# APV FOCUS GROUP DRUG DELIVERY

COMBINING SCIENCE & TECHNOLOGY TO CREATE ADVANCED DRUG DELIVERY SYSTEMS

INTERNATIONAL ASSOCIATION FOR PHARMACEUTICAL TECHNOLOGY

NEWSLETTER ISSUE 1/2013




## TABLE OF CONTENTS



## DRUG DELIVERY EVENTS


BACK TO TABLE OF CONTENTS


Provided by Christoph Blümer

◇ **APV Course 6481: Workshop Nanomedicine(s)**
April 8-9, 2013, Berlin, Germany

Chairs: Horst-Dieter Friedel, Bayer Pharma AG, Berlin, Germany; Rogério Gaspar, University of Lisbon & iMed.UL, Lisbon, Portugal

Details

- Lessons Learnt from First Generation Products
- Challenges for introduction of "Follow-On" Products
- Mechanisms to ensure Safe and Timely Introduction of Emerging Nanomedicines/Nanomaterials

**40th Annual Meeting & Exposition of the Controlled Release Society**
July 21-24, 2013, Honolulu, Hawaii, U.S.A.

Details

***Suggest a meeting to be announced!***

## DRUG DELIVERY PRODUCTS


BACK TO TABLE OF CONTENTS


Provided by Dr. Louise Rosenmayr-Templeton

### ZECUITY™ (sumatriptan iontophoretic transdermal system) (NuPathe Inc.)

On 17 Jan 2013 the FDA approved Zecuity™(sumatriptan iontophoretic transdermal system) from NuPathe Inc. (Conshohocken, PA, USA) for the acute treatment of migraine with or without aura in adults [1, 2]. Zecuity is a disposable, single use, battery operated system that delivers the selective 5-hydroxy-tryptamine receptor subtype 1 (5-HT1) agonist, sumatriptan, across the skin by iontophoresis. It is comprised of an iontophoretic device and a drug reservoir card. The reservoir card contains 2 non-woven pads and 2 different gel formulations; one a sumatriptan succinate formulation and the other a sodium salt formulation. The sumatriptan succinate formulation and pad contains purified water, basic butylated methacrylate copolymer (polyamine), lauric acid, adipic acid, methylparaben and a non-woven viscose pad. The salt formulation and pad contains purified water, hydroxypropylcellulose, sodium chloride, methylparaben and a non-woven viscose pad.

Each device contains 86 mg sumatriptan. It is applied to dry, intact, non-irritated skin on the upper arm or thigh and is activated by pressing a button on the device. Zecuity delivers 6.5 mg of sumatriptan through the skin over 4 hours. The device's electronics continually monitor skin resistance and adjust the current applied to control the rate and amount of sumatriptan delivered. Approval was based Phase III trials involving 800 patients. In the Phase III pivotal study, twice as many patients treated with Zecuity were free from headache pain after two hours compared with placebo (18% and 9%, respectively) (primary end-point). 53% of patients treated with the iontophoretic device achieved relief from headache pain and 84% were nausea free at two hours compared to 29% and 63% respectively for placebo. The most common (greater than 5%) side effects of Zecuity were application site pain, tingling, itching, warmth and discomfort.

Zecuity is expected to be launched in Q4 2013.

### **Adasuve® (loxapine) inhalation powder** (Alexza Pharmaceuticals)

In December 2012 Adasuve™ inhalation powder was approved by the FDA and received a positive opinion from the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) [3, 4]. This product contains the antipsychotic, loxapine, without excipients. It was developed by Alexza Pharmaceuticals (Mountain View, CA, USA) using its Staccato® technology for the acute treatment of agitation associated with schizophrenia or bipolar I disorder in adults. This technology involves a hand-held disposable inhaler that delivers a thermally generated drug aerosol to the deep lung. The inhaler consists of a heating substrate, a thin film of unformulated drug coated onto the substrate, and a mouth-piece through which the patient inhales. On oral inhalation controlled and rapid heating of the thin-film of drug occurs. This vapourises the drug which then condenses into particles of 1 to 3 microns which, in turn, are dispersed into the airstream created by inhalation through the mouth-piece [5]. Adasuve 10 mg inhaler delivers 9.1 mg loxapine base in this way. As absorption of the drug is very rapid from the lungs, the pharmacokinetics obtained are similar to that of an intravenous injection with a median time to maximum plasma concentration ($T_{max}$) of 2 minutes and decreased agitation being evident after 10 minutes.

Approval was based on two short-term (24-hour), randomized, double-blind, placebo-controlled, fixed-dose trials in acute agitation. Study 1 involved 344 schizophrenic patients and Study 2 314 patients suffering from bipolar I disorder, manic or mixed episodes with or without psychotic features.

Due to the potential of Adasuve to produce bronchospasm, it can only be administered in the US in certified specialist centres taking part in the Adasuve Risk Evalation and Mitigation Strategy program. In addition, it is contraindicated in patients who have or have a history of asthma, chronic obstructive pulmonary disease (COPD) or other pulmonary conditions, as well as elderly patients with dementia-related psychosis due to the increased risk of death.

**References and Further Information**


[1] Entry for Zecuity on Drugs@FDA
http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/202278s000lbl.pdf (Accessed on 31.01.2013)

[2] Nupathe website
http://www.nupathe.com/products/zecuity-migraine (Accessed on 31.01.2013)

[3] Entry for Adasuve on Drugs@FDA
http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.DrugDetails
(Accessed on 31.01.2013)

[4] Meeting highlights from the Committee for Medicinal Products for Human Use (CHMP) 10-13 December 2012
http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2012/12/news_detail_001673.jsp&mid=WC0b01ac058004d5c1 (Accessed on 31.01.2013)

[5] Alexza Pharmaceuticals website
http://www.alexza.com/ (Accessed on 31.01.2013)

[6] The CHMP Delivers a Positive Opinion Recommending Grant of Marketing Authorization for ADASUVE® (Staccato® Loxapine) in the European Union
http://nocache-phx.corporate-ir.net/phoenix.zhtml?c=196151&p=RssLanding&cat=news&id=1767327
(Accessed on 31.01.2013)


## DRUG DELIVERY COMPANIES

BACK TO TABLE OF CONTENTS

Provided by Jeffry Grunkemeyer

### **PARI PHARMA GMBH** (Starnberg, Germany)

Based on over 100 years as a successful business, PARI recognizes the future of aerosol therapies in the simultaneous optimization of drug and device. This approach is the key focus of PARI Pharma GmbH. PARI Pharma is part of the global network of PARI Worldwide companies. PARI Pharma optimizes Advanced Aerosol Delivery platforms, such as eFlow®, with newly formulated liquid medications. The goal is to develop extremely short and effective treatments that lead to increased patient adherence, symptom control and an improved quality of life for patients. By optimizing drug and device under one roof, PARI Pharma increases the speed of development for our pharmaceutical partners due to its well established track record with Advanced Aerosol Delivery platforms. Our projects include the re-invention of existing medications and the development of new medications.

**Fact sheet:**

| | |
|---|---|
| Founded: | 2007 |
| Location: | Moosstr. 3, 82319 Starnberg, Germany |
| Ownership: | Part of PARI Medical Holding, the company is privately held |
| Employees: | 75 |
| Key technology: | **Name of the key technology/ies**<br>PARI Pharma's eFlow® Technology is a portable, electronic aerosol platform that utilizes advanced technology to increase the efficiency and effectiveness of medication delivery while significantly decreasing standard nebulizer treatment times. eFlow Technology can be customized and optimized for each drug formulation and formulations can be modified or adjusted to eFlow Technology.<br>Proven track record in the development and characterization of orally inhaled products. |
| Products: | - ColiFin® 1 MIU / 2 MIU: Colistimethate Sodium<br>- Range of commercial nebulizer systems based on eFlow® Technology |
| Partnerships: | Gilead, Aptalis, Sunovion, Insmed, Kamada, Alnylam and other undisclosed pharmaceutical companies |
| Website: | http://www.paripharma.com |
| Contact: | Friedrich Gruber<br>Lochhamer Schlag 21<br>82166 Gräfelfing<br>Phone: +49 89 74284676<br>Fax: +49 89 74284678<br>e-mail: f.gruber@pari.de |

## DRUG DELIVERY PEOPLE

BACK TO TABLE OF CONTENTS

Provided by Prof. Dr. Karsten Mäder

**MARK PRAUSNITZ** is Regents' Professor and Love Family Professor of Chemical and Biomolecular Engineering and serves as Director of the Center for Drug Design, Development and Delivery at the Georgia Institute of Technology. His research interests focus on biophysical methods of drug delivery, which employ microneedles, lasers, ultrasound, electric fields and other physical means to control the transport of drugs, proteins, genes and vaccines into and within the body. Current research in his laboratory focuses on drug delivery to the skin, into the eye and into cells.

Prof. Prausnitz earned a B.S. degree from Stanford University and a Ph.D. degree from the Massachusetts Institute of Technology (in the laboratory of Robert Langer), both in chemical engineering. He worked for one year at Alza Corporation carrying out research on transdermal drug delivery systems and for one year at ORBIS International teaching biomedical engineering in developing country hospitals.

At Georgia Tech, Prof. Prausnitz teaches an introductory course on engineering calculations, as well as two advanced courses on pharmaceuticals, both of which he developed. He also serves the broader scientific and business communities as a frequent consultant, advisory board member and expert witness.

Prof. Prausnitz has published more than 175 research articles; given 150 invited lectures at conferences, universities and companies; filed 35 issued or pending patents; and supervised more than 30 doctoral theses. He has been honoured with the Young Investigator Award, Outstanding Pharmaceutical Paper Award and Outstanding Work in Transdermal Drug Delivery Award from the Controlled Release Society, among other awards from the American Society for Engineering Education, National Science Foundation and Sigma Xi Scientific Research Society.

## ACADEMIC GROUPS WITH EXTRUSION CAPABILITIES

This newsletter section is intended to give a brief overview of academic groups working on hot-melt extrusion. It is the third of an occasional series giving brief details of European research teams exploring different aspects of drug delivery research. It is not intended to be a comprehensive list of those involved in the area. As it is a living document, our readers are most welcome to suggest other research teams they are aware of for inclusion in our next edition.

### Belfast, UK

| | |
|---|---|
| Institution | School of Pharmacy, Queen's University Belfast |
| Address | 97 Lisburn Road<br>Belfast BT9 7BL, UK |
| Contact | Dr. Gavin Andrews |
| eMail | g.andrews@qub.ac.uk |

### Bonn, Germany

| | |
|---|---|
| Institution | Pharmazeutisches Institut der Universität Bonn, University of Bonn |
| Address | Gerhard-Domagk-Str. 3<br>53121 Bonn, Germany |
| Contact | Priv.-Doz. Dr. Hubert Rein |
| eMail | rein@uni-bonn.de |

### Bradford, UK

| | |
|---|---|
| Institution | Centre for Pharmaceutical Engineering Science, University of Bradford |
| Address | University of Bradford,<br>Bradford,<br>West Yorkshire, BD7 1DP, UK |
| Contact | Dr A L Kelly, CEng MIMechE |
| eMail | A.L.Kelly@bradford.ac.uk |

### Düsseldorf, Germany

| | |
|---|---|
| Institution | Institut für Pharmazeutische Technologie und Biopharmazie. Heinrich-Heine-Universität Düs-seldorf |
| Address | Universitätsstr. 1 / Gebäude 26.22<br>40225 Düsseldorf, Germany |
| Contact | Dr. Markus Thommes |
| eMail | markus.thommes@uni-duesseldorf.de |

### Gent, Belgium

| | |
|---|---|
| Institution | Laboratory of Pharmaceutical Technology, University of Gent |
| Address | Harelbekestraat 72,<br>9000 Gent, Belgium |
| Contact | Prof. Dr. Jean Paul Remon |
| eMail | JeanPaul.Remon@UGent.be |

**Greenwich, UK**

| | |
|---|---|
| Institution | University of Greenwich, School of Science |
| Address | Medway Campus,<br>Central Avenue,<br>Chatham Maritime,<br>Kent ME4 4TB, UK |
| Contact | Dr. Dennis Douroumis |
| eMail | D.Douroumis@greenwich.ac.uk |

**Leuven, Belgium**

| | |
|---|---|
| Institution | Laboratory for Pharmacotechnology and Biopharmacy, University of Leuven |
| Address | Campus Gasthuisberg O+N2;<br>Herestraat 49 b921<br>3000 Leuven, Belgium |
| Contact | Prof. Dr. G. Van den Mooter |
| eMail | guy.vandenmooter@pharm.kuleuven.be |

**Lille, France**

| | |
|---|---|
| Institution | College of Pharmacy, Université Lille Nord de France |
| Address | 3, rue du Professeur Laguesse<br>59006 Lille, France |
| Contact | Prof Jürgen Siepmann |
| eMail | juergen.siepmann(at)univ-lille2.fr |

**Milan, Italy**

| | |
|---|---|
| Institution | Dipartimento di Scienze Farmaceutiche "P. Pratesi", Universita Degli Studi di Milano |
| Address | via G. Colombo 71<br>20133 Milan, Italy |
| Contact | Dr. Matteo Cerea |
| eMail | matteo.cerea@unimi.it |

**Norwich, UK**

| | |
|---|---|
| Institution | School of Pharmacy, University of East Anglia |
| Address | Norwich Research Park<br>Norwich<br>Norfolk NR4 7TJ, UK |
| Contact | Dr Sheng Qi |
| eMail | Sheng.Qi@uea.ac.uk |

## RECENTLY PUBLISHED LITERATURE REVIEWS IN THE FIELD OF DRUG DELIVERY

**Passive lung-targeted drug delivery systems via intravenous administration**.
Wei Y, Zhao L. Pharm Dev Technol. 2013 Jan 22.

**A review of hot-melt extrusion: process technology to pharmaceutical products.**
Maniruzzaman M, Boateng JS, Snowden MJ, Douroumis D. ISRN Pharm.2012

**Epithelial cell adhesion molecule-targeted drug delivery for cancer therapy**
Simon M, Stefan N, Plückthun A, Zangemeister-Wittke U . Expert Opin Drug Deliv. 2013 Jan 14.

**Improving the prediction of drug disposition in the brain**
Lanevskij K, Japertas P, Didziapetris R. Expert Opin Drug Metab Toxicol. 2013 Jan 8.

**Niosomes as a propitious carrier for topical drug delivery**
Hamishehkar H, Rahimpour Y, Kouhsoltani M. Expert Opin Drug Deliv. 2013 Feb;10(2):261-72

**Recent Patents and Advances on Anti-Tuberculosis Drug Delivery and Formulations**
Vora C, Patadia R, Mittal K, Mashru R.. Recent Pat Drug Deliv Formul. 2012 Dec 13.

**Oral delivery of anticancer drugs I: general considerations**
Mazzaferro S, Bouchemal K, Ponchel G. Drug Discov Today. 2013 Jan;18(1-2):25-34

**Impact of the emulsification-diffusion method on the development of pharmaceutical nanoparticles**
Quintanar-Guerrero D, Zambrano-Zaragoza Mde L, Gutierrez-Cortez E, Mendoza-Munoz N.; Recent Pat Drug Deliv Formul. 2012 Dec;6(3):184-94

**Development of a platform of antibody-presenting liposomes**
Garnier B, Tan S, Gounou C, Brisson AR, Laroche-Traineau J, Jacobin-Valat MJ, Clofent-Sanchez G. Biointerphases. 2012 Dec;7(1-4):11

**Stimuli-responsive polymers and their applications in nanomedicine.**
Cabane E, Zhang X, Langowska K, Palivan CG, Meier W. Biointerphases. 2012 Dec;7(1-4):9

**The oral delivery of peptides and proteins: established versus recently patented approaches.**
Rosenmayr-Templeton L. Pharmaceutical Patent Analyst. 2013 Jan 2(1):125

## ABOUT THE FOCUS GROUP

BACK TO TABLE OF CONTENTS

**The APV Drug Delivery Focus Group (APV DD) is a section of the APV (Arbeitsgemeinschaft für Pharmazeutische Verfahrenstechnik e.V. / International Association for Pharmaceutical Technology), a major European society for those sharing a professional interest in pharmaceutical sciences. The Focus Group was established in 2003 in response to the increasing importance of drug delivery within modern pharmaceutics.**

***Read more.*** ***Contact us.***

### COMBINING SCIENCE AND TECHNOLOGY TO CREATE ADVANCED DRUG DELIVERY SYSTEMS

### OUR MISSION STATEMENT:

Modern drug delivery research and development is a truly multidisciplinary approach and must combine all relevant scientific, technical, medical and regulatory aspects required for the design, preparation, testing, manufacturing and registration of drug delivery systems and their components. It is the mission of the APV Drug Delivery Working Group to foster and promote all aspects of research and development required to transform drug molecules into safe, applicable and acceptable drug delivery systems, which provide therapeutic benefit, convenience to the patient and improve patient compliance.

**Our mission includes in particular the following tasks:**

- Thoroughly understanding the physical-chemical and biopharmaceutical properties of the drug substance to be delivered and the components of the drug delivery system
- Understanding the biological barriers and the interactions of the drug molecule and its delivery system with the biological environment and the biological target including PK/PD and PK/safety relationships
- Research on excipients, materials and technologies required for the design, preparation and manufacturing of drug delivery systems for a selected route of administration
- Development and understanding of methods for in vitro and in vivo evaluation of drug delivery systems and their components
- Knowledge of regulatory requirements for clinical testing, manufacturing and registration of drug delivery systems

**All disciplines relevant to the above mentioned areas of drug delivery R&D are invited to contribute to the APV Drug Delivery Group:**

Pharmaceutics, Biopharmaceutics, Analytics, Biology, Physical Chemistry, Biochemistry, Physics, Engineering Sciences, Nano Technology, Material Sciences, Polymer Science, Toxicology, Drug Safety, Clinical Research, Drug Regulatory Affairs, etc.

### MEMBERS OF THE APV DRUG DELIVERY FOCUS GROUP

**Karsten Cremer, PhD**
*Focus Group Chairman*
Pharma Concepts GmbH, Basel (CH)

**Georg Böck, PhD**
*Deputy Focus Group Chairman*
Boehringer Ingelheim Pharma GmbH & Co. KG
Biberach/Riß (D)

**Achim Göpferich, PhD**
*APV Liaison Officer*
University of Regensburg (D)

**Johannes Bartholomäus, PhD**
Pharmakreativ Consulting, Aachen (D)

**Karsten Mäder, PhD**
Martin Luther University, Halle/Saale (D)

**Oskar M. Kalb, PhD**
F. Hoffmann-La Roche AG, Basel (CH)

**Stefan Bracht, PhD**
Bayer Pharma AG, Berlin (D)

**Bianca Brögmann, PhD**
Evonik Industries, Darmstadt (D)

**Jeffry L. Grunkemeyer, MBA**
Patheon UK Ltd., Basel Area (CH)

**Michael Horstmann, PhD**
tesa SE, Hamburg (D)

**Gerben Moolhuizen, MBA**
OctoPlus B.V., Leiden (NL)

**Thorsten Schmeller, PhD**
BASF SE, Limburgerhof (D)

**Carsten Timpe, PhD**
F. Hoffmann-La Roche AG, Basel (CH)

**Bernd-Ulrich Riebesehl, PhD**
Novartis Pharma AG, Basel (CH)

**Louise Rosenmayr-Templeton, PhD**
Tower Pharma Consulting, Vienna (A)

**Jürgen Zirkel, PhD**
Lipoid GmbH, Ludwigshafen (D)

**Lea Ann Dailey, PhD**
Kings College, London (UK)

***Contact us!***

### EDITORIAL GROUP OF THE NEWSLETTER

**Editor:** Dr. Louise Rosenmayr-Templeton, Tower Pharma Consulting, Vienna, Austria
**Compilation/Layout:** Christoph Blümer, Catalent Pharma Solutions, Schorndorf, Germany