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CRS Goes to Capitol Hill

Chapter News



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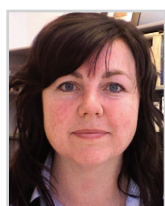
*Must meet all criteria for the Michelson Prize as stated at michelson.foundanimals.org



Charles Frey
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Arlene McDowell
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Rod Walker
Editor

CRS Newsletter

Leading
Delivery Science
and Technology

Vol. 29 • No. 4 • 2012

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

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*Yvonne Perrie
Aston University, School of Life and Health Sciences
Aston Triangle, Birmingham, U.K.*

Olympics and Nobel Prizes—Not an Easy Combination

Dear Reader,

Within this issue you will see a round-up of the 39th CRS Annual Meeting & Exposition held in Québec City, which was another great meeting. Whilst not perhaps as big as the Olympic Games, it was a great gathering of people working in the arena of Controlled Release from across the world. I will not dwell on the conference too much, but it is a little like a party—if you were there you know all about it, and if you were not, you really don't want to hear people going on and on about it. However, I hope you do enjoy the photos from the meeting. There are pictures of this year's award winners, which include the Outstanding Paper awards, the Distinguished Service Award, the College of Fellows appointments, the Founders Award, the Young Investigator Award, and two postdoctoral awards. Again, these photos are perhaps not quite as inspiring as those we are seeing from the Olympics—there are no photos of our Keynote speakers walking around draped in their national flag, and thankfully no one collapsed at the end of a presentation due to exhaustion, although I did see a few very tired delegates at some of the early starting sessions.

Regarding the Olympics, an interesting bit of trivia for you—only one or possibly two people have ever won both an Olympic medal and a Nobel Prize:¹ Philip Noel-Baker of Great Britain won the silver in the 1,500 metres in 1920 and captained the British track team at the 1920 and 1924 Games (which are the Games immortalised in the film *Chariots of Fire*). He received the Nobel Peace Prize in 1959 for his lifelong commitment to disarmament and international peace, and he participated in the formation of the League of Nations and the United Nations. It is also reported that Niels Bohr, who was awarded the Nobel Prize in Physics in 1922 for his quantum structure of the atom and other work in quantum theory, also won a silver Olympic medal (along with his younger brother Herald) in the 1908 summer Olympics as members of the Danish football team. However, there is some debate about this, as records show that only Herald Bohr was selected for the team.

Part of me wonders, with all the media coverage and celebration that the Olympics is quite rightly generating, wouldn't it be good if we had the Geek Olympics? That said—compared to a 100 metre sprint, perhaps the 100 micron electron scan might not be quite as exciting. So with that thought, I will go back to watching the Olympics; it is great to see Team GB doing so well. This is indeed good news for Britain and, with the gold medals we're winning, perhaps we can cash them in and help our ailing economy.

Best regards,

Yvonne

¹ <http://nobelprizewatch.wordpress.com/2011/11/30/when-a-nobel-prize-just-isnt-enough/> ■



*Martyn C. Davies
University of Nottingham
Nottingham, United Kingdom*

Olympic Spirit

The Olympics have just started in London. It means a great deal to us British; it's such an honour to host it, and we hope it has a lasting legacy for our youth. I was thinking of the ethos of the games, which are based on respect for others, bringing people together from all over the world, and the idea that taking part and giving your best is as important as winning. These are great ideals. I hope you all enjoyed the opening ceremony, including the Queen parachuting into the stadium—I never knew she could do that.

I have just returned from the 39th CRS Annual Meeting in Québec City, and in a much smaller way than the Olympics, it was also a time for people from our community drawn from all over the world to meet and discuss our science and technology. With an attendance of nearly 1,300 delegates from 40-plus countries, it was a conference to remember set in a beautiful location right at the heart of the city which added to the rich cultural and historical backdrop of Québec.

It was a great honour to be President during this conference. The program team—Hamid Ghandehari and Dusica Maysinger (Bioactive Materials), Christopher McDaniel and Teresa Virgallito (Consumer & Diversified Products), and Arlene McDowell and Thierry Vandamme (Veterinary)—did such a great job of generating a strong scientific theme with over 750 presentations, including 80+ invited speakers, 500+ poster presentations, and over 160 podium presentations. It was a great conference centre with rooms often full to bursting to hear the latest developments in science. The new format of the meeting worked well, with a huge standing-room-only attendance for the final plenary speaker, the venerable Vladimir Torchilin, on late Wednesday morning. Our CRS staff led by Susan Kohn did a superb job in ensuring all events ran smoothly—a big thank you to them.

There were outstanding awardees this year as CRS honoured all stages of what it means to be a delivery scientist, from recognising tomorrow's leaders with the Postdoctoral Achievement Award or the CRS Foundation's prestigious Sung Wan Kim Postdoctoral Fellowship to celebrating the lifelong dedication of our newest inductees into the College of Fellows. You can see all our awardees and other meeting pictures on our CRS website, www.controlledreleasesociety.org/meetings/annual/overview/photos. Congratulations to them all!

It wasn't all just about the science at the meeting but also there were great opportunities for networking. We had a great turnout to the Women in Science Luncheon organized by Diane Burgess, and over 150 people attended the first timers event to

learn more about the society and meet the CRS Board Members. We had over 100 new members sign up for the Mentoring Program run by the CRS Young Scientist Mentor-Protégé Subcommittee, and the Young Scientist Networking Evening was sold out. There were many representatives of our local chapters present, and I was delighted to meet up with a large group of young scientists that I had spoken to at the India Local Chapter meeting in Mumbai earlier in the year. I am personally very grateful to Kinam Park for such an entertaining speech at the superb Banquet; he really is quite amusing.

Our annual meeting was a chance for our committees to meet, to discuss the new CRS Strategic Plan, and to plan their work for the coming year. This year there are five new committees and a task force, all with new volunteers, helping CRS develop our activities into new emerging areas such as the translational and regulatory arena and also new ways to recruit, train, and develop CRS volunteers to help CRS grow in the coming years. It will be a busy 12 months, and we look forward to reporting back to the membership on the progress made over the coming year.

The final moments of the annual meeting also saw the transfer of the Presidency to Professor Kazunori Kataoka. A highly distinguished scientist and a true leader in scientific research and technological exploitation, Kazunori will bring his clear strategic thinking, wisdom, and tireless energy to the role. It has been a pleasure working with him on the Board over the last year, and I am sure he will be a great President.

The Olympic events have been sold out, well attended, and supported by the British public and visitors over the period of the games. The games are largely staffed by volunteers who have given their time for free. In that vein, this year we have also monitored attendance at Board Meetings and calls through the year, and the average attendance was well over 70%, demonstrating the strong commitment of the elected board members to the CRS cause.

Finally, I would like to thank all the colleagues who helped me during the past year—you know who you are, and I am very grateful for all your support, hard work, and guidance. I particularly wish to thank Mark Tracy (Past President), Ian Tucker (Secretary), and Debra Bingham (Treasurer). I am in your debt. As I sign off, I am just going to see if Britain has got any more medals at the Olympics, but from past experience, I am not hopeful! However, I see Team GB is to our astonishment exceeding expectations, but for many, their Olympic dream ends with no medal. For those competitors, it is taking part and giving your best that really counts. ■

Une Réunion Extraordinaire! 39th Annual Meeting & Exposition of the Controlled Release Society

Thank you to the more than 1,300 attendees who came to beautiful Québec City, Canada, to be a part of the 2012 CRS Annual Meeting. This year's annual meeting was full of breakthrough science and unique findings, top-notch presenters, and some of the best opportunities to build relationships with colleagues throughout the world. Watch for a full recap in the next issue of the *CRS Newsletter*.



Martyn Davies welcomes attendees to the 39th CRS Annual Meeting & Exposition during the Opening Session.



The Grand Opening Exposition and Welcome Reception was full, as attendees spoke with exhibitors and enjoyed time with colleagues.

2012 CRS Awards

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

Distinguished Service Award

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



Art Tipton has spent 25 years in the pharmaceutical industry and has participated in all growth aspects of three drug delivery start-ups. The company he founded in 2005 as Brookwood Pharmaceuticals became part of Evonik in November 2011, where he now heads global drug delivery.

College of Fellows

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



Theresa M. Allen is a professor emeritus of pharmacology at the University of Alberta, Canada, and adjunct professor of biochemistry and molecular biology at the University of British Columbia. She has been active in the drug delivery field for 35 years.



David Brayden is an associate professor of drug delivery at the School of Veterinary Medicine, University College Dublin (UCD), Ireland, and also a fellow of the UCD Conway Institute of Biotechnology. He is the current director of Science Foundation Ireland's Irish Drug Delivery Network, a public-private research consortium.

Founders Award

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



Yechezkel Barenholz is head of the liposome and membrane research laboratory and is the Daniel G. Miller Professor in Cancer Research at Hebrew University of Jerusalem, Israel. His current research focuses on the development of drugs based on drug delivery systems best exemplified by the anticancer drug DOXIL[®], the first nanoliposomal and the first FDA-approved (1995) nanodrug used worldwide.



Mansoor Amiji is a distinguished professor and chairman of the Department of Pharmaceutical Sciences, School of Pharmacy, Northeastern University, U.S.A. His research is focused on development of biocompatible materials from natural and synthetic polymers, target-specific drug and gene delivery systems for cancer and infectious diseases, and nanotechnology applications for medical diagnosis, imaging, and therapy.

Young Investigator Award

Cosponsored by Aptalis Pharmaceutical Technologies

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



Cory Berkland is a professor in the Department of Chemical and Petroleum Engineering and in the Department of Pharmaceutical Chemistry at the University of Kansas, U.S.A. His lab studies colloids, polymers, and biomaterials. He is a cofounder of Orbis Biosciences and Savara Pharmaceuticals.



Tram Dang completed her Ph.D. at the Massachusetts Institute of Technology, U.S.A., in the laboratories of Robert Langer and Daniel G. Anderson. For her thesis research, she developed new noninvasive imaging techniques to assess and understand the effects of controlled release anti-inflammatory drugs on the immunological response to biomaterials in rodent models.

CRS/T. Nagai Postdoctoral Research Achievement Award

Cosponsored by The Nagai Foundation Tokyo

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



Arun Iyer is currently an associate research scientist in Prof. Mansoor Amiji's laboratory. He has broad research interests in polymeric biomaterials for tumor drug targeting, biomedical imaging, advanced drug and gene delivery systems, and nanomedical technologies.



Christine Allen
University of Toronto,
Canada



David A. Jaffray
Techna Institute of Health
Technology Development, Canada

APN/CD13-targeting as a strategy to alter the tumor accumulation of liposomes
Michael Dunne, Jinzi Zheng, Joshua Rosenblat, David A. Jaffray, and Christine Allen

Drug Delivery and Translational Research Outstanding Paper Award

Cosponsored by Springer

This newly established award recognizes outstanding research in the field of drug delivery and translational research that was published during 2011 in Drug Delivery and Translational Research. This is the first year the award is being presented.



Tamara Minko
Rutgers University, U.S.A.

Non-viral systemic delivery of siRNA or antisense oligonucleotides targeted to Jun N-terminal kinase 1 prevents cellular hypoxic damage
Seema Betigeri, Min Zhang, Olga Garbuzenko, and Tamara Minko

CRS Outstanding Chapter of the Year Awards

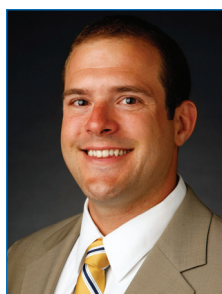
The CRS Chapter of the Year Awards recognize both a local chapter and a student chapter that have provided exceptional service to their members and to the Controlled Release Society. These chapters were chosen for their balanced, comprehensive events, as well as for maintaining a record of committed chapter activities.

**United Kingdom-Ireland Local Chapter
Connecticut Student Chapter**

Outstanding Consumer & Diversified Products Paper Award

Cosponsored by Fleet Laboratories Inc.

This award recognizes a CRS member whose winning abstract relates specifically to delivery of active ingredients in consumer or industrial products.



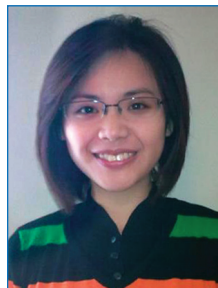
Craig Duvall
Vanderbilt University, U.S.A.

MMP-responsive, proximity-activated targeting polymeric nanoparticles for siRNA delivery
Coauthors: Hongmei Li, Shann S. Yu, Martina Miteva, Chris Nelson, and Todd Giorgio

Outstanding Oral Drug Delivery Paper Award

Cosponsored by Banner Pharmacaps

This award recognizes a CRS member whose winning abstract relates specifically to oral drug delivery.



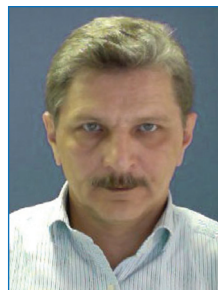
Angel Tan
Ian Wark Research Institute, Australia

Nanostructured microparticles that mimic the food effect for enhancing oral drug absorption
Coauthors: Tri-Hung Nguyen, Ben Boyd, and Clive Prestidge

Outstanding Pharmaceutical Paper Award

Cosponsored by Medimetrics

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



Mikhail Papisov
Massachusetts General Hospital, U.S.A.

Delivery of enzyme replacement therapeutics to CNS in rats and monkeys as seen and measured by PET
Coauthors: V. Belov, A. J. Fischman, J. Titus, M. Gagne, P. Calias, T. McCauley, and M. Hertlein

Outstanding Transdermal Drug Delivery Paper Award

Cosponsored by 3M Drug Delivery Systems

This award recognizes a CRS member whose winning abstract relates specifically to transdermal drug delivery research.



Gerold Lukowski
Institute of Marine Biotechnology, Germany

Prevention of the dermal colonization of MRSA by the application of algae microparticles
Coauthors: Ulrike Lindequist, Sabine Mundt, and Wolf-Dieter Jülich

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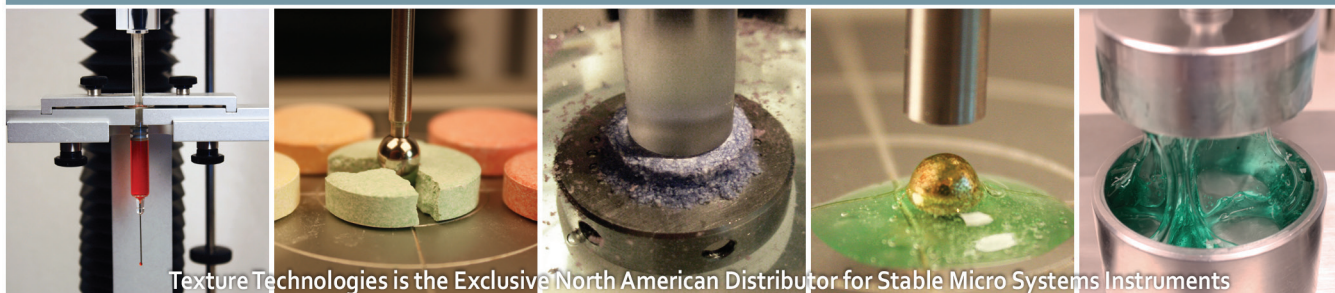
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Effect of Temperature and Time on the Coating and Loading Processes of Aquasome Manufacture

Deborah Lowry and Fadi Abdulrazzaq, Aston University

Introduction

With increasing numbers of protein and peptide therapeutics being developed, alternative delivery systems are being investigated. Many proteins and vaccines are delivered by parenteral routes; however, these have limitations, for example, poor patient compliance. The oral route is the most popular; however, delivery is limited for a number of reasons, for example, degradation by the gastrointestinal enzymes.

Aquasomes can be described as natural delivery systems. They were first proposed in 1996 by Nir Kossovsky as nanoparticulate carrier systems.¹ Aquasomes, or “bodies of water,” can protect fragile drugs, as they are composed of natural molecular stabilisers.² They are three-layered self-assembled structures with a solid phase nanocrystalline core. Aquasomes have the potential to deliver actives through sustained release, with the advantage of molecular shielding.

Hydroxyapatite (HA) has shown potential as a core. It occurs naturally in the body and is widely used in implants for drug delivery. High energy levels on the surface of the HA will allow adsorption of a carbohydrate coating through noncovalent, ionic, and van der Waals forces.³

The carbohydrate coating can prevent destructive denaturing interactions between the drug and solid carriers. A number of carbohydrates may be used to coat the core. In the present study, trehalose was selected because, in the absence of water, the hydroxyl group on disaccharides such as trehalose can replace the water around proteins, thus protecting against dehydration. In the plant kingdom, *Selaginella*, which grows in desert and mountainous areas, will revive when watered, even after it appears dead. This is due to trehalose. Therapeutic proteins are adsorbed to the glassy molecular stabilization film formed by the carbohydrate.⁴

There are a number of variables that may be investigated to optimize the manufacture of aquasomes. This short study investigated the effect of temperature on the coating step (trehalose) and temperature and time of the loading step (bovine

serum albumin [BSA]). A number of techniques may be used to characterize after each step, for example, size analysis, differential scanning calorimetry (DSC), and IR spectroscopy. Here we present the zeta potential and *in vitro* release data of aquasomes loaded with BSA.

Methods

Coating

HA of 99% purity was purchased from Sigma-Aldrich (Dorset, U.K.). A measured amount of HA was mixed with a trehalose solution for 2.5 hr at 4°C and 25°C. The coated cores were centrifuged, washed to remove unadsorbed trehalose, and freeze-dried. Zeta potential measurements were investigated after the coating step.

Loading

The coated cores were mixed with a BSA solution for 2.5 hr at 4°C and 24 hr at 25°C. A description of the manufacturing conditions is presented in Table 1. The loaded aquasomes were centrifuged, washed to remove any unadsorbed BSA, and freeze-dried. Zeta potential measurements were investigated after the coating step.

In Vitro Release

In vitro release studies were carried out in phosphate buffered saline (PBS, pH 7.4). The samples were placed in 10 mL of PBS and placed in a shaking water bath (37°C, 100 rpm). Hourly sampling with partial replacement of release medium was performed over 7 hr. All samples were analysed using HPLC with UV and fluorescence detection.

Table 1. Manufacturing conditions of each formulation.

Formulation	Coating		Loading	
	Time (hr)	Temperature (°C)	Time (hr)	Temperature (°C)
1	2.5	4	2.5	4
2	2.5	4	24	25
3	2.5	25	2.5	4
4	2.5	25	24	25

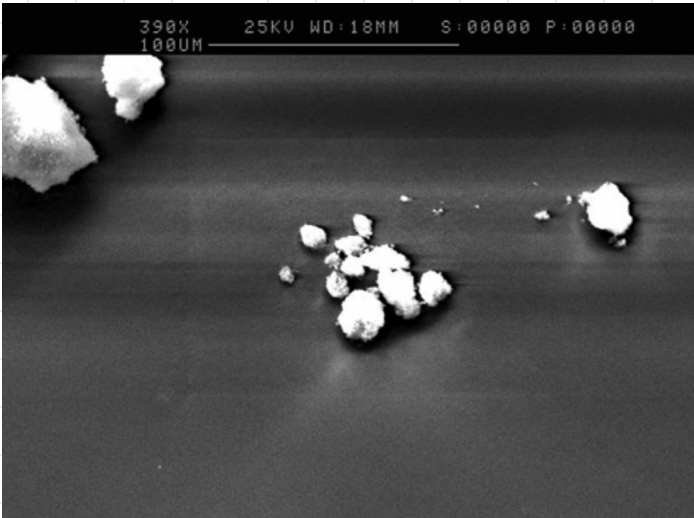


Figure 1. Scanning electron microscopy image of HA cores.

Results and Discussion

Coating the HA Cores

Figure 1 shows a scanning electron microscopy (SEM) image of the HA cores. The HA was observed to be round and have a semismooth surface. These properties should provide good attachment of the trehalose coating.

The HA cores were coated for 2.5 hr using two temperatures (4 and 25°C). Zeta potential may be used to confirm the adsorption of trehalose onto the HA cores. The surface charge of the cores was measured. This is the exterior charge of the delivery system, which is used to deliver the therapeutic to its target site.⁵ The HA cores had a charge of -8.30 ± 0.5 before coating. No significant change in charge was found between the two coating conditions (-1.3 ± 0.2 at 4°C and -1.15 ± 0.2 at 25°C); however, the change in charge confirms the HA cores were coated. The trehalose formed layers around the HA cores by physical adsorption.

Loading the BSA

The surface charge following loading of BSA is presented in Table 2. No significant differences were found between the formulations; however, the decrease in charge showed that BSA was adsorbed onto the trehalose coating. For any oral delivery system, interactions will occur between the particles and the thick negatively charged mucosal layer of the GI tract.⁵ This may be an advantage, as the aquasomes, which have a negative charge, may become stuck in the thick mucosal layer, causing the negative charges to repel and force the aquasomes through the layers and to the target.

Table 2. Surface charge (after loading), total *in vitro* cumulative release (mg), percentage release (%), and r^2 values for BSA released from aquasomes over 7 hr.

Formulation	Surface Charge	BSA Release (mg)	Percentage Release (%)	r^2
1	-11.2 ± 0.3	6.2	88.0	0.999
2	-17.9 ± 0.8	10.4	88.1	0.998
3	-12.2 ± 0.3	5.8	88.4	0.998
4	-17.3 ± 0.2	8.4	87.1	0.997

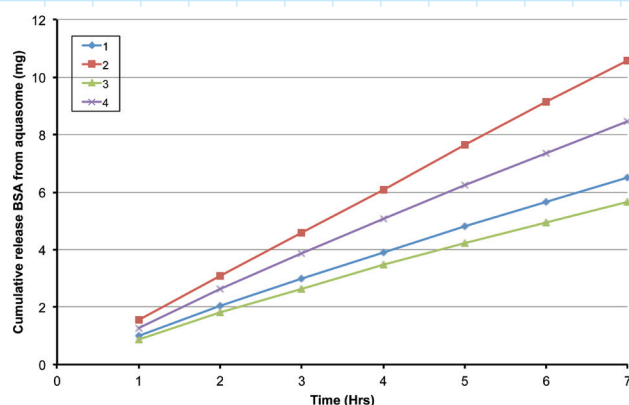


Figure 2. In vitro cumulative release of BSA (mg) from aquasomes manufactured under various conditions over 7 hr.

The manufacturing conditions for each aquasome formulation are listed in Table 1. The BSA loading efficiency of the aquasomes for each formulation (1, 2, 3, and 4) was 36, 59, 31, and 47%, respectively. It was found that the percentage of BSA was higher on aquasomes loaded at 25°C. This may be related to the viscosity of the trehalose coating. The viscosity of trehalose is increased at higher temperatures (25°C). Higher viscosity causes reduced particle motion in solutions and results in an increased rate of physical adsorption.^{6,7}

The *in vitro* release of BSA from the aquasomes over 7 hr is presented in Figure 2. No burst was observed from the formulations, and the cumulative release plots show zero-order kinetics over the 7 hr study (r^2 values are listed in Table 1). The aquasome formulations have shown diffusion controlled release.

Conclusion

This study has shown that BSA adsorbs well to the trehalose coating of the aquasomes. Following *in vitro* release, $88 \pm 1.8\%$ of the BSA was released over 7 hr for the formulations tested. The temperatures investigated for coating and loading showed no significant differences. However, the time required showed no significant differences; therefore, the loading step can be carried out in 2.5 hr, compared with longer processes. Further investigation of the manufacturing process is ongoing to optimize the use of aquasomes for the release of bioactive molecules.

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Method to Analyze Fish Oils Stabilized with Antioxidants Using HP-DSC

*Mathieu Zongo, Alexandre Zegels, and Craig Duckham
Laboratoires Meiners Sàrl, Colombier, Switzerland*

Introduction

Fish oils are typically composed of fatty acids with chain length C14–C18 along with docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), two polyunsaturated fatty acids with well-documented health benefits. These two compounds are the two major sensitive elements central to the degradation caused by external factors such as oxygen, temperature, and light.

The mechanisms of chain reactions are extremely complex and are largely dependent on a combination of external and internal factors such as the composition of the matrix material, traces of contamination of metallic origin, dissolved oxygen, and other compounds favoring the catalysis of oxidation.

It is, however, possible to delay significantly the process of decay by the addition of antioxidants, more precisely compounds with a continuous reaction that is more favorable than the reactions of the compounds requiring protection.

Sample Preparation

Determination of the Pro-oxidant Reaction

Fish oil (5 mL) was placed in 22 mL vials, tightly closed. The head space of the vials was saturated with oxygen to demonstrate the role of oxygen in the oxidation process. The vials were stored at 25°C and protected from light. The head space of the other samples was purged with argon. With the purpose of measuring their thermosensitivity, the sample vials were placed in climate cabinets at 40, 60, and 80°C, protected against light and moisture. To investigate the influence of light, the vials were exposed to light at a constant temperature of 25°C and a relative humidity of 0%. To measure the effect of humidity, the argon in the head space was evacuated, and 15 mL of pure water was added to the vial. These samples were also stored at 25°C, without exposure to light. All samples were stored under the selected conditions for seven days.

In the second part of the investigation, antioxidants, singly or as blends, were added to the fish oil samples at different concentrations. These antioxidants were selected on the basis of publications related to their functionality and unpublished findings from earlier studies at this laboratory. They were not exposed to the same oxidation conditions as the other samples. The objective was to demonstrate an improvement in the stability of the oils, using the direct measurement of oxidation onset temperature (OOT) with a high-pressure differential scanning calorimeter (HP-DSC). The selected antioxidants were

- mixed tocopherols (provider of hydrogen to peroxide-induced free radicals)
- rosmarinic acid (provider of hydrogen to peroxide-induced free radicals)

- curcumin (provider of hydrogen to peroxide-induced free radicals and singlet oxygen).

Methods for the Experiments

Calorimetric Assay

Our assay to measure stability was based on HP-DSC. This technology measures the energy produced during an oxidative reaction and calculates its enthalpy. The instrument can be seen as a mini-reactor under pressure using a specific gas or mixture of gases (air, oxygen, or nitrogen), while increasing the temperature to accelerate the start of the oxidative reaction. A mass of 5–15 mg of oil was weighed into an aluminum crucible of 40 µL and placed in the chamber of the HP-DSC827e instrument (Mettler Toledo, Greifensee, Switzerland).

The initiation of the degradation was identified at an accurate temperature. This value is the OOT. The relative stability of an oil, a polyunsaturated fatty acid, or an antioxidant can be determined using such a value.

The higher the OOT value, the more resistant to decay the compound; consequently, it can be considered to have better shelf-life stability. The method can be viewed as an accelerated shelf-life test, which allows prediction of long-term stability. Thus, it has the potential for screening large numbers of formulations to identify the most suitable for long-term storage stability.

Furthermore, a second measurement can be utilized, defined as the oxidation induction time (OIT). The time required to induce the oxidation, measured at a constant temperature (isothermal) is another indicator of the stability of the lipid. The OIT value can be compared with a reference oil (for example, when evaluating the addition of antioxidants) to obtain information about the changes in oxidative stability of such ameliorated oils.

Such methods allow identification of the source of pro-oxidative reactions in industrial processes and identify the critical control points to improve product quality.

Results and Discussion

The following results demonstrate the importance of oxygen compared with other sources of oxidation.

This is in contrast to a sample that was exposed to a treatment comprising the combination of four pro-oxidative sources, in a controlled climate at 80°C and 70% relative humidity in the presence of air and light. This sample had an OOT of $90.6 \pm 0.50^\circ\text{C}$.

The second part of the work consisted of the evaluation of the impact of antioxidants and blends.

Increasing concentrations of single antioxidants were added to the oil. Having identified the most efficient antioxidant, as well as its optimal dosage, a second antioxidant was added to the blend.

During our experiments, it was recognized that antioxidants can have synergetic effects with other antioxidants, but—depending on the nature of the oxidative environment—they also are potentially incompatible. The quantity must be defined precisely; when overdosed, they may turn pro-oxidative.

In this study, we could conclude that the origin of the oxidation was primarily oxygen; the other factors (humidity, temperature, and light) were rather catalysts for reactions, based on lowering the activation energy for the reaction.

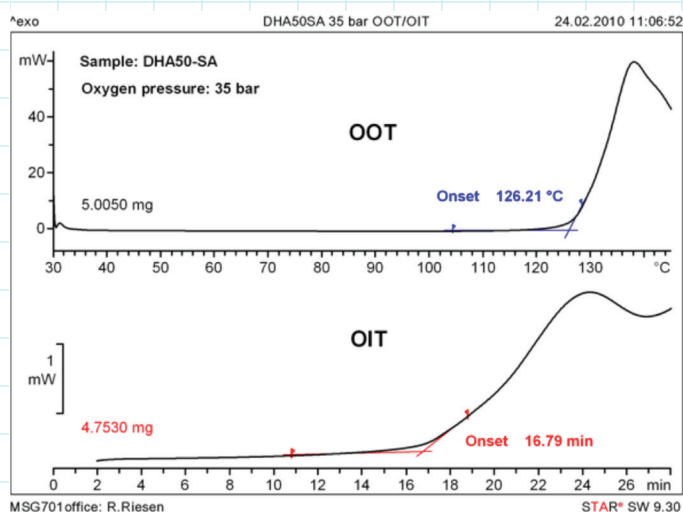


Figure 1. Typical HP-DSC curves showing the determination of the oxidation induction time (OIT) and oxidation onset temperature (OOT) of DHA 50% fish oil.

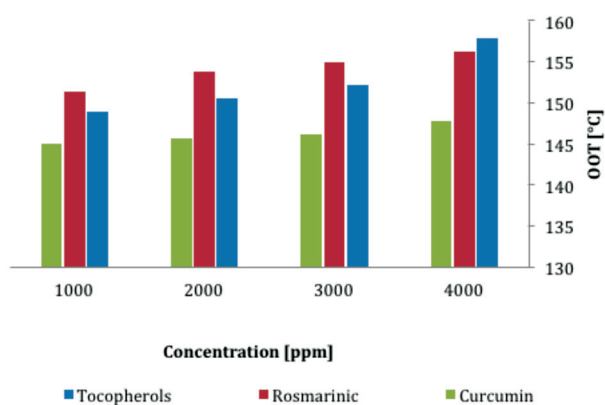


Figure 2. Oxidation onset temperature (OOT) for fish oil containing three antioxidants at different concentrations.

Table 1. OOT values vs. pro-oxidant factors.

	OOT (°C)	
	Mean	STD
Standard	141.2	0.07
Temperature	143.3	0.57
Humidity	141.8	0.29
Oxygen	130.8	1.88
Light	140.1	1.53

Table 2. Changes in OOT as a function of antioxidant concentration.

ppm	Light					
	Tocopherol		Rosmarinic Acid		Curcumin	
	°C	STD	°C	STD	°C	STD
4,000	158.0	0.04	156.2	0.02	147.8	0.02
3,000	152.2	0.02	155.0	0.07	146.2	0.02
2,000	150.6	0.03	153.8	0.02	145.7	0.02
1,000	148.9	0.04	151.4	0.55	145.1	0.02

Table 3. Changes in OOT as a function of antioxidant blend.

	OOT (°C)		STD
	°C	STD	
Toco8000	156.5	0.03	
Toco6000	157.5	0.04	
Toco4000–Ros4000	160.0	0.02	
Toco4000–Ros2000	156.6	0.02	

Toco = Tocopherol, Ros = Rosmarinic acid, and number indicates ppm.

Conclusions

The importance of oxygen versus other pro-oxidant conditions was demonstrated.

HP-DSC has allowed the formulation of a blend of antioxidants capable of improving the stability of omega-3 oils.

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Drug Delivery and Translational Research (DDTR) Update

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

Announcing the DDTR Outstanding Research Paper Award Winner

The DDTR Outstanding Research Paper Selection Committee is pleased to announce the first recipient of the DDTR Outstanding Research Paper Award, designed to honor excellent research published in DDTR.

Seema Betigeri, Min Zhang, Olga Garbuzenko, and Tamara Minko. Non-viral systemic delivery of siRNA or antisense oligonucleotides targeted to Jun N-terminal kinase 1 prevents cellular hypoxic damage. *Drug Deliv. Transl. Res.* 1: 13-24 (2011).



Tamara Minko, corresponding author of the paper, is professor II (distinguished) and chair of the Department of Pharmaceutics at Ernest Mario School of Pharmacy at Rutgers, the State University of New Jersey, U.S.A. She accept-

ed the award during the Tuesday plenary session of the CRS Annual Meeting & Exposition. Please join CRS in congratulating the authors of the paper for their outstanding achievement.

Consider submitting your best translational drug delivery research to compete for the 2012 outstanding paper award. The award will be selected from the research articles published in DDTR during 2012 and will be presented during the 2013 CRS Annual Meeting & Exposition. Visit the CRS website for more information.

DDTR Special Focus Issue on "Drug Delivery to the Central Nervous System" Vol. 2, Issue 3, Pages 143-221, 2012

In July 2011, the CRS held a workshop designed to bring together leading scientists in the fields of drug delivery, vascular biology, imaging, animal model development, and clinical research, with the goal of engaging in multidisciplinary discussions of the strategies needed to develop drug and biological products targeted to the central nervous system (CNS), from drug discovery through to clinical evaluation. This special issue, based on the theme of the workshop, contains an important collection of work describing the challenges and strategies being investigated to effectively deliver therapeutics to the CNS. Visit the CRS website to access these and other articles published in DDTR. Log in to the CRS website first, and then click the Publications tab to get to the DDTR member access link.



*Pericles Calias,
Senior Director,
Nonclinical Development
Shire HGT, U.S.A.*

About the Focus Issue Guest Editor

Perry Calias specializes in the development of targeted therapies to the CNS. As a senior director for Shire Human Genetic Therapies, he has led the investigational effort for the intrathecal administration of recombinant enzymes for the treatment of the CNS manifestations associated with lysosomal diseases. In this capacity, he has also led the research effort in regard to regulatory filings both within the United States and abroad. He has held various R&D

positions at EyeGate Pharmaceuticals (vice president, research and development), Eyetech Pharmaceuticals (senior director, drug delivery/chemistry), Draper Laboratories (senior technical lead), and Genzyme Corporation (senior scientist, biomaterials and surgical products research department). Perry is listed as an inventor on over 30 domestic and foreign patents and applications spanning 18 different patent families, including intrathecal delivery, CNS formulations, new polyethylene glycol-linker chemistries, noninvasive ocular delivery devices, nucleic acid-protecting strategies, and combination anti-angiogenic therapies. He obtained his Ph.D. in bio-organic chemistry in 1996 and his M.S. in 1993 from Tufts University.

Upcoming New Special Issues

A DDTR Special Focus Issue on "Biomimetic and Biofunctional Materials in Regenerative Medicine," with V. Prasad Shastri, University of Freiburg, as Guest Editor

The main objective of this themed issue is to highlight the evolution of concepts in materials engineering for inducing autologous regeneration and the challenges associated with clinical translation. In this context, material design that incorporates principles of directed self-assembly, surface engineering, metabolic engineering, extracellular matrix mimicry, and synthetic biology for driving functional cellular organization and recapitulation of signaling environments in embryonic and fetal development will be highlighted.

A DDTR Special Focus Issue on "Cancer Stem Cells" with Jayanth Panyam, University of Minnesota, 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. ■

CRS Goes to Capitol Hill in Support of Delivery Science and Technology

Mark A. Tracy, Tracy BioConsulting, U.S.A.



Mark A. Tracy

CRS, represented by former president Mark A. Tracy, met with U.S. Senate and House of Representatives staff on Capitol Hill on June 21, 2012, in support of prioritizing key science, technology, regulatory, and business issues of importance to CRS members. The event, called the Federal Symposium, was organized by the American Institute for Medical and Biological Engineering (AIMBE). AIMBE is a nonprofit organization headquartered in

Washington D.C. that promotes public policies that foster continued advancement in medical and biological engineering and related fields, including delivery science and technology. CRS is a member of AIMBE's Council of Societies, which provides CRS the opportunity to participate in and impact AIMBE's public policy initiatives, including the Federal Symposium.

Dr. Tracy was joined by about 30 AIMBE Council of Societies members and fellows, who met with the staffs of approximately 40–50 members of the U.S. Congress from across the country. Dr. Tracy and his colleagues highlighted delivery-based and other products that are improving people's lives and have spawned the growth of companies and jobs today that began with government-supported research. They emphasized the importance of prioritizing investments in science, engineering, and technology as well as STEM education (science, technology, engineering, and math) through this period of severe fiscal constraints. Dr. Tracy and his colleagues also discussed the importance of a consistent, transparent, and well-funded FDA to



facilitate the translation of research into products as well as the importance of strong, clear intellectual property law protecting inventions and a strong, well-funded Patent Office.

Dr. Tracy said, "As engineers and scientists and CRS members, it is critical for our voices to be heard by our lawmakers around the world, but especially now in these challenging economic times when new priorities are being set. Through our research and the products we develop, we create great value for society, including a higher quality of life and jobs. Lawmakers want and need to hear that story—our story—directly from us. Our membership in AIMBE's Council of Societies allows the CRS the opportunity to help develop important relationships with lawmakers and promote our achievements and issues that will allow us to continue to receive the government support that helps us enhance the quality of life of people world-wide." ■

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"Successful Integration in English-Speaking Communities" Event at the Hebrew University CRS Student Chapter

*Oren Giladi and Gali Umschwief
CRS Student Chapter, the Hebrew University of Jerusalem, Israel*

The CRS supports its chapters worldwide in a variety of activities, from academic and professional events to social activities. One such event was held on February 29, 2012, at the Givat Ram campus of the Hebrew University of Jerusalem. The day focused on professional skills that are inseparable from academic life but are not studied in lecture halls—integration in an English-speaking environment, which is a major concern for Hebrew-speaking graduate students. The event was planned in



an effort to assist in coping with this difficulty. The objectives of the event included equipping students with proficiencies to lecture in English in front of an English-speaking crowd and to upgrade the writing capabilities of the students, as well as to familiarize them with American academic and pharmaceutical culture. Those who participated were graduate students in the Institute for Drug Research at the School of Pharmacy of the Hebrew University of Jerusalem, and the day was planned by the institute's CRS student chapter.

The day was divided into two main sessions. The first part of the day opened with greetings from the head of the Institute for Drug Research, Prof. Simon Benita, who stressed the importance of the contents of the day and of the cooperation between Israeli and American academic institutions and industrial companies. The next speaker of this session was Dr. Sara Eyal, who gave an overview of the various types of cultural Israeli-American interrelations in the field of pharmaceuticals, addressed conversational dos and don'ts, and shared some of her experiences as a postdoctoral fellow at the University of Washington in Seattle.

During the second part of the day, the students divided into two groups and attended workshops dealing with the required skills for optimized performance in English-speaking communities.

The workshops were conducted by Dr. Sharon Hirsch and Dr. Helen Levy, two senior lecturers from the Hebrew University Department of English as a Foreign Language, and included techniques for improving students' preparation of academic articles for peer-reviewed journals, dissertations, M.A. theses, and oral presentations for international conferences.

Gadi Cohen, a Ph.D. student who participated in the event, summed up the feelings of the participants in her comments to the chapter: "As most of the important industry and academic affairs in the world are done in English, some of the skills that have been acquired today could be keys for my future career in an academy or international drug company." In short, the event was a success on all levels. It was enjoyable, insightful, educational, and informative, and the students left feeling inspired, encouraged, and confident with their newly gained knowledge. ■

Welcome New Members

Chandan A. S. Alam	Brice Moulari
Joaquim Amela	Xavier Mulet
Kuljit S. Bhatia	Berenice Ortiz
Jin Chen	Subin Park
Eugene Chow	Shilpa B. Pawar
Dhanunjay Kumar	Harvinder Popli
Dogiparti	Gerald Price
Orlagh Feeney	David Scher
Sangita Ghosh	Gina Song
Abhijit Gokhale	Mark Stella
Herve Guillard	Gert Storm
Nadiel Hernandez	Victoria B. Tran
Kasper Huus	Cristian Andrés Vilos
Jelena M. Janjic	David R. Virgallito
Christian J. Kastrup	Kapil Arvindbhai Vithani
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Courtesy of the Hawaii Convention Center / David Cornwell

People in the News

*Compiled by Steven Giannos, Chrono Therapeutics Inc.
Industrial Editor*

Wake Forest Baptist Names President of Piedmont Triad Research Park and Chief Innovation Officer

PRNewswire: June 26, 2012 – WINSTON-SALEM, NC, U.S.A. – Eric Tomlinson, D.Sc., Ph.D., a scientific and business leader whose career incorporates academia, product innovation, and economic development, has been named president of Piedmont Triad Research Park (PTRP) and chief innovation officer of Wake Forest Baptist Medical Center. He will join the Medical Center July 2, 2012.

“Eric will focus on the commercialization of research and innovation, along with the business development of PTRP, which is the area’s top regional economic project priority and one of the largest urban life science research parks in the country,” said John D. McConnell, M.D., chief executive officer of Wake Forest Baptist Medical Center. “His unique background in academic science, large pharmaceutical and small startup companies, product design and commercialization, and government policy made him the ideal candidate to build on our successes.”

Tomlinson has also worked as an advisor to venture capital, government, and professional agencies on biopharmaceutical sciences and has held academic appointments in the United States and in Europe, including at the University of Amsterdam as professor in the department of pharmacy. He is currently chairman of the board of directors of Metacclipse Therapeutics Corp., an early-stage company based in Atlanta, Georgia, that develops patient- and tumor-specific immunotherapies.

As former CEO, president, and member of the board of directors of Altea Therapeutics Corp., Tomlinson brought several high-value pharmaceutical products into clinical development for the treatment of diabetes, blood disorders, and pain. As the head of GeneMedicine, Inc., of Woodlands, Texas, a pioneering gene therapy company, he raised more than \$100 million in private, public, and partnership income, brought gene products into clinical trials for treatment of cancer, cardiovascular diseases, and neuromuscular disorders, and transacted a merger to form Valentis Inc.

Additionally, Tomlinson served as worldwide head of advanced drug delivery research and as a member of the international research board of Ciba-Geigy Pharmaceuticals in Horsham, U.K. He has also served as chairman of the Georgia Biotechnology Industry Organization and as a member of the U.S. National Research Council task force on the high technology/information technology workforce that reported to the U.S. Congress. Tomlinson is a fellow of the Royal Pharmaceutical Society of Great Britain, the Royal Society of Chemistry, and the American Academy of Pharmaceutical Sciences.

Tomlinson received his bachelor of pharmacy, his doctor of philosophy, and his doctor of science degrees from the University of

London. He has authored or coauthored 230 research publications in the life sciences and the pharmaceutical sciences (solution thermodynamics, drug design, site-specific drug delivery, and gene therapy). He is the cofounder and emeritus editor of the review journal *Advanced Drug Delivery Reviews*.

“Eric brings a wealth of talent and commercialization experience that will be invaluable as we work together to pioneer breakthroughs and create innovative solutions to improve our lives, our future, and the world around us,” said Edward Abraham, M.D., dean of Wake Forest School of Medicine.

With the recent completion of the state-of-the-art Biotech Place, the Medical Center has 10 departments in the park. Other park tenants include approximately 40 companies, professions, firms, and organizations that employ about 1,000 people.

BIND Biosciences CEO Scott Minick and Founder Omid Farokhzad Win Ernst & Young New England Entrepreneur of the Year Award

Business Wire: June 22, 2012 – CAMBRIDGE, MA, U.S.A. – BIND Biosciences, a clinical-stage biopharmaceutical company developing a new class of highly selective targeted and programmable therapeutics called Accurins™, today announced that its chief executive officer, Scott Minick, and its founder and an associate professor at Harvard Medical School, Omid Farokhzad, M.D., have been awarded the prestigious Ernst & Young New England Entrepreneur of the Year in the category of life sciences. The Ernst & Young award recognizes accomplished entrepreneurs for their development of new technologies, improvement of quality of life, and creation of strong and vibrant corporations. Mr. Minick and Dr. Farokhzad were honored last night at an event hosted by Ernst & Young in Boston, Massachusetts.

In selecting the BIND leaders for the Entrepreneur of the Year award, the Ernst & Young judges particularly recognized the accomplishments with BIND-014, the company’s lead drug candidate for cancer, which had promising antitumor effects in patients with advanced or metastatic cancers reported from a clinical study in April 2012. BIND-014 is a targeted and programmable nanomedicine that has been shown in preclinical models to deliver up to tenfold more cell-killing agent, docetaxel, to tumors than an equivalent dose of conventional docetaxel. BIND-014 demonstrates the potential of Accurins to have unique targeting to the site of disease, as the increased accumulation of docetaxel specifically to cancer tumors translated to marked improvements in antitumor activity and tolerability. In addition to BIND-014, BIND is developing a pipeline of novel Accurins based on the company’s proprietary platform for engineering programmable nanomedicines to create best-in-class drugs in the areas of oncology, cardiovascular, and inflammatory diseases.

“This award reflects the focus, passion, and dedication of two outstanding leaders, Scott and Omid, who have worked collaboratively to build BIND and develop transformative new medicines to benefit patients,” said Robert Langer, Sc.D., BIND founder and David H. Koch Institute Professor at MIT. “Scott has been an incredible entrepreneurial leader for the BIND team, focusing the team’s effort to bring the first Accurin, BIND-014, into human clinical trials and positioning the company to deliver a pipeline of Accurins for many diseases. Omid has shown at BIND his unique combination of skills as a great physician-scientist and inventor, along with his inspirational talent as a visionary and big thinker who can launch strong and vital biotech companies, as he has done with BIND and several other companies developing breakthrough medicines.”

Scott Minick is the president and CEO of BIND Biosciences. Prior to BIND, Mr. Minick was a managing director of ARCH Venture Partners and was director, president, and COO of SEQUUS Pharmaceuticals, a public biopharmaceutical company that was acquired by ALZA. Mr. Minick was formerly an executive at Baxter International, Inc., and Eli Lilly & Company and was chairman of the board of California Pacific Medical Center through 2009. He received his postgraduate training in neurobiology at the Salk Institute, an M.B.A. from Northwestern University, and a B.A. with honors from the University of California at San Diego.

Omid Farokhzad, M.D., is an associate professor at Harvard Medical School and a physician-scientist in the Department of Anesthesiology at Brigham and Women’s Hospital. He is a cofounder of BIND Biosciences, Selecta Biosciences, and Blend Therapeutics. Dr. Farokhzad’s research group is focused on developing novel nanotechnologies for medical applications. He has pioneered the application of micro- and nanotechnology for high-throughput development and screening of targeted drug delivery systems for a myriad of clinical applications. Dr. Farokhzad has authored more than 80 papers and is an inventor of more than 65 issued and pending patents. He completed his postdoctoral clinical and research trainings, respectively, at the Brigham and Women’s Hospital/Harvard Medical School and the Massachusetts Institute of Technology in the laboratory of Dr. Robert Langer. He received his M.D. and M.A. from Boston University School of Medicine.

Across the United States, hundreds of inspiring and innovative individuals were selected as Ernst & Young Entrepreneur of the Year finalists. Beginning in June, winners in 26 regions are honored locally for their vision, leadership, and ability to grow the successful businesses that help sustain our economy. These winners, including Mr. Minick and Dr. Farokhzad, will be eligible for the national awards, to be presented by Ernst & Young in Palm Springs in November. ■

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In the News

*Compiled by Steven Giannos, Chrono Therapeutics Inc.
Industrial Editor*

June 2012

Unigene's Oral PTH Phase 2 Proof-of-Concept Data to Be Presented at Upcoming Scientific Conferences

PRNewswire: June 28, 2012 – BOONTON, NJ, U.S.A. – Unigene Laboratories, Inc. (OTCBB: UGNE), a leader in the design, delivery, manufacture, and development of peptide-based therapeutics, today announced that data from the company's oral parathyroid hormone (PTH) analog phase 2 proof-of-concept trial results will be part of two presentations by Dr. Lorraine Fitzpatrick, medicine development leader for GlaxoSmithKline (GSK), at prestigious scientific conferences.

5th International Workshop on Advances in the Molecular Pharmacology and Therapeutics of Bone Disease, "(Mis)Adventures In Drug Discovery," Thursday, June 28, 2012, at 11:30 a.m. GMT, St. Catherine's College, Oxford, UK. Focus: Examination of PTH secretory dynamics via the comparison of PK data from ronacaleret, oral PTH, and PTH 1-34 and 1-84.

GIOSEG 5th Meeting Skeletal Endocrinology, Session 4—Anabolic Therapies for Osteoporosis—"New PTHs: Modalities, Duration, Combinations," Friday, September 21, 2012, 2:30 – 4:00 p.m. BST, University of Brescia, Main Hall School of Medicine, Brescia, Italy. Focus: Examination of PTH secretory dynamics via the comparison of PK data from ronacaleret, oral PTH, and PTH 1-34 and 1-84.

"We are extremely pleased Dr. Fitzpatrick has chosen to present the data from our oral PTH phase 2 proof-of-concept trial at two highly prestigious scientific conferences," stated Nozer Mehta, Ph.D., vice president of research and development for Unigene. "Both presentations will serve to highlight data that strongly validate Unigene's proprietary Peptelligence™ technology and, importantly, that the oral delivery of PTH is technically feasible."

The phase 2 proof-of-concept oral PTH study was conducted by Unigene under a now terminated, amended, and restated exclusive worldwide license agreement and related development services and clinical supply agreement with GSK pertaining to an oral formulation of a recombinantly produced PTH analog for the treatment of osteoporosis in postmenopausal women.

On November 9, 2011, Unigene announced positive top-line results of its phase 2 clinical study evaluating an experimental oral PTH analog for the treatment of osteoporosis in 97 postmenopausal women. The study achieved its primary endpoint with statistical significance.

Unigene has the exclusive worldwide rights to its oral PTH program and is actively seeking a development and commercialization partner. Unigene will publish the full data set of the phase 2 results in a peer-reviewed scientific journal and appropriate scientific conferences in the second half of 2012.

Landec Sells Seed Coating Business and Partners with INCOTEC to Gain Global Access for Landec Agriculture Seed Coating Technology

Business Wire: June 26, 2012 – MENLO PARK, CA, U.S.A. – Landec Corporation (Nasdaq: LNDC), a company that develops and markets patented products for food, agricultural, and biomedical applications, announced today that it has entered into three agreements with INCOTEC® Coating and Seed Technology Companies, a leading provider of seed and coating technology products and services to the seed industry. The partnership provides Landec access to growing global markets for its polymer technology and enables Landec to exit the day-to-day operations of its agricultural seed coating business. These agreements enable Landec to focus on developing new polymer formulations for an agricultural market increasingly dependent on seed coating technology and to leverage INCOTEC's global presence in the seed treatment markets.

In the first agreement, Landec sold its seed subsidiary, Landec Ag LLC, to INCOTEC Holding North America, Inc. Landec Ag was sold to INCOTEC for \$600,000, which will result in a gain of approximately \$400,000.

In the second agreement, Landec entered into a seven-year exclusive technology license and polymer supply agreement with INCOTEC Field Crops North America LLC for the use of Landec's Intellicoat® polymer seed coating technology for male inbred corn, which is sold under the Pollinator Plus® label. This license does not include the use of Intellicoat for the controlled release of an active ingredient for agricultural applications, which will be retained by Landec. Landec will be the exclusive supplier of Pollinator Plus polymer to INCOTEC during the term of the license agreement, and Landec will receive a royalty equal to 20% of the revenues realized by INCOTEC from the sale of or sublicense of Pollinator Plus coatings during the first four years of the agreement and 10% for the last three years of the agreement.

In the third agreement, Landec entered into a five-year exclusive technology license and polymer supply agreement with INCOTEC Holdings B.V. for the joint development of new polymer and unique coatings for use in seed treatment formulations. In this agreement, Landec will receive a value share, which will be mutually agreed to by both parties prior to each application being developed.

In the News continued on page 20

In the News continued from page 19

Gary Steele, Landec's chairman and CEO, stated, "These agreements with INCOTEC allow Landec to focus on its two core businesses, food products and biomedical materials, while capitalizing on our Intelimer® polymer technology for agricultural applications by leveraging INCOTEC's existing global distribution channels. Landec will retain all rights to its controlled release technology for agriculture. INCOTEC has worldwide operations and is rapidly growing its North American operations for supplying seed treatment formulations to major seed companies. Landec Ag's facility and operations in Oxford, Indiana, will now be operated by INCOTEC, and Landec will provide polymer supply and R&D support from our Menlo Park, California, location. We are very pleased to be working with INCOTEC, a market leader in seed coating formulations."

SCOLR Pharma Launches Redesigned Website to Support Their CDT® Formulated Supplements

PRNewswire: June 25, 2012 – BELLEVUE, WA, U.S.A. – SCOLR Pharma, Inc. (PINK: SCLR) today launched a new website to support their CDT® (Controlled Delivery Technology) formulated vitamins, minerals, and dietary supplements. The website, www.scolr.com, is part of SCOLR's initiative to provide consumer-related education on the industry and how its CDT® based products enhance performance and provide value.

The website contains product information and consumer "touch-points," including a Q&A section to address frequently asked questions and a "blog" feature. In addition, the website will contain information on SCOLR's development activities on over-the-counter (OTC) and prescription drug formulations. The company will continue to add new features to the website, which may include coupons and rewards programs.

Stephen Turner, president and CEO of SCOLR, said: "SCOLR seeks to define 'value' as the ideal combination of safety, efficacy, convenience, and cost. Our goal is to deliver the best overall experience to consumers shopping for value, by providing products with the optimal release of their active ingredients over time. Our new website provides us with an efficient vehicle to reach out and educate consumers. I am excited about our plans for this website, and how we will utilize it to support continued growth and awareness on CDT®. The closer we are to the consumer, the better we will be at meeting their needs."

Tocagen to Utilize ClearPoint® Neuro Intervention System for MRI-Guided Delivery of Toca 511 in a Study of Patients with Brain Cancer

Business Wire: June 25, 2012 – MEMPHIS, TN, U.S.A. and MUNICH, Germany – MRI Interventions, Inc. (OTCBB: MRIC) and Brainlab AG today announced an alliance with Tocagen Inc. in the fight against the most aggressive form of brain cancer, recurrent high-grade gliomas, including glioblastoma multiforme (GBM). Under the arrangement, MRI Interventions' ClearPoint® Neuro Intervention System will be utilized at selected sites in Tocagen's ongoing investigational clinical trial for the delivery of Toca 511 into brain tumors under

real-time magnetic resonance imaging (MRI) guidance. Patient recruitment is currently underway at one of several potential trial centers for this arm of this multicenter phase I/II study.

Traditionally, delivery of drug therapies to brain tumors has been performed with neuro-navigation, a computer-assisted technology utilized by neurosurgeons that does not provide for direct visualization of drug delivery in real time. The ClearPoint system, which is in commercial use in the U.S. for a variety of minimally invasive neurosurgery procedures, is designed to allow real-time, direct visualization during neurosurgery. MRI Interventions and Brainlab have partnered to enable neurosurgeons to visualize local drug delivery to the brain and central nervous system using the ClearPoint platform.

"We are enthusiastic about the potential of combining our new Toca 511 investigational therapy with the next generation brain delivery platform represented by the ClearPoint system," said Harry Gruber, M.D., CEO of Tocagen.

Tocagen is currently enrolling patients in its investigational clinical trial of Toca 511 in combination with Toca FC (flucytosine, extended-release) tablets. This multicenter, open-label trial is evaluating the safety and efficacy of Toca 511 injected into the brain tumor and followed by oral administration of Toca FC in patients with recurrent high-grade glioma.

Toca 511 is a retroviral replicating vector (RRV) that is designed to deliver a cytosine deaminase (CD) gene selectively to cancer cells. After Toca 511 spreads through the tumor, the CD gene in the cancer cells converts the prodrug, flucytosine, into the anticancer drug 5-fluorouracil (5-FU).

Under this new alliance, at selected trial centers, neurosurgeons participating in the Tocagen clinical trial plan to use the ClearPoint system to precisely place the drug delivery catheter in the brain tumor and then deliver Toca 511 directly into the tumor while observing this delivery real-time via MRI.

"Excitement among researchers and drug companies to explore use of the ClearPoint system for direct drug delivery began to build last year, on the heels of two research publications from UCSF," noted Kimble Jenkins, CEO of MRI Interventions. "We are pleased to announce today our first drug development alliance that brings together our ClearPoint platform with a promising experimental brain cancer therapy from Tocagen."

Joseph Doyle, CFO of Brainlab, added, "By offering a platform for delivering therapeutic agents direct to the central nervous system, we hope to make promising therapies more accessible to patients."

According to the National Brain Tumor Society, 620,000 people are currently living with a form of brain cancer. Each year 10,000 new glioblastoma multiformes (GBM, grade IV gliomas) are diagnosed in the United States.

Moberg Derma AB: Moberg Derma Signs Agreement for Nalox™/ Emtrix® in Iran

Business Wire: June 25, 2012 – STOCKHOLM, Sweden – Moberg Derma AB (STO: MOB) has entered into a distribution agreement with Ana Darou P.J.S. for Nalox™/ Emtrix®—for discolored and damaged nails caused by nail fungus (onychomycosis) or nail psoriasis. Under the agreement Ana Darou is granted exclusive rights to market and sell Nalox™/Emtrix® in Iran. Moberg Derma assumes production and supply responsibility.

“The agreement is part of our international commercialization of Nalox™/Emtrix®. We are looking forward to make the product available to the patients in Iran through the cooperation with Ana Darou,” says Peter Wolpert, CEO and founder of Moberg Derma.

Depomed Announces Acquisition of Zipsor® (Diclofenac Potassium) from Xanodyne Pharmaceuticals, Inc.

PRNewswire: June 21, 2012 – MENLO PARK, CA, U.S.A. – Depomed, Inc. (NASDAQ: DEPO) today announced that it has acquired all rights to Zipsor® (diclofenac potassium) liquid filled capsules from Xanodyne Pharmaceuticals, Inc. Zipsor is a nonsteroidal anti-inflammatory drug (NSAID) indicated for relief of mild-to-moderate acute pain in adults. The product uses proprietary ProSorb® delivery technology to deliver a finely dispersed, rapidly absorbed formulation of diclofenac.

Zipsor, which was introduced by Xanodyne in 2009, achieved approximately \$19 million of net sales in the 12 months ended May 31, 2012. Depomed acquired the product in return for \$25.9 million of cash and potential milestone payments based on sales of Zipsor and assumption of certain liabilities.

“We are pleased to expand our portfolio of pain products with the addition of Zipsor to our sales force of 164 reps and 78 flex reps that today are detailing Depomed’s Gralise® (gabapentin),” said Jim Schoeneck, president and CEO of Depomed. “Zipsor is an NSAID that we believe is differentiated in the pain space, allowing rapid absorption of the lowest available oral dose of diclofenac. With current sales of approximately \$19 million annually, Zipsor will have an immediate positive impact on Depomed’s financials. We believe we will have the runway to achieve significant returns for our shareholders from this acquisition, with the Orange Book listed patents for Zipsor expiring in 2019 and 2029. We plan to utilize our sales force to promote Zipsor to pain specialists, neurologists, and high-prescribing PCPs, including those we currently detail for Gralise in addition to current prescribers of Zipsor.”

Bend Research and Catalent Partner to Provide Integrated Solutions for Oral Controlled-Release Technologies

Business Wire: June 21, 2012 – BEND, OR and SOMERSET, NJ, U.S.A. – Bend Research Inc. and Catalent Pharma Solutions, Inc. have entered into an agreement to provide integrated solutions for pharmaceutical companies seeking to

develop and manufacture specialized multiparticulate oral controlled-release products.

Under the agreement, Bend Research and Catalent will provide an integrated approach to bring complex controlled-release products to market faster and more efficiently with optimal therapeutic and release profiles.

The companies’ combined expertise in formulation development and Catalent’s breadth of services in analytical/CMC, solid-state optimization, clinical and commercial supply will provide pharmaceutical companies with optimal dosage forms and a more efficient path to market. Catalent and Bend Research are developing joint operations and technology-transfer protocols to make the customer experience seamless and efficient while leveraging the strengths of both companies to develop better treatments for patients globally.

“Our integrated approach is geared toward complex, multiparticulate controlled-release products, which traditionally have presented a high scale-up risk when they are transferred to commercial manufacturing sites,” said Rod Ray, CEO of Bend Research. “This partnership with Catalent will provide an efficient pathway for these medicines from early development through commercialization. We believe that Catalent’s breadth of services and demonstrated success in bringing controlled-release products to market, as well as supplying them globally, makes them an ideal complement to our development strengths.”

Ian Muir, president of Catalent’s modified release technologies business, indicated that “Catalent and Bend are aligning their scientific expertise and processes to ensure that developments are undertaken from day one based on Quality by Design principles. Bend’s added laboratory-scale modeling expertise will enhance and increase the efficiencies that Catalent will provide to customers to bring difficult to formulate and manufacture controlled-release compounds to market faster, with optimal product profiles. This should enable optimal and seamless scale-up within Catalent’s controlled release network, and particularly at our Winchester, Kentucky, facility, which is widely regarded as the leading commercial facility for multiparticulate products.”

MicroDose Therapeutx and Moerae Matrix Announce Collaboration to Develop Novel Inhaled Treatment for Idiopathic Pulmonary Fibrosis (IPF)

Business Wire: June 20, 2012 – MONMOUTH JUNCTION, NJ, U.S.A. – MicroDose Therapeutx, Inc. and Moerae Matrix, Inc. announced today that they have signed a collaboration agreement to develop a dry powder inhalation product of Moerae’s novel MK2 inhibitor, MMI-0100, for the treatment of idiopathic pulmonary fibrosis (IPF), a serious and fatal lung disease for which there are no approved treatments in the U.S. The collaboration will involve the development and supply of a pulmonary drug delivery system for Moerae and/or its partners utilizing MicroDose’s proprietary inhaler technology in support of chronic administration.

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“We are pleased to be partnering with a recognized industry leader in pulmonary drug delivery to advance development of MMI-0100 for IPF,” said Cynthia Lander, Ph.D., Chairman and Chief Executive Officer of Moerae Matrix. “MicroDose’s piezo-driven dry powder inhaler platform is the optimal technology for delivering our first-in-class peptide therapeutic for treatment of IPF.”

Commenting from MicroDose, Scott Fleming, Sr. Vice President, Sales and Marketing, said, “Moerae has assembled an impressive team to advance this promising treatment approach for this debilitating disease, and we are pleased to be able to contribute to its advancement. This collaboration in IPF expands the utilization of MicroDose’s inhalation technology into yet another extremely important disease area.”

MMI-0100 is a selective inhibitor of MAPKAP kinase 2 (MK2), a key terminal kinase in the transforming growth factor beta (TGF- β)/p38 signaling pathway. By targeting a terminal kinase, MMI-0100 has the potential for greater specificity of action and lower off-target toxicity than other anti-fibrotic agents that address targets higher in this important pathway.

“IPF represents an enormous unmet medical need, and delivering a drug directly to the lung that inhibits a down-stream kinase in the TGF-beta/p38 pathway is extremely appealing. It is very likely that multiple drugs that interfere with different components of fibrosis will be needed to combat IPF, and MK2 inhibition is a novel and exciting target for drug development in this devastating disease,” said Paul W. Noble, M.D., Professor of Medicine and Chief, Division of Pulmonary, Allergy, and Critical Care Medicine, Duke University Medical Center.

“Developing therapeutics for local delivery is a very desirable approach for the treatment of lung diseases in general, and IPF in particular. Doing so should minimize the risk of systemic effects while targeting a kinase now known to be involved in fibrogenesis. Accordingly, this is an attractive approach for treating such a lethal disease,” said David S. Wilkes M.D., Executive Associate Dean for Research Affairs, August M. Watanabe Professor for Medical Research, Indiana University School of Medicine.

Development of MMI-0100 for treatment of IPF is being funded in part with federal support from the National Heart, Lung, and Blood Institute (NHLBI), part of the National Institutes of Health (NIH) in the Department of Health and Human Services (DHHS), under the Science Moving toward Research Translation and Therapy (SMARTT) program (NHLBI contract no. HHSN268201100017C).

Femina Pharma Announces Issuance of United States Patent 8,178,123 to Improve Drug Absorption for Cancer and HIV/AIDS Populations

PRNewswire: June 19, 2012 – MIAMI, FL, U.S.A. – Femina Pharma Incorporated announced the issuance of U.S. Patent 8,178,123. This patent covers methods of improving drug

delivery, particularly for cancer and HIV/AIDS populations. Prof. Giovanni Pauletti, a named inventor of the patent, explains the background and significance of the ’123:

“The gastrointestinal tract is physiologically designed to digest food, absorb nutrients, and serve as an effective barrier protecting the internal milieu of the body from microorganisms and other disease-causing agents. Consequently, it is not surprising that blood concentrations for the majority of our drugs are less than expected due to incomplete absorption and/or significant degradation after oral administration.

“This patent describes new opportunities for patients to obtain greater therapeutic benefit from drugs that are not completely absorbed after oral administration and/or cause significant gastrointestinal side effects such as nausea, vomiting, and bleeding. Specifically, this invention aims at improving treatment options for patients diagnosed with cancer or HIV/AIDS. Most drugs used in the management of these diseases are poorly absorbed after oral administration and required either high doses that can cause significant gastrointestinal side effects or administration via injection.

“To overcome this unsatisfactory limitation, the inventors of this patent created novel pharmaceutical compositions that protect a drug from extensive enzymatic degradation and, simultaneously, augment drug permeation across biological membranes. These unique formulations comprise of a mixture of plant-based inhibitors of the dominant metabolic cytochrome P450 enzyme system and FDA-approved excipients that enhance drug absorption across biological membranes by inhibiting specific transport proteins that prevent drug absorption (i.e., efflux systems such as P-glycoprotein). As many drugs are effectively eliminated by the liver, these novel compositions are designed for patient-controlled self-administration in anatomical regions where absorbed drug is not directly transported to the liver (e.g., oral or vaginal cavity). As a consequence, patients will experience greater therapeutic efficacy and reduced side effects due to lower drug doses administered.”

Joseph Fuisz of Femina commented: “We are very proud of this issuance, the benefits for these critical patient areas, and our continuing progress at Femina.”

Valeant Pharmaceuticals Agrees to Acquire OraPharma

PRNewswire: June 15, 2012 – MONTREAL, Canada – Valeant Pharmaceuticals International, Inc. (NYSE: VRX and TSX: VRX) announced today that Valeant has agreed to acquire OraPharma, a specialty oral health company that develops and commercializes products that improve and maintain oral health, from Water Street Healthcare Partners, a private equity firm focused exclusively on the health care industry. Total consideration is approximately \$312 million and up to \$114 million in potential contingent payments based on certain milestones, including revenue targets. OraPharma’s lead product is Arestin, a locally administered antibiotic for the treatment of periodontitis that utilizes an advanced controlled-release delivery

system and is indicated for use in conjunction with scaling and root planing for the treatment of adult periodontitis. OraPharma currently has the largest specialized pharmaceutical sales force in the dental industry and, as of March 31, 2012, OraPharma's trailing twelve month net revenue was approximately \$95 million with the business growing at a high-single-digit rate.

"We are excited to enter a new attractive market segment with an already established sales infrastructure focused entirely on the dental community," said J. Michael Pearson, chairman and chief executive officer. "We believe that this market segment has similar characteristics to the dermatology, podiatry, and ophthalmology markets and should offer us the opportunity to cross-sell some of our current products, most notably our new topical prescription cold sore medication, Xerese. We believe the OraPharma business is a new growth platform from which to build additional opportunities in the future."

Impel NeuroPharma Announces Commercial Milestones and First-in-Human Use of Pressurized Olfactory Delivery (POD) Technology

Business Wire: June 14, 2012 – SEATTLE, WA, U.S.A. – Impel NeuroPharma, a medical device company developing a novel drug delivery device that enables drugs to bypass the blood-brain barrier (BBB) using direct nose-to-brain delivery, today announced a set of important milestones in its drive to commercialize its POD technology.

The key milestones announced today are:

- Successful first-in-human pilot study of the POD technology,
- Three (3) collaborations with leading pharmaceutical companies to pursue applications of the POD technology in three different CNS therapeutic applications, and
- Award of a Small Business Investigational Research (SBIR) grant from the National Institutes of Health (NIH) and National Institute of Drug Abuse to evaluate a first-in-class biologic analgesic.

The results of the first-in-human study using the POD technology will be discussed at the 2012 BIO International Convention in Boston, MA, on June 18–21. The study showed a 2:1 overall preference for the POD technology over conventional nasal spray devices. "This is an encouraging result, which indicates the POD technology can be easily utilized in clinical research and incorporated into commercial drug-device combination products," said John Hoekman, Ph.D., Impel NeuroPharma's chief scientific officer. "We have designed the POD device with the end user in mind. We want to ensure it is easy to use for both patients and clinical investigators."

The collaborations announced today are the direct result of Impel NeuroPharma's focus on incorporating its drug delivery technology into meaningful therapeutic initiatives of pharmaceutical companies. One of Impel NeuroPharma's current collaborations is designed to demonstrate the effectiveness of the

POD technology in humans. Results from this human study will be presented this fall.

"We are extremely pleased by the response of the pharmaceutical industry to our inventive nose-to-brain delivery technology. These collaborations validate Impel NeuroPharma's technology in a wide range of therapeutic indications and CNS agents. Our goal is to collaborate with pharmaceutical companies who have CNS agents that can benefit from nose-to-brain delivery. Our next wave of projects will continue to broaden the range of therapeutic applications in which we can provide the greatest impact," stated Michael Hite, Impel NeuroPharma's Chief Executive Officer.

Impel NeuroPharma has been awarded a phase 1 SBIR grant of \$150,000 which will be used to evaluate a novel biologic analgesic therapeutic. Nose-to-brain delivery may enable the delivery of analgesic therapeutics that have fewer side effects and have lower potential for abuse. Dr. Hoekman will serve as the PI for the grant. Dr. Hoekman currently serves as the PI on a phase 2 SBIR grant received in 2011 from the Department of Defense and as an investigator on the commercialization grant from the Life Science Discovery Fund (LSDF) received in 2011. Impel NeuroPharma has received over \$1.9 million in grants since its inception.

The announced milestones build upon Impel NeuroPharma's recent accomplishments as it moves rapidly toward the commercialization of its POD technology.

Fuse Science Sets New Standard of Transdermal Delivery with Groundbreaking Scientific Results

PRNewswire: June 13, 2012 – MIAMI LAKES, FL, U.S.A. – Fuse Science Inc. (OTCQB: DROP) (www.fusescience.com) is pleased to announce the results of a study that begins to indicate the significant capabilities that reside in their proprietary technology. A third-party study, which is being released today at www.fusescience.com, reveals unique and differentiated transdermal delivery capabilities that the company believes have the potential to significantly improve drug delivery and minimize side effects. The results of the study center around four basic principles that matter to everyone when it comes to nutrition, energy, and pharmaceutical delivery options:

Speed—Fuse Science is the first to report the ability to deliver caffeine through the epidermis in less than 3 minutes in an *in vitro* study. This opens the door for a wide variety of acute delivery options transdermally, which will significantly improve medical treatment options. Imagine the transformation of the \$2 billion dollar internal analgesic category from a pill that takes 30 minutes to an hour to help provide relief vs. a roll-on with "Powered by Fuse™" technology that begins to work in less than 3 minutes.

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Variability—The study indicates that our proprietary delivery technology can influence the amount of medications and nutrients delivered through the skin at varying rates. This will allow for pediatric and adult dosing, as well as the ability to introduce a wide variety of new treatment applications designed to improve medical care, health and beauty, and anti-aging therapies.

Duration—The study reports the superior progressive delivery of caffeine that has not peaked at 2 hours vs. current published data of oral consumption, which peaks at 45–60 minutes and thereafter falls off. We believe that this sets the stage for Fuse Science to deliver therapeutic levels of medications and nutrients over longer periods of time, creating better health outcomes.

Functionality—Fuse Science delivery technology can take products that are currently in patch form like nicotine, birth control, and lidocaine, as a few examples of many, and turn them into simple transdermal roll-ons that deliver the same or better results without the constraints and drawbacks of wearing a patch.

“We believe that proof of concept demonstrated by the study will be a key enabler in our global licensing efforts, and it further documents superior capabilities that reside within our technology,” said Jeanne Hebert, vice president of marketing and clinical research. “It is our objective to leverage our technology, which we believe extends well beyond these initial findings, to redefine the standard of performance in many multi-billion dollar pharmaceutical and nutritional categories and improve the lives of people around the world.”

“Needless to say, we are very pleased with the results of this initial study,” said Brian Tuffin, CEO of Fuse Science Inc. “We have been very deliberate and calculated with every action we’ve taken as a company, and this study provides the first of several significant steps we’re taking to fully commercialize our proprietary delivery technology. We anticipate announcing in the coming days and weeks more successes in this area, which began with the licensing of some of our transdermal technology to Mission Athletecare early this year.”

Analytical Solutions, Inc., Expands, Changing Name to Tergus Pharma—New Name Reflects Expanded Services in Dermatology Product Development

PRNewswire: June 12, 2012 – RESEARCH TRIANGLE PARK, NC, U.S.A. – In response to company growth and expansion of topical pharmaceutical product development services, Analytical Solutions, Inc. (ASI) is pleased to announce today that it is changing its name to Tergus Pharma, LLC, to better echo the company’s new growth trajectory.

Tergus cofounder and CEO, Dr. Vijendra Nalamothu, most recently head of dermatology R&D for Promius Pharma and Dr. Reddy’s Laboratories, brings 18 years of topical drug product development and commercialization experience to Tergus clients. Since 1994, Tergus cofounder and president, Dr. Kailas Thakker, has been providing quality analytical services to the

pharmaceutical industry with an emphasis on *in vitro* release testing (IVRT), functional testing for semisolids and topical products.

Tergus (Latin for “skin”) is now providing dermatology drug development services from concept to commercialization. With the acquisition of new equipment and strategic additions to the scientific team, Tergus Pharma is pleased to announce that it is now servicing its clients with a broader range of topical drug development services, including product development strategy and design; target product profile development; formulation development; analytical method development and validation; preclinical and clinical supplies manufacturing; program management and logistics leadership; scale-up and technology transfer oversight; regulatory CMC consulting; disease model development; clinical development strategy; and development plan creation to ensure fastest path to *in vivo* or clinical proof of concept studies.

Tergus’ core expertise will remain focused in topical dosage forms, including creams, ointments, lotions, liquids, suspensions, gels, hydrogels, pastes, pump sprays, topical aerosols, foams, microencapsulation, liposomes, suppositories, and nail lacquers.

Tergus Pharma, LLC is a privately held dermatology-focused organization offering complete pharmaceutical product development services. Tergus’s GMP/GLP compliant, state-of-the-art laboratories are located in Research Triangle Park, North Carolina. For additional information, please visit www.TergusPharma.com.

Groundbreaking Clinical Evidence Demonstrates Benefit of PROPEL Implant for Chronic Sinusitis Patients

Business Wire: June 6, 2012 – MENLO PARK, CA, U.S.A. – Intersect ENT, Inc., an innovator in treatment solutions for ear, nose, and throat clinicians and their patients, today announced two key clinical publications demonstrating the benefit of the PROPEL™ steroid-releasing implant for chronic sinusitis patients.

A meta-analysis of two separate, randomized, controlled, multicenter clinical studies was published in *International Forum of Allergy & Rhinology*, the official journal of the American Rhinologic Society and the American Academy of Otolaryngic Allergy. Results of the meta-analysis demonstrate that, compared to controls, use of PROPEL reduced postoperative interventions by 35 percent ($p = 0.0008$) following endoscopic sinus surgery (ESS). PROPEL also decreased adhesion lysis by 51 percent ($p = 0.0016$), the need for oral steroids to treat inflammation by 40 percent ($p = 0.0023$), and frank polyposis by 46 percent ($p < 0.0001$). Early postoperative healing, including reduced inflammation, is a predictor of longer-term success after sinus surgery.

“The level of clinical evidence in these two publications is unparalleled in the management of chronic sinusitis,” said Joseph Han, M.D., director of rhinology and endoscopic sinus surgery

and associate professor at the Eastern Virginia Medical Center, the lead author of the meta-analysis publication. “The results clearly demonstrate that the PROPEL implant offers significant advantages for patients undergoing endoscopic sinus surgery.”

“We are proud to have collaborated with clinicians across the country to develop a product that delivers meaningful clinical benefits to chronic sinusitis sufferers. PROPEL is the first and only product for patients undergoing sinus surgery to be backed by Level 1-A clinical evidence,” said Lisa Earnhardt, the company’s president and CEO. “We are very pleased with the success of our limited launch and look forward to bringing PROPEL to additional U.S. markets later this year.”

The meta-analysis included results from 105 patients at 11 centers enrolled in the ADVANCE II pivotal trial of the PROPEL implant and from 38 patients undergoing ESS for chronic sinusitis at four centers in a pilot study of the device.

In addition, results of the prospective, randomized, controlled, double-blind, multicenter ADVANCE II pivotal trial of the PROPEL implant were published in the June issue of *Otolaryngology—Head and Neck Surgery*.

Results of the study demonstrate that use of the PROPEL mometasone furoate implant significantly improves outcomes for patients undergoing ESS for chronic sinusitis. In the study, PROPEL provided a 29 percent reduction in the need for postoperative interventions ($p = 0.0280$) relative to controls, including a 52 percent reduction in surgical lysis of adhesions or scar formation ($p = 0.0053$) and a 29 percent reduction in the need for oral steroids to resolve recurrent inflammation ($p = 0.0881$). These results, which were graded by an independent and blinded panel of ENT surgeons, show that the improvements clinicians see endoscopically translate into significant patient benefits.

Intersect ENT Inc., located in Menlo Park, California, is an innovator in local drug delivery focused on advancing clinically proven therapy solutions that improve quality of life for patients with ear, nose, and throat conditions. The company’s initial product, the PROPEL™ dissolvable steroid-releasing implant, is clinically proven to improve sinus surgery outcomes for patients suffering from chronic sinusitis, a common condition that affects one out of seven adults in the U.S. and greatly impacts quality of life. The company holds 17 issued U.S. patents and more than 75 patents and pending applications worldwide. Intersect ENT is backed by Kleiner, Perkins, Caufield & Byers; U.S. Venture Partners; PTV Sciences; and Medtronic. For more information, please visit www.intersectENT.com.

Orexo Acquires All U.S. Rights for Abstral and Receives a Net Cash Consideration of MSEK 610

Business Wire: June 4, 2012 – UPPSALA, Sweden – Orexo AB (“Orexo”) today announced the acquisition of the U.S. rights to Abstral® from ProStrakan Group plc (“ProStrakan”) and the restructure of the existing royalty arrangement for the product in EU and rest-of-the-world (ROW) markets. Completion of the

transaction in the U.S. is anticipated by January 1, 2013, while the EU and ROW were completed as of June 1, 2012.

Fixed payments of 610 MSEK to be received by Orexo as part of the revised agreement, combined with expected future royalties and milestone awards from Abstral sales in ex-U.S. markets, will secure a strong financial position from which to execute future U.S. commercial activities.

This development is fully in line with the company’s strategy, as communicated during the last year, where Orexo itself will seek to commercialize the proprietary products that arise from application of its patented sublingual delivery technology. Abstral was originally developed by Orexo and out-licensed to ProStrakan. Abstral is a rapid-acting formulation of fentanyl, employing Orexo’s proprietary sublingual delivery technology, which is approved and marketed for the treatment of breakthrough pain in cancer patients in both the U.S. and EU. With acquisition of the U.S. rights, Orexo has taken an important step toward establishing a commercial presence in the U.S.

Since 2010, Orexo has committed to establishing a commercial presence in the U.S. through which to launch its proprietary products. In Abstral, Orexo has secured its first U.S. commercial brand as of January 1, 2013.

The establishment of a commercial presence in the U.S. will now be in advance of the FDA filing of Orexo’s lead value driver, OX219. From early 2014, it is expected that Orexo will be very well positioned in the U.S. market through full ownership of two commercial specialty pharmaceutical brands.

- Abstral—the leading, new fast-acting fentanyl product in the EU intended for treatment of breakthrough pain in cancer patients. The product is already approved and available in the U.S.
- OX219—sublingual reformulation of buprenorphine and naloxone using Orexo’s technology. The program is developed for maintenance treatment of opioid dependence and may be the first new entrant in to a rapidly growing \$1.3 billion market. Orexo expects to file OX219 with the FDA in Q1 2013.

The new agreement will see the existing commercial infrastructure continue to market Abstral in the U.S. until December 31, 2012, under ProStrakan’s direction. In the seven-month period until Orexo assumes full operational responsibility, a detailed commercial plan will be developed to ensure the establishment of Abstral as the leading, new fast-acting fentanyl product in the U.S., as has been achieved in the EU. Orexo will in Q4 2012 present the commercial plan for Abstral in the U.S.

Anders Lundström, chief executive of Orexo, said, “Since launch in 2008, Abstral has gained the position as the leading new treatment of breakthrough pain in cancer patients in EU markets. Orexo is confident that the success we have witnessed

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in EU can be mirrored in the U.S., through execution of an optimized commercial strategy.”

Martin Nicklasson, chairman of the board of directors at Orexo, commented, “I am very satisfied with the revised Abstral agreement, as it sees Orexo gaining full U.S. rights to the brand, monetising much of the current value of the existing EU and ROW agreements, while reducing financial risks. Furthermore, with the revised royalty structure, Orexo still retains much of the upside associated with increasing EU and ROW sales, which can be expected to contribute to Orexo’s cash flow in the years to come.”

Orexo AB is an emerging specialty pharma company developing improved treatments using proprietary drug delivery technology. Orexo’s expertise is within the area of reformulation technologies and especially sublingual formulations. Orexo has a portfolio of revenue-generating EU- and U.S.-approved products currently marketed under licence and a pipeline of several reformulations of approved compounds for areas of unmet medical need. Orexo also has collaboration projects with several international pharma companies. Orexo AB is Swedish-headquartered with 100 employees and listed on NASDAQ-OMX. The largest shareholders are Danish Novo A/S and Swedish HealthCap. For information about Orexo, please visit www.orexo.com.

May 2012

Royer Biomedical, Inc., Receives FDA Approval to Proceed with Human Testing (IND 111446) on 5/25/2012 for Its AppliGel Polymer Drug Delivery System

Business Wire: May 31, 2012 – FREDERICK, MD, U.S.A. – Royer Biomedical, Inc. (RBI) received FDA approval to proceed with human testing of AppliGel-G (Gentamicin) in management of diabetic foot ulcers (DFU). AppliGel is a patented proprietary dissolvable nonimmunogenic polymer drug delivery system platform. It has demonstrated efficacy in biofilm and infection eradication, without significant systemic API levels.

“This represents an important milestone in the development of AppliGel,” said William Wolf, M.D., RBI’s president and CEO. “We are excited at the prospect of helping diabetics and their physicians in the management of this difficult and limb-threatening disorder. We look forward to gaining final approval for topical, injectable, and implantable drug delivery applications for antibiotics, chemotherapeutics, and analgesics to address DFU, cancers, and other conditions requiring sustained medication in a dissolvable platform without immunogenic reaction or the need for removal. Our AppliGel polymer platform’s shelf stability, ease of application, and ability to deliver pharmaceuticals without significant adverse effects has been well-demonstrated in the veterinary world, and the prospect of collaborating with Johns Hopkins University Hospital and Georgetown University Hospital to improve patient outcomes in cancer and diabetes is truly exciting.”

A.P. Pharma Announces Study Finding Continuous Exposure to a 5-HT3 Antagonist Using APF530 Provides Better Emetic Control

Business Wire: May 31, 2012 – REDWOOD CITY, CA – A.P. Pharma, Inc. (OTCBB: APPA.OB), a specialty pharmaceutical company, today announced that an abstract analyzing a subset of efficacy results from its phase 3 trial of APF530 has been published in conjunction with the American Society of Clinical Oncology’s (ASCO) 2012 Annual Meeting. APF530 is the company’s lead product candidate being developed for the prevention of both acute- and delayed-onset chemotherapy-induced nausea and vomiting (CINV). The abstract concludes that continuous exposure to a 5-HT3 receptor antagonist, through the administration of an extended-release formulation such as APF530, results in better emetic (nausea and vomiting) control than administration of a standard, short-acting 5-HT3 receptor antagonist. The title of the abstract is “The effect of continuous exposure to serotonin receptor antagonism on delayed emesis: An analysis of 1,535 patients in two randomized clinical trials with granisetron (G), APF530, and palonosetron (palo).” Abstract No.: e19635. Authors: Harry Raftopoulos, Erin O’Boyle, Richard J. Gralla, Martin Rosenberg, and John Barr.

APF530 contains the 5-HT3 antagonist granisetron, formulated in the company’s proprietary Biochronomer™ drug delivery system, which allows therapeutic drug levels to be maintained for five days with a single subcutaneous injection. Intravenous and oral formulations containing granisetron are approved for the prevention of acute-onset CINV but not delayed-onset CINV. Granisetron was selected because it is widely prescribed by physicians based on a well-established record of safety and efficacy. For further information, please visit the company’s website at www.appharma.com.

Bio-Path Holdings Successfully Completes Third Cohort in Phase I Clinical Trial of Lead Product Candidate Liposomal Grb-2 in Leukemia

Business Wire: May 29, 2012 – HOUSTON, TX, U.S.A. – Bio-Path Holdings, Inc. (OTC BB: BPTH) (“Bio-Path”), a biotechnology company developing a liposomal delivery technology for nucleic acid cancer drugs, today announced that it has completed treatment of the third dosage cohort in its phase I clinical trial of its lead product candidate, BP-100-1.01 (liposomal Grb-2), which is a systemic treatment for blood cancers, including acute myeloid leukemia (AML), chronic myelogenous leukemia (CML), acute lymphoblastic leukemia (ALL), and myelodysplastic syndrome (MDS). The trial is being conducted at the MD Anderson Cancer Center. The drug’s safety profile continues to be favorable, with no treatment-related serious adverse events reported, and data continues to suggest some possible antileukemia activity.

A total of three patients were enrolled and dosed in the third cohort of the study. All three patients completed the 28-day treatment cycle and were evaluable. Liposomal Grb-2 is systemically delivered by intravenous injection. Patients received a dose of 20 mg/m² twice a week for four weeks, for a total of

eight doses. Preliminary results suggest that liposomal Grb-2, at a dose of 20 mg/m², is well tolerated. The protocol for the clinical trial includes dose escalation of 5, 10, 20, 40, and 50 mg/m². The expected dose for treatment is 45 mg/m² based on preclinical studies in animals.

As was the case with the two previous cohorts, there continued to be a suggestion of possible antileukemia activity, as all three patients stabilized. As such, all three patients are receiving or will receive additional treatment cycles. In the protocol of the clinical trial, a patient exhibits stable disease if, in the opinion of the principal investigator, there is no clinically significant change in the disease. One patient, from this cohort, with AML had bone marrow blasts reduced by 60 percent during the first treatment cycle to within normal parameters and continued with a second treatment cycle.

“The preliminary results being reported today for the third cohort of our clinical trial demonstrate consistent safety results with the previously reported data, as well as a continuation of possible antileukemia activity related to the drug. Patients in our clinical trial are refractory or relapsed to current therapies and have failed other approved treatments. These patients have very advanced stages of the disease and are often in very poor condition. The fact that all three patients in the third cohort stabilized to qualify for extended treatment is very promising,” said Peter Nielsen, president and chief executive officer of Bio-Path. “It is clear that the momentum of the trial has significantly changed to the better, with markedly shortened times to complete a cohort and the minimum number of patients needed. The increase in the number of patients needing drugs for extended treatments has caused us to accelerate our plans to upgrade the capacity of our supply chain. We expect new supplies to become available to continue treatment of patients in June. The fourth cohort is ready to be opened for enrollment once the new drug supplies have arrived, as well as the continued treatment of third cohort patients on extended treatment plans.”

Bio-Path’s drug delivery technology involves microscopic-sized liposome particles that distribute nucleic acid drugs systemically and safely throughout the human body, via simple intravenous infusion. The delivery technology can be applied both to single stranded (antisense) nucleic acid compounds and double stranded (siRNA) with the potential to revolutionize the treatment of cancer and other diseases where drugable targets of disease are well characterized. However, the company is currently only developing liposomal antisense drug candidates. Bio-Path also anticipates developing liposome tumor targeting technology, representing next-generation enhancements to the company’s core liposome delivery technology. For more information, please visit the company’s website at www.biopathholdings.com.

Pearl Therapeutics Phase 2b Twice-Daily Dosing Data Suggest Morning and Evening Benefit of PT003 in Patients with COPD

PRNewswire: May 14, 2012 – REDWOOD CITY, CA, U.S.A. – Pearl Therapeutics Inc. announced plans to make 11 presentations at upcoming medical meetings to report clinical and product development information pertaining to PT003 (GFF MDI), a proprietary, fixed-dose combination of glycopyrrrolate (GP), a long-acting muscarinic antagonist (LAMA) and formoterol fumarate (FF), a long-acting beta-2 agonist (LABA). PT003 and its components, PT001 (GP MDI) and PT005 (FF MDI) are being developed for the treatment of patients with moderate-to-severe COPD. Among these presentations will be previously undisclosed results of a phase 2b study in which PT003 was shown to be associated with a significant improvement in home peak expiratory flow rate (PEFR), a measure of lung function, when compared to placebo, individual components of PT003, and open-label active controls ($p < 0.03$ for all comparisons). Importantly, this improvement was observed for both morning and evening PEFR assessments, which may suggest a morning and evening bronchodilator effect with twice-daily administration of PT003. In addition to improvement in home PEFR, phase 2b results being presented at ATS demonstrate that PT003 is associated with a reduction in rescue albuterol use compared to placebo and controls. The product development data being presented at the RDD meeting demonstrate Pearl’s ongoing commitment to designing PT003 and its component inhalers for reliable drug delivery that will be further evaluated in late-stage clinical development.

“At ATS this year, we are presenting a compendium of phase 2b clinical findings that provide further support for PT003 as a potential treatment for patients with moderate-to-severe COPD,” stated Dr. Colin Reisner, chief medical officer and executive vice president of clinical development for Pearl Therapeutics. “It is well documented that patients with COPD experience worsening of their symptoms in the morning and evening. The significant improvement with twice-daily administration of PT003 vs. placebo in home PEFR in both the morning and the evening pre- and post-dose assessments suggests that PT003 may provide benefit at the times when patients’ symptoms are known to worsen. The potential benefits of this dual-peak effect following morning and evening dosing will be evaluated further in late-stage studies.”

Clinical results are also being presented supporting the selection of the FF MDI (PT005) dose to be tested in the company’s phase 3 fixed-dose combination studies of PT003. CMC data on Pearl’s “triple” combination of GP, FF, and an inhaled corticosteroid (ICS) is described in another Pearl presentation at ATS, and a late-breaking presentation on the formulation of MDIs that deliver nanogram-level doses of GP and FF will also be presented.

Chuck Bramlage, Pearl’s chief executive officer, added, “We believe the depth and strength of the clinical data, and the

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achievements by Pearl scientists in designing robust and reproducible inhalers, substantially de-risk the Pearl bronchodilator family of products for late-stage development. We also believe that the innovations Pearl has made in respiratory drug delivery truly differentiate PT003 development from conventional inhaled product development, and set a new benchmark in capital and time efficiency in the field of pulmonary product development. We look forward to concluding the phase 2b program in 2012 and commencing with a plan to support registration of PT003 thereafter.” For more information, please visit www.pearltherapeutics.com.

April 2012

Imprimis Pharmaceuticals Closes \$7.95M Financing and Provides Progress Report to Shareholders

PRNewswire: April 27, 2012 – SOLANA BEACH, CA, U.S.A. – Imprimis Pharmaceuticals, Inc. (OTC Markets: IMMY) announced that it has closed a \$7.95M private placement of stock and warrants and is providing an update to shareholders and the market.

Imprimis Pharmaceuticals, Inc., CEO Mark L. Baum stated, “We are pleased to announce the closing of a \$7.95M private placement. The financing was completed at a price of \$0.79 per unit and included one share of common stock and a 25% three-year warrant, giving the investor the right, for three years, to buy additional Imprimis common shares at \$1.185 per share. Imprimis has the unilateral right to call for the mandatory exercise of the warrants with 90 days’ notice to the holders, upon notice from the FDA that our lead drug candidate—Impracor—has been approved for sale in the United States. No brokerage or investment banking fees were paid related to the financing, so the net cash received by the company was approximately \$7.95M.”

Baum added, “We believe that closing this common stock and warrant financing transaction is a strong sign that the recent changes at Imprimis have had a positive effect on our ability to secure the capital we need to drive value for our stakeholders. We believe that the market opportunity for our technology and our lead drug candidate is significant, and this capital will certainly provide momentum for us to begin to execute on our clinical and other strategic initiatives.”

Imprimis’ chief medical officer, Dr. Joachim Schupp, commented, “Our science team has been hard at work as we transition towards the re-initiation of clinical studies for our lead drug—Impracor, a ketoprofen-based topical NSAID—as well as additional strategic initiatives that we hope to execute in the future. We have been in communication with the FDA regarding our IND and our objective to file a 505(b)2 for Impracor following successful phase 3 development.”

Baum continued, “Our mission is to be the leader in topical drug delivery solutions. With the guidance of a team of experts, Imprimis has recently developed an intellectual property strategy that is being aggressively implemented. Our patented platform

technology, called Accudel, allows us to deliver medicines through the skin (topical drug delivery), and we intend to monetize this platform through a pipeline development program that will be guided by pharmaceutical and medical industry thought-leaders and a disciplined approach to development expenditures. Our science team, including Dr. Joachim Schupp, Dr. Balbir Brar, and Dr. Paul Finnegan, has provided our board of directors with tremendous support, and we are confident that our clinical efforts are being guided by a pressure-tested winning strategy, and are being executed by seasoned scientific leaders. We look forward to moving these programs forward in the near term.”

“Imprimis’ balance sheet has been dramatically improved in the past four months, as we have reduced our debt by approximately 86%. Concurrent with the closing of this financing, our secured debtholder agreed to roll 100% of its secured debt into common stock on the same terms as this \$7.95M financing. Now, we are a company with a promising vision, a world class team to execute on this vision, and we have a financeable balance sheet.”

Baum concluded, “Looking towards the future, we have hired MDB Capital, LLC, of Santa Monica, CA, to represent Imprimis for our future investment banking needs. In the coming months, we also intend to make an application to NASDAQ to list our common shares. Much has been done, and there is much more to be done. We appreciate the patience of our shareholders, their commitment to our business and our team, and their interest in our shared vision to better people’s lives by providing choices to the traditional methods that medicines are delivered.”

Imprimis Pharmaceuticals is dedicated to creating value for our shareholders by improving patient health and their quality of life by leveraging Accudel, a patented topical drug delivery platform that enables highly targeted site-specific treatment. Imprimis is made up of a team of scientists and seasoned executives who are focused on the development and commercialization of noninvasive topically delivered medications. Our lead phase 3 drug, Impracor, utilizes our Accudel™ cream formulation to deliver Ketoprofen, a nonsteroidal anti-inflammatory drug (NSAID), to target underlying tissue where Impracor exerts its localized anti-inflammatory effect. Accudel™ technology has the ability to bring numerous promising new products to the prescription drug, over-the-counter, and cosmeceutical markets, improving the way people have been treated in a number of large market categories. The Imprimis Pharmaceuticals, Inc. website is currently under construction and is expected to launch in May of 2012. For more information, contact Mark L. Baum, Esq., (858) 433-2800.

Generex Announces Publication of Paper on Buccal Spray Insulin

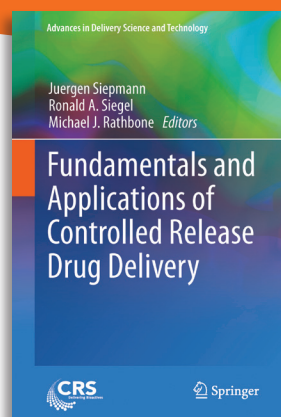
PRNewswire: April 26, 2012 – WORCESTER, MA, U.S.A., and TORONTO, Canada – Generex Biotechnology Corporation (OTCBB: GNBT.OB) announced today that a paper in respect of Generex Oral-lyn™, the company’s

proprietary buccal insulin spray product, has been published in the peer-reviewed journal *Expert Opinion on Biological Therapy*. The paper, titled "Buccal spray insulin (Oralgen) for type 2 diabetes: What evidence?," is authored by Professor Paolo Pozzilli and Drs. Andrea Palermo and Ernesto Maddaloni of the Department of Endocrinology and Diabetes, University Campus Bio-Medico, Rome, Italy. The abstract of the paper can be viewed online at the U.S. National Library of Medicine, National Institutes of Health at www.ncbi.nlm.nih.gov/pubmed/22515262.

The paper notes that, while the achievement of glycemic control, particularly the management of postprandial hyperglycemia, is

the most significant treatment target for the management of diabetes, and that multiple daily insulin injections are required to achieve treatment goals, both patients and healthcare professionals are reluctant to initiate insulin therapy (which the authors term "psychological insulin resistance"). The paper suggests that noncompliance with injected insulin therapy, which compromises glycemic compensation processes, may be remedied by novel noninjectable insulin formulations and that Generex Oral-lyn™ (referred to as "Oralgen" in the paper), which provides insulin absorption via the buccal mucosa, appears "suitable to manage the postprandial hyperglycemia without hypoglycemic risk." ■

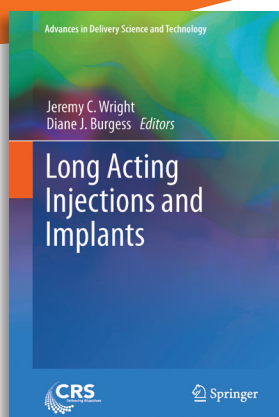
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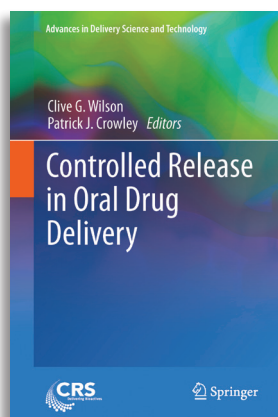
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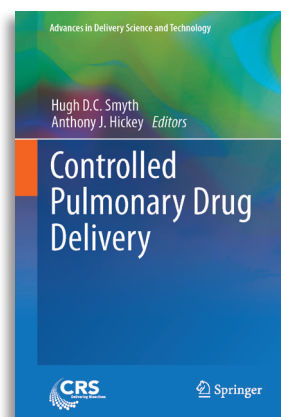
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Calendar of Events

2012

8th Annual Meeting of the Israeli Chapter

September 5–7
Western Galilee, Israel
<http://www.icrs.org.il>

2nd Symposium on Innovative Polymers for Controlled Delivery (SIPCD 2012)

September 11–14
Suzhou, China
<http://www.sipcd.cn>

10th International Nanomedicine and Drug Delivery Symposium (NanoDDS '12)

Sponsored by CRS
October 28–30
Atlantic City, NJ, U.S.A.
<http://nanodds2012.com>

Drug Delivery Australia Conference

Sponsored by CRS
November 26–27
Melbourne, Australia
<http://www.crsaustalia.org>

2013

ISAA 2012—10th International Symposium on Adjuvants for Agrochemicals

April 22–26
Foz do Iguaçu, Paraná, Brazil
<http://events.isaa-online.org>

40th Annual Meeting & Exposition of the Controlled Release Society

Sponsored by CRS
July 21–24
Hawaii Convention Center
Honolulu, Hawaii, U.S.A.
www.controlledreleasesociety.org