Nanopharm
an Aptar pharma company

SPRING 2023

WELCOME!

Welcome to our new-look newsletter covering all the latest exciting developments here at Nanopharm.

Spring is synonymous with new growth, and it feels appropriate that we are launching this newsletter at a time when Nanopharm's R&D and analytical services are being extended through a series of important developments.

Preparations are continuing ahead of the opening of our new cGMP-compliant analytical facilities, which are scheduled for launch in July. As part of this move, we will be integrating the market-leading expertise from our sister company, NextBreath, into an expanded Nanopharm offering.

This is a major development for our customers, enhancing our range of services from developmental, early-stage analysis and CMC support through to submission into regulatory dossiers and cGMP clinical and commercial batch release. For our customers, it means a smoother transition, whatever stage you are at in the development cycle and whatever services you require.

All of these services will be available under the single roof of our state-of-the-art new facility here in Cwmbran, Wales, which opened its doors for the first time in Q2 2022. With vastly expanded capacity and capabilities, we offer a highly robust and highly advanced platform for the successful development of orally inhaled and nasal drug products (OINDPs).

We also continue to recruit new people, adding ever more depth to the R&D and analytical talent within our team. After all, it is our investment in people as well as our investment in technology that provide the springboard for customer success and growth.

Thank you for reading this newsletter and please get in touch if you would like to discuss any of the points raised in this issue.

Gemma Budd
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RESPIRATORY UPDATE

Clinical end-point studies can be problematic on many levels, from time and cost to predictability of results. But what if there was a smarter alternative?

With Nanopharm, there is. SmartTrack™ is the result of our pioneering work to open the alternative bioequivalence regulatory pathway for U.S. FDA approval of generic orally inhaled and nasal drug products (OINDPs). It employs a combination of in vitro and in silico models to help pharmaceutical companies to file Abbreviated New Drug Application (ANDA) dossiers and support 505(b)(2) filings.

In August 2022, the SmartTrack™ offering was strengthened through an exclusive collaboration with long-term partner Fluidda, a leader in the field of Functional Respiratory Imaging (FRI). Fluidda's in silico platform, when combined with in vitro data and physiologically-based pharamacokinetic (PBPK) modelling from Nanopharm, generates critical information on the activity of a drug at the site of action in the lungs.

Our complementary technologies combine to deliver far more value than the sum of their parts, providing pharma customers with clinically relevant scientific evidence of bioequivalence using only in vitro and in silico methodologies.

NASAL UPDATE

Interest in intranasal drug delivery has continued to intensify in recent years, with pharma companies focused on turning the benefits of this highly effective, patient-friendly pathway into commercial opportunities.

At Nanopharm, we have continued to expand our expertise in this area, helping guide molecules on the most efficient route to regulatory approval. For both dry powders and liquids, we are experienced in optimising formulation and device in unison to target delivery to the nasal cavity.

Having previously provided support for development and pre-clinical trials, we are now able to directly support our customers all the way through to early Phase 1/2 clinical trials thanks to our position within the Aptar Pharma family and the services available from our CDMO partners, accelerating and derisking the next step of your development by allowing you to rely on Nanopharm to supply and release your clinical materials.

This offering employs the following device platforms from Aptar Pharma: Unidose (UDS), which delivers a reliably precise single dose of a formulation in liquid or powder form, and Bidose (BDS), which delivers a dual-shot of a liquid formulation via nasal spray.

Partners benefit from extensive expertise in the development and handling of both small molecules and biologics, including cGMP manufacturing of intranasal clinical trial materials, commercially-representative device filling and assembly, and process validation for technology transfer to CMO.

Contact us today to discuss how Nanopharm can provide end-to-end support for your nasal drug product on the pathway to regulatory approval.

TEAM PROFILE: *Irene Rossi*

Irene, how did you start your journey?

I started my adventure in inhalation and nasal drug delivery back in 2013 as an undergraduate at the University of Parma, with my thesis focussing on particle engineering, especially for antibiotics. Interestingly, the first powder I developed back then, I have now revisited having recently tested it in a device over 10 years later!

Following my undergraduate studies, for the next two years I worked in a fellowship programme at the University specialising in nebulisers and particle engineering. This was my first exposure to the commercial world as contracts were undertaken by the University and research centre for a range of different pharma companies.

I found I loved the nasal and inhalation field in particular, and so in 2015, I started my PhD focussing on pulmonary vaccination. Using my background in particle engineering and formulation development, I turned my attention to large molecules such as proteins. In collaboration with the in-house biotech group, together we were able to deliver a novel HPV antigen as a dry powder inhaler. Also, during that time, I spent six months in the US where I began to work with cells and bacteria. This was also the first time I had experience of working with in-vivo animal pre-clinical studies.

What does your current role and responsibilities look like at Nanopharm?

In 2019 I joined Nanopharm starting as a senior scientist in pharmaceutical development, moving then to a lab supervisor role before being promoted to a principal scientist. Today, I work on the formulation development of biologics and new chemical entities as well as the repurposing of molecules from other drug delivery forms into respiratory or nasal devices.

What do you see as the key strengths of the Nanopharm offer?

Firstly, this is a great place to work! I see the way we work as one of our key strengths – we aren't like a typical CRO or CDMO with a straight through process irrespective of the nuances of the project.

Secondly, we are all scientists which makes us very curious by nature and drives us to bring as much value as we can to our client's projects.

Finally, we don't just deliver great quality data, we impart science and share our insight to offer another perspective. Our focus is on driving collaboration and embedding understanding in specific device performance, while at the same time advancing the knowledge in our industry as a whole.

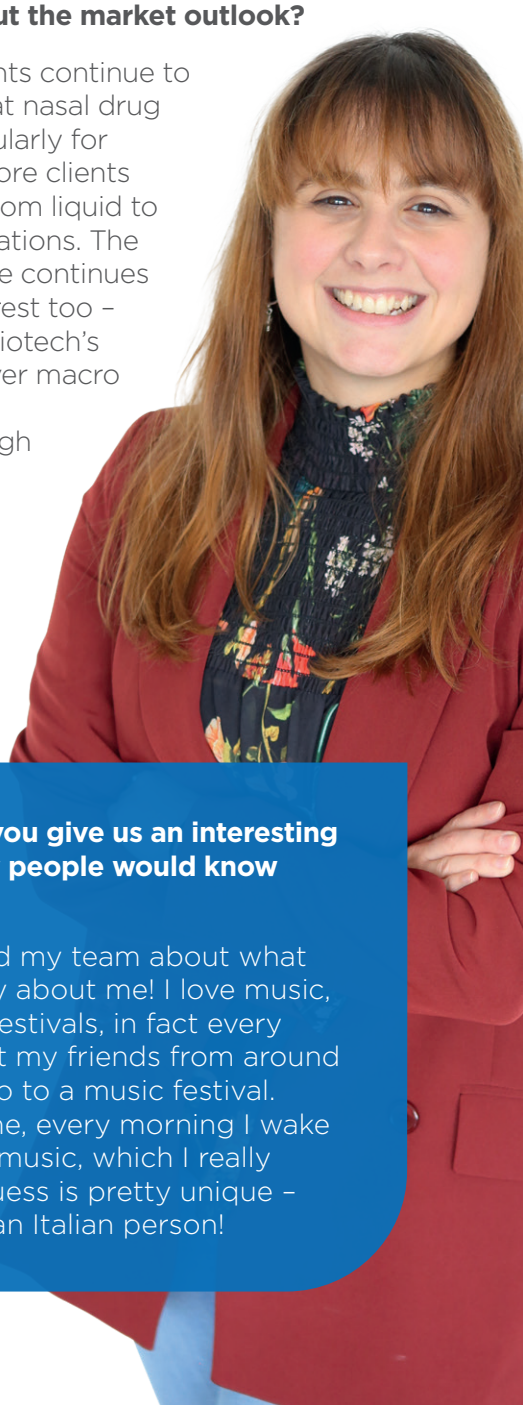
As we enter the second half of 2023, what are your priorities for the rest of the year?

To continue our collective understanding of biologics as well as my personal understanding of large molecules. Post pandemic, more customers are exploring nasal as a viable route for the delivery of macro molecules, an area where we have delivered huge amounts of work in the past two years – and a bit of a departure for the industry.

We are also focussing on testing and generics development, as well as looking at NCE's and the innovative ways in which we can deliver perhaps DPIs to better treat patients.

And what about the market outlook?

Our global clients continue to ask us to look at nasal drug delivery, particularly for biologics, as more clients look to move from liquid to powder formulations. The inhalation space continues to grow in interest too – especially for biotech's looking to deliver macro molecules and biologics through nebulisation and perhaps then a further transition to DPIs in the future.



Finally, could you give us an interesting fact only a few people would know about you?

I actually asked my team about what they would say about me! I love music, concerts and festivals, in fact every summer I meet my friends from around the world to go to a music festival. Confession time, every morning I wake up to country music, which I really love and is I guess is pretty unique – especially for an Italian person!

PBPK MODELS FOR OINDPS

Physiologically-based Pharmacokinetic (PBPK) models are an incredibly valuable tool in the development of orally inhaled and nasal drug products (OINDPs). In the first of a series of articles exploring their importance, Dr. Will Ganley, Nanopharm's Head of Computational Pharmaceutics, goes back to basics with an explanation of what is meant by a PBPK model.

A PBPK model is a mathematical description of drug transportation from the point of entry into the body to excretion.

Conventional pharmacokinetic (PK) models are often empirical in nature and are fitted to clinical data, reducing their predictive capabilities. What we do in PBPK modelling is use differential equations to mechanistically describe the organs, tissues, and other physiological features associated with the ADME (absorption, distribution, metabolism and excretion) processes associated with PK investigations. The result, the PBPK model, is a multi-layered system of differential equations.

PBPK modelling is therefore a 'bottom-up' approach. The starting point is the modelling of each individual process that transports the drug through the body. From these building blocks, we work up towards a complete model that ties together data from multiple sources, from different in vitro tests, for example, or clinical trials. The endpoint is observed clinical outcomes, which are used to validate the model.

By constructing a model that weights input data in a physiologically meaningful way we can produce a solution that reliably predicts clinical outcomes; a credible PBPK model."

Read Will's full article **here**.

Head of Computational Pharmaceutics

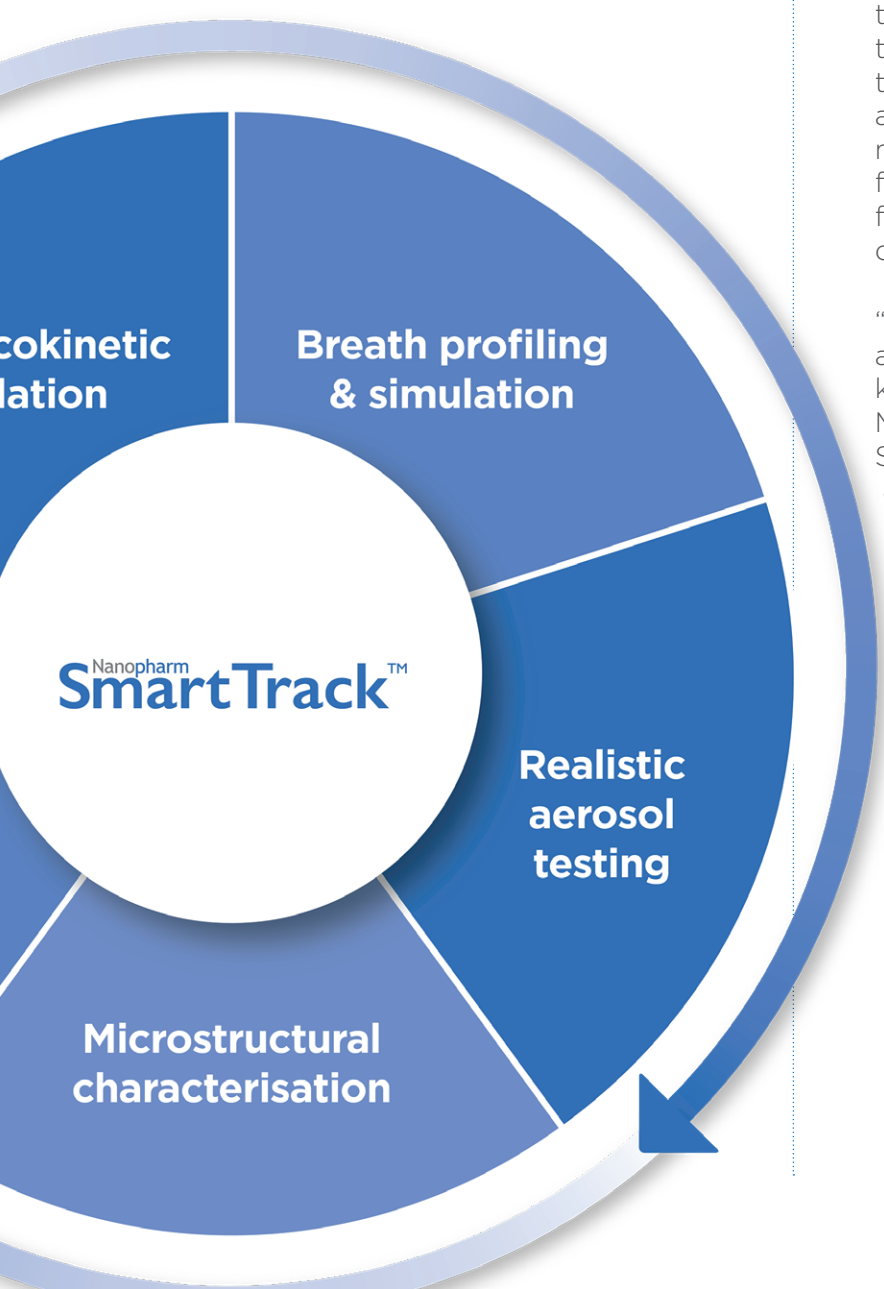
Dr. Will Ganley

> "A PBPK model is a mathematical description of drug transportation from the point of entry into the body to excretion."

A HOLISTIC DEMONSTRATION OF SMARTTRACK™ AND NEW WAYS OF COLLABORATING COMBINE FOR A SUCCESSFUL FDA WORKSHOP

Dr. Jag Shur, Vice President, Science & Technology at Nanopharm, and Dr. Will Ganley, Head of Computational Pharmaceutics, recently discussed SmartTrack™ and Nanopharm's extended capabilities in support of alternative bioequivalence at a workshop which was held jointly between the FDA and the Center for Research on Complex Generics (CRCG) at the University of Maryland, Baltimore and the University of Michigan.

Jag Shur's presentation focused on realistic in vitro tools. Our partner Jan De Backer from FLUIDDA spoke on their in silico CFD models for studying regional deposition in patient-specific models.



Will Ganley, whose presentation on how in silico patient-specific PBPK models form part of a platform as an alternative to CCEP BE studies for inhaled generics, said this about the event itself: "The event was unique in that of the 85 in-person attendees a large proportion of them were from the FDA. This allowed us to have conversations and ask questions during the sessions and over lunch or coffee, which I had never experienced before. The workshop opened with a statement that only 4/33 of currently approved inhaled medicines in the US have approved generics which was motivating."

Will said, "The talks covered a wide range of topics from the shortcomings of current bioequivalence approaches to novel or alternative in silico, in vitro and in vivo studies that could help us better demonstrate bioequivalence for orally inhaled products. There was a lot of healthy discussion, especially during the small group discussions and panel sessions. There were a lot of differences of opinion on the best way to bring the industry's expertise together to solve this problem, but it was clear that the basic research is mainly done. We have already established the tools we need to make this happen. The final challenge is figuring out how to bring them all together for each of the remaining products that don't have approved generics."

"Overall, the event was excellent. We covered a lot of ground, and the attendees were keen to share experience and opinions. My perspective has shifted on a few things. Still, I am confident that Nanopharm's approach of bringing relevant in vitro studies and in silico methods together ticks all the boxes."

More information about the event can still be found **here**.

Vice President,
Science & Technology

Dr. Jag Shur

Head of Computational
Pharmaceutics

Dr. Will Ganley

EVENTS

RDD EUROPE 2023, MAY 2-5

The Nanopharm team is attending RDD Europe 2023 in Antibes, France. We are on the podium, hosting a workshop, and presenting a number of posters.

Dr. Will Ganley (Podium Presentation)

Alternative Bioequivalence Approaches: Combining In Vitro and In Silico Models to Demonstrate BE of Orally Inhaled Drug Products.

Lucas Silva (Workshop)

Accelerating and De-Risking the Development of Low Global Warming Potential (GWP) pMDIs.

Dr. Will Ganley (Poster)

Using a Physiologically Based Pharmacokinetic (PBPK) Model to Investigate the Relationship Between Device, Orientation, Deposition Pattern and the Systemic Exposure of Sumatriptan Nasal Solutions.

Dr. Irene Rossi and Antonia Zapata (Poster)

Assessment of the Realistic Performance of Orbital™ Device Loaded with Model Fluticasone Proprionate Blends Manufactured by Low Shear and Isothermal Dry Particle Coating.

Dr. Irene Rossi (Poster)

Formulation Technologies Assessment for the Development of Intranasal Powders Comprising a Peptide.

More information about RDD Europe 2023 can be found here.

NOVEL NASAL FORMULATION & DELIVERY SUMMIT, MAY 16-18

Gemma Budd will speak at the forthcoming Summit in San Diego, California, US.

ATS 2023, May 19-24

The Nanopharm team will be co-presenting a poster with Fluidda at this event in Washington, US.

Dr. Irene Rossi

In-silico/In-Vitro Assessment of Deposition Patterns of Two Dry Powder Inhalers in Cystic Fibrosis and Healthy Subjects.

COMING UP...

8th Pulmonary Drug Delivery Workshop, May 31-June 2
Istanbul, Turkey

IPI Academy, June 6
Virtual

Rescon Summit Europe, June 20-21
Porto, Portugal

24th ISAM, August 26-30
Saarbrücken, Germany

Drug Delivery Summit Europe, September 6-7
Berlin, Germany

Inhalation Drug Delivery Forum, September 14-15
Philadelphia, US

American Association of Pharmaceutical Scientists (AAPS) PharmaSci 360, October 22-25
Orlando, US

CPhI Worldwide, October 24-26
Barcelona, Spain

SPOTLIGHT ON NEW FACILITY

It is one year since Nanopharm's relocation to its state-of-the-art facility in Cwmbran, Wales. The 25,000 sq. ft. facility, four times the size of its previous location, spans three floors and has been completely redesigned.

Building on the company's heritage and belief that fundamental materials science drives behavior in aerosol science, the addition of new characterization and analytical capabilities, as well as increased capacity, has enabled our scientists to provide specialist services, benefit from in-house evaluation and facilitate the customers' desire to get to the clinic quickly, yet safely.

Within the facility, you will now find:

- State-of-the-art research and development (R&D) and cGMP-compliant analytical laboratories (scheduled to open July 2023)
- Expanded in-house particle engineering capabilities
- One-of-a-kind spray dryer with world-class flexibility and scalability to multiple commercial platforms
- Potent suite giving Nanopharm the ability to handle OEB (Occupational Exposure Band) Class 5 compounds, BSL (Biosafety Level) Class 2 biological materials and a license to handle Schedule 1-5 controlled substances.

Moreover, our team has access to a range of new micronization techniques to enable unique formulation approaches for sensitive molecules, including biologics, and the manufacture of complex suspensions and powders, including nanoparticles for both inhaled and nasal products.

Aside from the contract development and analytical services, the new facility also provides ample R&D space for our team to develop the next generation of services and technologies to continue its work at the forefront of the industry. Flexible laboratories that can house equipment on a short-term basis, including customer-owned assets, where appropriate, give Nanopharm the flexibility to use the best tools for the project.