology is simpler and results in less costly drug manufacturing than other systems.

Under the terms of the agreements, OPKO has acquired a world-wide license for the development and commercialization of products utilizing BioZone's proprietary drug delivery technology, including QuSomes, exclusively for OPKO in the field of ophthalmology and non-exclusive for all other therapeutic fields, subject in each case to certain excluded products. Additionally, OPKO acquired exclusive world-wide distribution rights to BioZone's enhanced formulation of propofol that utilizes its proprietary technology to produce a clear solution, which may address many of the drawbacks with current emulsion formulations of propofol.

Propofol is a short-acting, intravenously administered hypnotic agent commonly used for the induction and maintenance of general anesthesia, sedation for mechanically ventilated adults, and procedural sedation.

OPKO is a multi-national biopharmaceutical and diagnostics company that seeks to establish industry-leading positions in large and rapidly growing medical markets by leveraging its discovery, development, and commercialization expertise and novel and proprietary technologies.

FDA Accepts Impax Pharmaceuticals NDA Filing for IPX066 for the Treatment of Idiopathic Parkinson's Disease

Business Wire: February 23, 2012 – HAYWARD, CA, U.S.A. – Impax Pharmaceuticals, the branded products division of Impax Laboratories, Inc. (Nasdaq: IPXL) today announced that the U.S. Food and Drug Administration (FDA) has accepted for filing the Company's New Drug Application (NDA) for IPX066 for the treatment of idiopathic Parkinson's disease (PD) submitted to the Agency on December 21, 2011. IPX066 is a patented extended release capsule formulation of carbidopa-levodopa (CD-LD). The Prescription Drug User Fee Date (PDUFA) for a decision by the FDA is October 21, 2012. IPX066 has been licensed to GlaxoSmithKline (GSK) for countries outside the U.S. and Taiwan for development and marketing.

IPX066 has undergone extensive clinical development, including multiple studies in early and advanced PD in the U.S. and in

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Europe. The NDA included data from three controlled Phase III studies and two open label extensions of IPX066 in both early and advanced PD. IPX066 has been investigated in more than 1,000 subjects.

IPX066 is an investigational extended release capsule formulation of CD-LD that is intended to maintain consistent plasma concentration of levodopa for a longer duration versus immediate release levodopa, which may have an impact on fluctuations in clinical response. It is not approved or licensed anywhere in the world.

Results from the pivotal Phase III studies of IPX066, APEX-PD (early PD), ADVANCE-PD (advanced PD), and ASCEND-PD (advanced PD) have previously been announced. Results of the ASCEND-PD study have been accepted for presentation to the American Academy of Neurology in April 2012.

Impax Pharmaceuticals and GSK announced an agreement for the development and commercialization of IPX066 in December 2010. Under the terms of the agreement, GSK received an exclusive license to register and commercialize IPX066 throughout the world except in the U.S. and Taiwan. For more information, please visit the Company's website at www.impaxlabs.com.

Inovio Researchers Successfully Demonstrate RNA Drug Delivery via Electroporation

PRNewswire: February 22, 2012 – BLUE BELL, PA, U.S.A. – Inovio Pharmaceuticals, Inc. (NYSE Amex: INO) announced today that its next generation surface skin electroporation technology was successfully used to significantly enhance the delivery of small interfering RNA (siRNA) molecules to skin in animal studies. The data was published in the journal *Molecular Therapy – Nucleic Acids* in a paper titled "Optimized *in vivo* transfer of small interfering RNA targeting dermal tissue using *in vivo* surface electroporation."

While Inovio has multiple ongoing human trials demonstrating the efficacy of its electroporation technology to deliver synthetic DNA-based vaccines to both skin and muscle, this is the first time that this technology has been applied to the delivery of siRNA molecules.

Recently, siRNAs have demonstrated their potential as novel therapeutics due to their ability to induce robust, sequence specific gene silencing in cells. Using siRNA to induce RNA interference (RNAi) could become a promising therapeutic approach to treat many currently untreatable disorders, such as some cancers and many viral and genetic diseases. This preclinical study of Inovio's novel delivery method demonstrated positive results using its minimally invasive, low-voltage surface electroporation technology to successfully deliver siRNA to the skin.

The primary point of this study was to establish whether electroporation is able to accomplish effective delivery of RNA *in vivo*. The successful outcome of this study highlights the far-reaching therapeutic potential for Inovio's electroporation technology. Preclinical and clinical studies have demonstrated that electroporation, as an effective physical delivery method, can improve both the expression and immunogenicity of DNA vaccines by up to 100-fold.

Dr. J. Joseph Kim, President and CEO, said: "Perhaps the biggest hurdle in realizing the full potential of RNA-based therapies is the lack of proper and efficient delivery of siRNA molecules. This study supports the idea that Inovio's proprietary electroporation technology can successfully deliver breakthrough RNA therapies with the same efficacy and safety in which we deliver DNA therapies. Most important, our delivery platform could pave the way for the development of targeted RNA-based therapies for diseases and conditions that are now considered untreatable."

Researchers in this study investigated the optimization of electrical parameters for a novel low-voltage electroporation (EP) method to deliver RNA to dermal tissue *in vivo*. Initially, the electrical parameters were optimized for dermal delivery of plasmid DNA encoding green fluorescent protein (GFP) using this novel surface dermal EP device at as little as 10V voltage parameters. The device was also assessed for the electronic transfer of siRNA into dermal tissue, and Inovio researchers observed robust transfection of tagged-siRNA in the skin. The researchers then assessed whether the successful transfer of siRNA led to gene knockdown (silencing) *in vivo*. Using a reporter gene construct encoding GFP and tagged siRNA targeting the GFP message, researchers demonstrated simultaneous transfection of the siRNA to the skin via EP and the concomitant knockdown of the reporter gene signal. The siRNA delivery was accomplished with no evidence of injection site inflammation or local tissue damage. The minimally invasive low-voltage EP method is able to efficiently deliver functional siRNA molecules to dermal tissue in a tolerable manner.

Santarus and Depomed Announce Settlement with Lupin of GLUMETZA Patent Litigation

Business Wire: February 22, 2012 – SAN DIEGO & MENLO PARK, CA, U.S.A. – Santarus, Inc. (Nasdaq: SNTS) and Depomed, Inc. (Nasdaq: DEPO) today announced that they have entered into a settlement agreement with Lupin Ltd. and its subsidiary, Lupin Pharmaceuticals, Inc., to resolve pending patent litigation involving GLUMETZA® (extended release metformin tablets) 1,000 mg and 500 mg.

The settlement agreement grants Lupin the right to begin selling a generic version of GLUMETZA on February 1, 2016, or earlier under certain circumstances. The settlement agreement is subject to review by the U.S. Department of Justice and the Federal Trade Commission, as well as entry by the U.S. District Court for the Northern District of California of an order dismissing the litigation.

Collegium Pharmaceutical Announces Series B Financing and Advancement of Development Program for its DETERx® Tamper-Resistant, Extended-Release Opioid

Business Wire: February 22, 2012 – CUMBERLAND, RI, U.S.A. – Collegium Pharmaceutical, Inc., a specialty pharmaceutical company focused on the development of innovative treatments for chronic pain, announced today that it has raised $22.5 million in a Series B financing round led by Longitude Capital and Skyline Ventures. Series A investors Frazier Healthcare Ventures and Boston Millennia Partners also participated in the round.

In connection with the financing, David Hirsch, M.D., Ph.D., of Longitude Capital and Stephen Hoffman M.D., Ph.D., of Skyline will join the Collegium board of directors that includes Patrick Heron of Frazier, Patrick Fortune, Ph.D., of Boston Millennia and Michael Heffernan, the Company's Founder and CEO.

The Series B financing will support the execution of the Company's full development program for COL-003, a tamper-resistant, extended-release oxycodone product utilizing its proprietary DETERx® technology. "We believe that with the ongoing national epidemic of prescription drug abuse, there remains a significant unmet clinical need for tamper-resistant formulations that can mitigate abuse/misuse of opioid products. We have initiated our Phase III trial for COL-003 and are working to complete the remaining development activities required for regulatory submission," stated Michael Heffernan, CEO, Collegium. The Company expects to file the NDA for COL-003 in 2013. The current financing will support the Company through FDA approval of COL-003.

Both chronic pain and prescription opioid abuse are highly prevalent. According to a recent Institute of Medicine report, approximately 116 million Americans suffer from chronic pain each year, and many of these patients are untreated or undertreated due to the significant concerns with the safety, abuse, and diversion of prescription opioids. Opioid formulations that incorporate barriers to common forms of tampering are an emerging component of risk management in prescription opioid therapy. "We were attracted to Collegium by the potential to develop an important and unique product that helps address the enormous and growing issue of prescription drug abuse. The DETERx technology provides market leading tamper-resistant properties that would substantially raise the bar for tamper-resistant opiates," stated David Hirsch of Longitude.

The DETERx® drug delivery platform consists of a multi-particulate matrix formulation in a capsule. While developed primarily to provide tamper-resistant properties to protect against common methods of tampering such as chewing, crushing, snorting, and extraction for IV injection, the multi-particulate design is expected to enable patients with difficulty swallowing to open the capsule and administer the contents on food or via a gastronomy tube, while maintaining the extended release properties of the product. DETERx technology can be used with drugs that are commonly abused such as opioids and amphetamines, as well as drugs that have narrow therapeutic windows that would benefit from protection against misuse such as breaking, crushing, grinding or dissolving the product. The formulation platform is covered by U.S. and international patents and patent applications. For more information, visit the Company's website at www.collegiumpharma.com.

Aerogen Gains Approval for Entry into Chinese Market

Business Wire: February 17, 2012 – GALWAY, Ireland – Aerogen (www.aerogen.com), the innovative medical device and drug delivery company, has announced receipt of authorisation to market its Aeroneb Pro and Aeroneb Go products in China. The Aeroneb Pro is a patented vibrating mesh nebuliser that creates a fine particle aerosol for targeted drug delivery to the lungs. This unique, easy to use, multi-patient nebuliser is aimed predominately at the critical care market for treatment of a broad spectrum of patient respiratory conditions. Aerogen has also received approval for its home care device, the Aeroneb Go. Based on the same vibrating mesh technology, the Aeroneb Go brings hospital grade efficiency to inhaled drug treatment in the home.

Aerogen, an Irish medical device company that currently sells its high-performance products in 65 countries, is continually expanding its operations into new markets. John Power, Aerogen CEO, commented, "The rapidly growing Chinese market is receptive to international products of the highest standard and plays a key role in Aerogen's ambitious plans for growth. We are looking forward to being a part of that market and bringing to Chinese patients for the first time the benefits enjoyed by users of our products across the globe."

Aerogen worked closely with Gaelmed, its distribution partner in China, to secure the approval from the State Food and Drug Administration (SFDA) for registration of two products from Aerogen. Gaelmed will act as a distribution channel for Aerogen, actively promoting and selling both the Aeroneb Pro and the Aeroneb Go within China.

Chinese annual spending on healthcare has an attractive 20% growth rate, representing a significant opportunity for advanced technologies to flourish. Aerogen is no stranger to high growth, having increased sales 30% year on year since its management buyout in 2008, an achievement recently recognised with the award of the Ruban d'Honneur for its international growth strategy at the European Business Awards.

"Aerogen is confident of a strong entry into the Chinese market. We expect to see Aerogen products in use in China by the end of March 2012, which will be a significant milestone in our planned move into emergent, high-growth regional markets," John Power said. www.Aerogen.com.

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MicroCHIPS Announces Clinical Results for First Successful Human Trial of Implantable, Wireless Microchip Drug Delivery Device

Business Wire: February 16, 2012 – WALTHAM, MA, U.S.A. – MicroCHIPS, Inc., a developer of implantable drug delivery devices and biosensors, announced today the results of the first successful human clinical trial with an implantable, wirelessly controlled and programmable microchip-based drug delivery device. The MicroCHIPS study was published in today's online edition of the journal *Science Translational Medicine*.

"These data validate the microchip approach to multi-year drug delivery without the need for frequent injections, which can improve the management of many chronic diseases like osteoporosis where adherence to therapy is a significant problem," said study lead author Robert Farra, MicroCHIPS President and Chief Operating Officer. "We look forward to making further progress to advance our first device toward regulatory approvals, as well as developing a range of products for use in important disease areas such as osteoporosis, cardiovascular disease, multiple sclerosis, cancer, and chronic pain."

In the trial, postmenopausal women diagnosed with osteoporosis received daily doses of the marketed osteoporosis drug teriparatide through microchip delivery rather than daily injection. The drug released from the implanted microchip demonstrated similar measures of safety and therapeutic levels in blood to what is observed from standard, recommended multiple subcutaneous injections of teriparatide.

In the study, seven osteoporotic postmenopausal patients between the ages of 65 and 70 received the microchip-based implant. The primary objective of the clinical trial was to assess the pharmacokinetics (PK) of the released drug teriparatide from the implanted devices. Safety measures included evaluation of the biological response to the implant and monitoring indicators of toxicity. Secondary objectives were to assess the bioactivity of the drug and to evaluate the reliability and reproducibility of releasing the drug from the device.

The device and drug combination were found to be biocompatible with no adverse immune reaction. The resulting PK profiles from the implant were comparable to and had less variation than the PK profiles of multiple, recommended subcutaneous injections of teriparatide. The study also demonstrated that the programmable implant was able to deliver the drug at scheduled intervals. Drug delivery and evaluation in patients occurred over a one month period and provided proof-of-concept measures of drug release and device durability that support implantable device viability for 12 months or more.

The microchip device was implanted and explanted using local anesthetic. Patient surveys found that the microchip device was well-tolerated, and patients indicated that they would repeat the implant procedure. "Each procedure lasted less than 30 minutes," said treating surgeon Pia Georg Jensen, M.D. "The patients were able to walk out of the facility and go home unescorted."

To assess efficacy and improvement in bone fracture risk, the study measured biological markers of bone formation (P1NP) and bone resorption (CTX). In the study, changes in serum calcium, P1NP, and CTX resulting from drug implant therapy were found to be qualitatively and quantitatively similar to those reported in previous studies during daily subcutaneous injections of teriparatide.

"A microchip that continues to deliver teriparatide with this or similar consistency and efficiency over 12 to 24 months could improve bone mass, density, architecture, and strength," said study co-author Robert Neer, M.D., Founder & Director of the Massachusetts General Hospital Bone Density Center and Associate Professor of Medicine at Harvard Medical School.

Implantable medical devices such as pacemakers and pain pumps perform important functions to help patients return to a healthier state and to manage their disease. The design of a next-generation microchip drug delivery device is the only approach to an implantable device that can be wirelessly programmed to release drugs inside the body without percutaneous connections in or on the patient. An implantable microchip device also provides real-time dose schedule tracking, and as part of a network, physicians can remotely adjust treatment schedules as necessary.

"This trial demonstrates how drug can be delivered through an implantable device that can be monitored and controlled remotely, providing new opportunities to improve treatment for patients and to realize the potential of telemedicine," said study co-author Robert Langer, Sc.D., Institute Professor at the David H. Koch Institute for Integrative Cancer Research at MIT and cofounder of MicroCHIPS, Inc. "The convergence of drug delivery and electronic technologies gives physicians a real-time connection to their patient's health, and patients are freed from the daily reminder, or burden, of disease by eliminating the need for regular injections."

MicroCHIPS is currently developing new designs of its microchip-based implant to include as many as 400 doses per device, providing daily dosing for one year or multi-year therapy for less frequent dosing regimens. Components of the original microchip technology, such as the array of micro reservoirs used to contain drug and the first microchip opening mechanism, were developed at the Massachusetts Institute of Technology and licensed to MicroCHIPS.

The study with the implantable microchip in osteoporosis patients was funded and managed by MicroCHIPS. In addition to osteoporosis, the company is advancing applications for the microchip device for other therapeutic applications in proprietary programs and through strategic partnerships. The company plans to file for regulatory approval for its first microchip device in 2014.

Xenogenics Received Rights to Polyanhydride Compounds Drug Delivery Patent

PRNewswire: February 16, 2012 – WOONSOCKET, RI, U.S.A. – Xenogenics Corporation, a subsidiary of MultiCell Technologies, Inc. (OTC Bulletin Board: MCET) has exclusive license rights to a polyanhydride compounds drug delivery patent recently granted in Canada.

The patent was granted to Rutgers University this July for polyanhydrides that link low molecular weight drugs containing a carboxylic acid group and an amine, thiol, alcohol, or phenol group within their structure into polymeric drug delivery systems. The patent also covers methods of producing polymeric drug delivery systems via these polyanhydride linkers and methods of administering low molecular weight drugs to a host via the polymeric drug delivery systems.

Xenogenics Corporation has exclusively licensed this patent from Rutgers University and believes it has applications in the company's coated cardiac stent business and other therapeutic applications that may be attractive to the pharmaceutical industry.

Xenogenics Corporation is a majority-owned subsidiary of MultiCell Technologies, Inc., which is developing novel therapeutics and discovery tools that address unmet medical needs. For more information about Xenogenics Corporation and MultiCell Technologies, please visit www.xenogenicscorp.com and www.multicelltech.com.

RedHill Biopharma Commences Advanced Clinical Trial with RHB-102 (Prevention of Nausea and Vomiting in Cancer Patients); Subjects Recruitment Completed; First Dosing Took Place; Results Expected Within Months

Business Wire: February 15, 2012 – TEL AVIV, Israel – RedHill Biopharma Ltd. (TASE: RDHL), an emerging Israeli biopharmaceutical company focusing primarily on development of late clinical-stage new formulations and combinations of existing drugs, has announced today the commencement of an advanced clinical trial with RHB-102 for the prevention of nausea and vomiting in cancer patients. RedHill completed screening and recruitment of all subjects for this clinical trial and announced subjects' first dosing on February 13, 2012.

Earlier this week RedHill Biopharma announced IND (Investigational New Drug Application) approval from FDA. RedHill previously obtained CTA (Clinical Trial Application) approval from Health Canada.

RHB-102 is a once-daily controlled release Ondansetron formulation referencing GSK's Zofran®—a leading and approved drug administered several times per day, with annual sales of hundreds of millions of dollars (including generic versions). The RHB-102 clinical trial is a bioequivalence study that aims to test the pharmacokinetic similarity between RedHill's once-daily controlled release tablet formulation and Zofran®. The RHB-102 clinical trial is expected to last several months up to final analysis of its results.

Based on advice from the Company's regulatory advisors and preliminary discussions held with FDA regarding the requisite regulatory route, if positive results are obtained and certain FDA requirements are met, the clinical trial may be considered a pivotal one (Phase III–equivalent), to be used by the Company for submitting a U.S. marketing approval application (NDA, New Drug Application).

RHB-102 is a patent protected once-daily controlled release tablet formulation of the active ingredient Ondansetron, a serotonin 5-HT3 receptor antagonist used mainly as an antiemetic (i.e., for prevention of nausea and vomiting). The drug market for serotonin receptor inhibitors (the drug family of RHB-102) is estimated at approximately $1 billion.

Mr. Gilead Raday, VP Corporate & Product Development at RedHill Biopharma, stated today: "We are excited about the commencement of the RHB-102 advanced clinical trial, which we hope will lead to a U.S. marketing application filing. RHB-102 is designed to prevent nausea and vomiting during a time window of up to 24 hours post administration, and is therefore expected to provide enhanced relief to cancer patients undergoing radiotherapy, relieving such patients from the requirement to take additional doses post radiotherapy treatment."

Nanologica Becomes Strategic Partner in €10M EU Project to Develop New Treatments for Tuberculosis

Business Wire: February, 15, 2012 – STOCKHOLM, Sweden – Nanologica AB today announced that the Company is a key player in the ORCHID project. The ORCHID alliance brings together tuberculosis (TB) expertise from academia, government research centres, non-profit organizations, and biotech companies. The project is funded by European Union's Seventh Framework Programme.

Within ORCHID, Nanologica's first goal is to deal with the immediate formulation problems associated with the poor water solubility of GSK's and other partner members' TB compounds.

"Nanologica's carrier materials are instrumental to the pharmaceutical industry," said Andreas Bhagwani, CEO of Nanologica. "Our approach can improve the formulation and solubility of water-insoluble active pharmaceutical compounds, to control their pharmacokinetic parameters, such as bioavailability. With this, we can achieve specific targeted release of active compounds."

After years of extensive research in the area of pharmaceutical excipients, Nanologica has shown the value of their silica-based porous materials. Through slow and controlled release from the porous particles, the materials significantly enhance the solubility of pharmaceutical compounds.

Nanologica's research team and other leading scientists worldwide will combine their expertise to investigate the potential of three different areas of research, all of which have shown potential effect against TB.

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The three areas to be investigated are:

β-Lactams—new evidence suggests that a novel approach could make these broad-spectrum antibiotics effective against TB. This approach will seek to design new animal models to demonstrate the potential of β-lactams as treatments against TB.

New InhA inhibitors—GSK, in collaboration with TB Alliance, has recently identified a chemical series that can inhibit recognised known TB target (InhA), which is essential for the bacterium's survival. Tool compounds in this series have shown active against multidrug resistant strains (MDR-TB) in the lab and have also demonstrated promising activity in animal models of *Mycobacterium tuberculosis*.

Whole-cell hits—Compounds that have been shown to be active against TB in High Throughput Screening but whose mode of action is unknown. The project will aim to understand this activity.

The €10M project is part of the Seventh Framework Programme for Research and Technological Development (FP7), led and partly funded by the European Union, which is providing €5.4M. The remainder of the funds will be provided by the ORCHID partners, largely from the provision of expertise and resources.

The 11 partners that make up ORCHID are:

- The University of Birmingham—Birmingham, U.K.
- Univerza v Ljubljani—Ljubljana, Slovenia
- Institut National de la Santé et de la Recherche Médicale (INSERM)—Toulouse, France
- Global Alliance for Tuberculosis Drug Development—New York, U.S.A.
- Nanologica AB—Stockholm, Sweden
- Cellzome AG—Heidelberg, Germany
- Université Pierre et Marie Curie—Paris, France
- École Polytechnique Fédérale de Lausanne—Lausanne, Switzerland
- The Federal State Scientific Institution Saint-Petersburg Scientific Research Pasteur Institute of Epidemiology—Saint Petersburg, Russia
- Microbiology and Federal State Institution Saint Petersburg Research Institute of Phthisiopulmonology of the Federal Agency for High Technology Medical Aid—Saint Petersburg, Russia
- Institut Pasteur Korea—Bundang-gu, Korea
- GSK Tres Cantos Medicines Development Campus—Madrid, Spain

FP7 is the European Community Framework Programme for Research, Technology, Development and Demonstration covering almost all scientific disciplines. It is a collection of efforts at EU level to fund and promote research.

The main objective of FP7 is to support the Lisbon strategy, in directing Europe toward becoming one of the most competitive, knowledge-based economies in the world. In order to ensure this objective and help create a European Research Area, FP7 will run for a period of seven years (2007–2013) and fund hundreds of projects originating from European players in research and innovation.

Nanologica is a materials development company that specializes in evolving innovative nanoporous structures as carrier materials for a variety of applications, ranging from drug delivery to cosmetics. The patented technique enables Nanologica to create structures that have novel properties and functions based on their size, shape and composition. Nanologica's unique technology is based on nanotechnology research from Stockholm University and Uppsala University. The Swedish-based company was founded in 2004. For more information, please visit www.nanologica.com.

BYDUREON™, First and Only Once-Weekly Type 2 Diabetes Treatment, Now Available in U.S. Pharmacies

PRNewswire: February 13, 2012 – SAN DIEGO, CA, U.S.A. and DUBLIN, Ireland – Amylin Pharmaceuticals, Inc. (Nasdaq: AMLN) and Alkermes plc (Nasdaq: ALKS) today announced that BYDUREON™ (exenatide extended-release for injectable suspension) is now available by prescription in U.S. pharmacies.

The U.S. Food and Drug Administration (FDA) approved BYDUREON, the first and only once-weekly treatment for type 2 diabetes, on January 27, 2012, as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes. The approval was based on safety and efficacy data from the DURATION clinical trial program, in which treatment with BYDUREON resulted in improvements in glycemic control in a once-weekly dose.

"Type 2 diabetes is a complex condition that can be very demanding for patients," said Steven Edelman, M.D., professor of medicine, Division of Endocrinology and Metabolism, University of California, San Diego. "I'm excited to be able to offer my patients BYDUREON, since it provides significant improvements in blood glucose control with just one dose per week."

BYDUREON is provided in a straightforward single-dose tray so that patients can self-administer the once-weekly subcutaneous (under the skin) injection. To help patients get off to a successful start, Amylin offers BYDUREON Steady Support℠ for patients and healthcare providers. BYDUREON Steady Support offerings include flexible resources for healthcare providers and their patients to learn about BYDUREON, how to administer it, and how to sign up to receive ongoing support to help manage type 2 diabetes. This support will include access to BYDUREON specialists seven days a week via a toll-free number, interactive tutorials online, and the opportunity to schedule in-person training sessions with a diabetes educator.

Amylin is committed to assisting patients with diabetes in accessing coverage for BYDUREON. Eligible patients will have access to the BYDUREON Steady Savings Card to help offset copay costs. With the Steady Savings Card, these patients can

save up to $50 per month on their BYDUREON prescriptions for up to 24 months. A patient assistance program is also available for eligible patients who have been prescribed BYDUREON but do not have insurance for prescription drugs. Additional information can be found at www.bydureonreimbursement.com.

Columbia Laboratories Transfers NDA for Progesterone Vaginal Gel 8% to Watson Pharmaceuticals

PRNewswire: February 13, 2012 – LIVINGSTON, NJ and PARSIPPANY, NJ, U.S.A. – Columbia Laboratories, Inc. (Nasdaq: CBRX), and Watson Pharmaceuticals, Inc. (NYSE: WPI), today announced that Columbia has transferred the new drug application for progesterone vaginal gel 8% for use in the reduction of risk of preterm birth in women with a singleton gestation and a short uterine cervical length in the mid-trimester of pregnancy (NDA 22-139) to Watson.

Watson has full rights and regulatory responsibility for all activities and sponsor obligations relating to this application as of February 10, 2012. The companies indicated that Watson is continuing to work with FDA in support of the review of the NDA.

The March 2010 Purchase and Collaboration Agreement between Columbia and Watson contemplates the transfer of the NDA. There are no incremental payments associated with the transfer, and Columbia maintains its financial interest in the product and its role in the companies' Joint Development Committee.

"We continue to enjoy a strong working relationship with Watson and believe this is the appropriate time to transfer the NDA," said Frank Condella, President and CEO of Columbia Laboratories, Inc. "As a result of this action, shareholders and other stakeholders can be assured that Watson will provide the resources available, as a result of its position as a $4.6 billion global pharmaceutical industry leader, to support continued progress of this application." The FDA is expected to take action on the NDA by February 26, 2012.

Impax Laboratories Provides Update on Status of Warning Letter Resolution for its Hayward Facility

Business Wire: February 9, 2012 – HAYWARD, CA, U.S.A. – Impax Laboratories, Inc. (Nasdaq: IPXL) today provided an update on the status of its resolution of the previously disclosed warning letter issued by the U.S. Food and Drug Administration (FDA) covering its Hayward manufacturing facility. Late last year, Impax received an acknowledgement letter from the FDA stating that it had received a complete response from Impax to the warning letter. However, a satisfactory re-inspection is required to close out the warning letter and the re-inspection by the FDA has not occurred to date. Therefore, the Company's previously stated goal for completing the closing out of the warning letter before the end of February 2012 may not occur. Until such re-inspection is completed and the warning letter is closed out, approval of the Company's pending drug applications listing the Hayward manufacturing facility as a manufacturing location may be withheld by the FDA.

"We worked as quickly and diligently as possible to ensure we addressed all FDA concerns, and look forward to a timely resolution," said Larry Hsu, Ph.D., president and CEO, Impax Laboratories. "At the same time, we have been successfully executing our growth strategy, including pursuing external growth opportunities, further advancing our generic and brand R&D pipeline, and servicing our customers. Our focus on achieving these objectives is evident in several recent positive events, including obtaining a long-term licensing agreement for Zomig®, advancing our pipeline with the filing of a New Drug Application for IPX066, and submitting 11 Abbreviated New Drug Applications in 2011."

As part of its Global Quality Improvement Program, the Company said it has revised its Standard Operating Procedures, made key staffing changes, revalidated manufacturing processes, conducted additional training, and purchased and validated new equipment.

Hsu added, "Improving the operation of all of our production facilities and company-wide quality systems has strengthened our Company, and continuous improvement will remain a top priority. We appreciate the communication and guidance provided by the FDA throughout this process and look forward to their re-inspection of our Hayward facility."

Moberg Derma AB: Further Studies May Be Required for MOB-015

Business Wire: February 9, 2012 – STOCKHOLM, Sweden – Moberg Derma AB (OMX: MOB) has analysed data from approximately fifty per cent of the patients in the ongoing open phase II study for MOB-015. Based on the analysis, the company assesses that there is low probability that the final results from the study will be sufficient for out-licensing the project. Further studies will probably be required before continuing to phase III. The ongoing phase II study will be completed and results are expected by the end of the year.

"In parallel with the completion of the study, we will get additional data and can identify possible product improvements. The project will be delayed, but our financial goals remain—to attain positive operating income and positive operating cash flow from and including 2013 and in the long-term to attain an operating margin of at least 25% with continued strong growth," said Peter Wolpert, CEO of Moberg Derma.

MOB-015 is a new topical treatment for nail fungus (onychomycosis) with fungicidal, keratolytic, and emollient properties. Moberg Derma's patent-pending formulation technology facilitates high concentrations of a fungicidal substance to be transported in and through nail tissue. In pre-clinical studies on human nails, more than tenfold concentrations of the antifungal substance have been detected,

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compared to the concentrations measured in the nail with successful oral treatment. As MOB-015 is applied locally, the side effects associated with oral treatment are avoided.

Nail fungus is the most common nail disease and afflicts approximately 10% of the general population and increasing with age. The estimated global market potential exceeds USD 1 billion. The untapped potential is significant, since many patients remain untreated. It is generally recognized that there is a need for new efficacious and safe topical treatments.

Ocular Therapeutix, Inc. Receives IDE Approval to Conduct a Pivotal Clinical Trial for ReSure™ Sealant

PRNewswire: February 6, 2012 – BEDFORD, MA, U.S.A. – Ocular Therapeutix, Inc. announced today that it has received IDE approval from the U.S. Food and Drug Administration to conduct a pivotal clinical trial with ReSure Sealant, a proprietary synthetic hydrogel polymer for ophthalmic use over clear corneal incisions.

The randomized, parallel-arm clinical trial will test the safety and efficacy of the device, relative to sutured closure, for prevention of postoperative fluid egress on clear corneal incisions following cataract or intraocular lens placement surgery. The trial will be conducted at up to 24 sites throughout the United States.

Cataract surgery is the most commonly performed surgery in the United States, with well over 3 million procedures conducted annually. Clear corneal wound leaks are widely thought to be a contributing factor to many post-surgical complications. Presently, ophthalmologists use stromal hydration to close these wounds; however, recent literature has shown that this technique may not be enough to create a watertight seal, and therefore more protection is necessary. "In a time where wound integrity is under scrutiny, this product fills a void where our only option for closure of vulnerable incisions was sutures," stated Steven Dell, Medical Director of Dell Laser Consultants. "ReSure Sealant could be a huge step forward for protecting our patients' eyes post-operatively."

"We are very excited to have developed a robust study with FDA's input to definitively demonstrate the utility of the ReSure Sealant compared to older methods of incision closure and management in clear corneal cataract surgery," stated Amar Sawhney, President and CEO of Ocular Therapeutix, Inc. "We look forward to completing the trial and making the ReSure Sealant available to U.S. physicians by next year."

OptiNose Files Investigational New Drug Application to Use Sumatriptan Delivered with Its Novel Drug Delivery Technology

Business Wire: February 2, 2012 – YARDLEY, PA, U.S.A. – OptiNose Inc. announced the filing of an Investigational New Drug (IND) with the U.S. Food and Drug Administration (FDA) in December 2011. The FDA has completed its review and has notified OptiNose that the studies under this IND may proceed. The Company will initiate Phase III trials in adults with acute migraine with or without aura utilizing its novel intranasal technology.

"This filing signals an important milestone in our quest to deliver improved relief to patients who suffer from migraine headaches," said Peter Miller, Chief Executive Officer (CEO) of OptiNose. "Based on our clinical study results to date, we are encouraged by the potential of the OptiNose technology and the significant impact it could have on patients with this debilitating condition."

OptiNose is a drug delivery company with breakthrough bi-directional nasal technology set to transform the static nasal drug delivery market. Founded in 2000, OptiNose's devices are designed to deliver intranasal drugs to target regions of the nasal cavity, including the sinuses and the olfactory region, while preventing lung deposition. The company offers both single and multi-use intranasal delivery devices for liquid and powder formulations. The technology has been tested in a number of clinical trials assessing both clinical efficacy and safety.

OptiNose's bidirectional nasal delivery technology significantly improves delivery to the targeted sites deep into the nose. While exhaling into the device, the soft palate automatically closes off the nasal cavity completely. The breath enters one nostril through a sealing nozzle and triggers the release of drug particles into the airflow. This action causes the narrow nasal passages to expand and carry these particles beyond the nasal valve to targeted sites. After delivering drug particles to the targeted sites, the air flow then exits the nasal cavity through the other nasal passage in the opposite direction.

Unigene Receives 2012 Drug Delivery Partnerships Industry Achievement Award

PRNewswire: February 1, 2012 – BOONTON, NJ, U.S.A. – Unigene Laboratories, Inc. (OTCBB: UGNE) today announced that it has received the 2012 Drug Delivery Partnerships™ ("DDP") Innovation Award in the Industry Achievement category in recognition of the Company's 2011 clinical advances in the oral delivery of peptides.

This year's DDP Award recipients were voted on and selected by conference attendees, including leading scientists, pharmaceutical executives, and drug delivery key opinion leaders, at the 16th annual DDP conference, held in Las Vegas, Nevada, January 25–27, 2012. This industry achievement award honors Unigene as the Company that has made the greatest contribution to the field of drug delivery throughout 2011.

Ashleigh Palmer, President and CEO, Unigene Laboratories, commented, "As the pharmaceutical industry's largest, longest running and most-respected drug delivery conference, acknowledgement from the DDP provides an exclamation point to Unigene's transformational 2011, which was marked by numerous business, clinical, and technological successes."

Dr. Nozer Mehta, Unigene's Vice President, Research and Development, said, "Among our achievements in 2011, Unigene saw two of its late-stage oral peptide programs successfully

advance in the clinic and serve to validate our proprietary oral delivery technology platform; OSTORA™, our oral calcitonin licensed to Tarsa Therapeutics, successfully completed a pivotal Phase 3 study and is targeted for an NDA submission by year-end 2012, and our oral PTH analog, for which we reported a successful outcome in a Phase 2 study with statistically significant results at the end of 2011, and are currently seeking a licensing partner. This progress not only marks major evolutionary steps in the administration of peptide-based therapeutics but is truly representative of the outstanding work by the entire Unigene team. We are extremely honored to accept the 2012 Drug Delivery Partnerships Industry Achievement Award."

As the leader in the design, delivery, manufacture, and development of peptide-based therapeutics Unigene is focused on advancing its own pipeline of novel, proprietary peptide product candidates focused on metabolic disease and inflammation as well as exploiting its industry-leading Peptelligence™ platform of peptide oral drug delivery and manufacturing assets, expertise, and capabilities by building a robust portfolio of strategically partnered opportunities.

"We are very proud to have Unigene as the 2012 DDP Innovation Award recipient," remarked Heather King, Program Director, Drug Delivery Partnerships. "Based upon voter response, it is clear that Unigene has cemented itself as a true innovator in oral peptide delivery and, more broadly, throughout the drug development and delivery industry."

Palmer concluded, "Unigene is proud of what it has accomplished thus far, and we are very excited by the tremendous opportunities on our horizon. We are committed to extending our leadership position and continue to firmly establish Unigene as the peptide development partner-of-choice for pharmaceutical companies interested in capitalizing on the significant opportunities that orally delivered peptides offer in the treatment of numerous debilitating diseases. Our goal is to continue to maximize our oral peptide development expertise, depth of technological know-how, and intellectual property housed within our Peptelligence™ platform."

January 2012

Oramed Pharmaceuticals Granted Australian Patent for Important Part of the Company's Core Technology in Oral Delivery of Proteins

PRNewswire: January 24, 2012 – JERUSALEM, Israel – Marking a major milestone for the Company, Oramed Pharmaceuticals Inc. (OTCBB: ORMP) (www.oramed.com), a developer of oral drug delivery systems, announced today that it has received approval for a key patent by the Australian Patent Office. The patent covers an important part of the Company's core technology, which allows for the oral delivery of peptides. Oramed's portfolio now consists of one issued patent and 34 patents pending for its technologies and products.
Oramed's core product is an oral insulin capsule. An oral delivery system for insulin may increase patient value, leading to a healthier lifestyle, especially at the earliest of stages of diabetes treatment. Higher patient compliance may result in improved patient outcomes and a reduction in the costs of healthcare and lost productivity.

According to a report by Medtech Insight, diabetes affects nearly 24 million people in the U.S. and an estimated 246 million adults worldwide. Being one of the most expensive diseases, it costs the U.S. healthcare system more than $130 billion per year, and the market for direct pharmaceutical care is close to $15 billion.

"Our patent position further strengthens Oramed and our competitive advantage in the development of an oral insulin capsule. The patent received will provide additional commercial protection for Oramed's technology and adds extended value to our existing IP-portfolio," said Nadav Kidron, CEO of Oramed.

FDA Grants Orphan Drug Designation to Ikaria® for Use of Inhaled Nitric Oxide in Pulmonary Arterial Hypertension

PRNewswire: January 23, 2012 – HAMPTON, NJ, U.S.A. – Ikaria, Inc., a critical care company focused on developing and commercializing innovative therapies for critically ill patients, today announced that the U.S. Food and Drug Administration (FDA) has granted orphan drug designation for the use of inhaled nitric oxide (iNO) with the INOpulse® DS drug-delivery system as a combination product for pulmonary arterial hypertension (PAH). An investigational new drug application (IND) for PAH was submitted to the FDA in November 2011, and the company is pursuing clinical development under this open IND.

Nitric oxide is naturally produced by many cells in the human body and is known as a "signaling molecule" due to its ability to penetrate cell membranes to deliver a signal to nearby muscles to relax. When inhaled, nitric oxide selectively relaxes the cells of the pulmonary vasculature, resulting in increased blood flow through the lungs and delivery of more oxygenated blood to the body. Inhaled nitric oxide is available as INOMAX® (nitric oxide) for inhalation, a vasodilator, which, in conjunction with ventilation and other appropriate agents, treats term and near-term newborns (>34 weeks gestation) with hypoxic respiratory failure associated with evidence of pulmonary hypertension.

Based on this use, Ikaria is investigating the use of iNO in patients with PAH, which is hypertension in the arteries between the heart and lungs. The delivery of iNO will be pulsed to synchronize with the patient's breathing pattern through Ikaria's next-generation INOpulse® DS drug-delivery system, which is specially engineered for use in spontaneously breathing patients. Ikaria's PAH development program, known as IK-7001, will investigate the use of iNO/INOpulse DS as a drug-device combination product.

"Our receipt of orphan drug designation for the use of iNO via the INOpulse in PAH, combined with the IND we submitted

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last year, speaks to the solid progress of our late-stage pipeline," stated Daniel Tasse, Chairman and CEO of Ikaria. "We're delighted to have PAH and bronchopulmonary dysplasia as additional indications under investigation for iNO, and also are planning its investigation with the INOpulse DS in chronic obstructive pulmonary disease."

Orphan drug designation is reserved for rare diseases or disorders that affect fewer than 200,000 people in the United States. PAH affects fewer than 200,000 Americans. This designation offers the sponsor tax credits on certain development costs, a waiver of the new drug application (NDA) user fee, and an exclusivity period of seven years following marketing approval. In addition to the seven-year marketing exclusivity period granted under the orphan drug designation, the INOpulse DS drug-delivery system would be further protected by developing a portfolio of patents, the last of which expires no earlier than 2029.

Alexza Announces Extension of the ADASUVE™ PDUFA Goal Date by Three Months

PRNewswire: January 23, 2012 – MOUNTAIN VIEW, CA, U.S.A. – Alexza Pharmaceuticals, Inc. (Nasdaq: ALXA) announced today that the U.S. Food and Drug Administration (FDA) will require additional time to complete its review of the New Drug Application (NDA) for ADASUVE™ (Staccato® loxapine).

In a notice received from the FDA, the Prescription Drug User Fee Act (PDUFA) date for the ADASUVE NDA has been extended from February 4, 2012, to May 4, 2012.

The FDA notified Alexza that its January 10, 2012, submission to the NDA, updating the proposed Risk Evaluation and Mitigation Strategy (REMS) program, has been designated as a major amendment. The FDA exercised its option to extend the PDUFA goal date to provide time to complete the review when a sponsor submits materials the FDA considers a major amendment to an NDA within three months of the PDUFA goal date. Alexza has submitted this amendment to the NDA, among others, to address topics discussed during the December 12, 2011, Psychopharmacologic Drugs Advisory Committee meeting on the ADASUVE application.

"We continue to believe that we are on a pathway to gain approval of ADASUVE in the United States," stated Thomas B. King, President and Chief Executive Officer of Alexza Pharmaceuticals. "We appreciate the efforts of the FDA to complete their review of our NDA, and we will continue to support the continued review of the NDA."

Patheon Adds Soft Gel Capsule Capabilities Through New Partnership with Procaps, S.A.

PRNewswire: January 19, 2012 – RESEARCH TRIANGLE PARK, NC, U.S.A. and BARRANQUILLA, Columbia – Patheon and PROCAPS S.A. are pleased to announce an agreement to provide the pharmaceutical industry a new world-class line of prescription pharmaceutical soft-gel product development and manufacturing services. The offering will be branded as "P-Gels" soft gels, and the partnership will give Patheon rights to market PROCAPS' soft gel technology and manufacturing capabilities in North America, Europe, and Asia.

"This exclusive agreement is part of our recently announced strategy to strengthen our core operations and product offerings," said Jim Mullen, Patheon's Chief Executive Officer. "By combining PROCAPS' manufacturing capabilities and proprietary technology with our global experience, reach, and customer service, we are positioned to provide our customers royalty-free soft gel capsule solutions for their products."

"PROCAPS is pleased to enter into this agreement with Patheon, one of the leading providers of contract development and manufacturing services in the world," said Ruben Minski, PROCAPS Chief Executive Officer. "This partnership truly provides us with a great opportunity to leverage our quality soft gel capabilities across the globe through Patheon's customers and beyond."

"The addition of commercial scale soft gel capacity to our full offering of dosage forms, which includes parenteral, solid, and liquid technologies, creates a more comprehensive array of options for our clients," commented Michael Lytton, Executive Vice President, Corporate Development and Strategy & General Counsel. "Soft gel oral drug delivery offers many advantages to some of the more challenging compounds being developed by the pharmaceutical industry today, and the collaboration with PROCAPS builds on Patheon's successful SoluPath™ solution set for compounds with solubility challenges. We look forward to partnering with our current and future customers to provide them with P-Gels soft gel capability." ■

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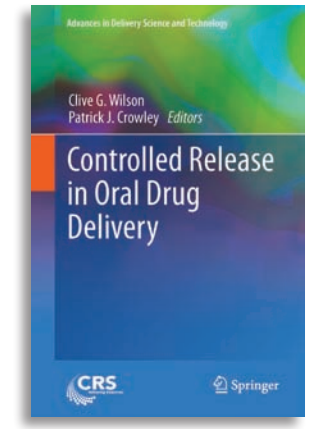

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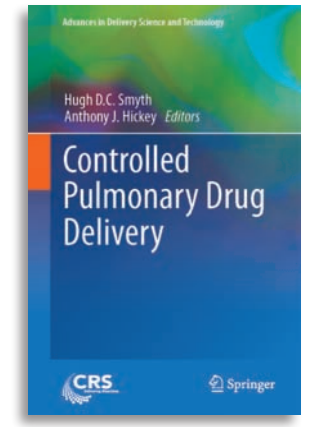

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