

Hello!

Welcome to our latest issue of the High Force Research Bulletin!

It's been a busy couple of months for High Force Research with the launch of a new website, new research and new services. This issue we're taking a closer look at some of our products and services as well as updating you on all our latest news.

I hope you enjoy reading our latest issue of the HFR Bulletin and I look forward to speaking and meeting with you soon, whether at one of our three sites around the UK or one of the many events HFR will be attending in the coming months.

If I can be of any assistance or if you would like to find out more about High Force Research and our work, please do not hesitate to get in touch.

Stella

Dr Stella James

stellajames@highforceresearch.com

+ 44(0)191 377 9098



Dates for your Diary

- 18th - 20th September - Chem Outsourcing, New Jersey
- 3rd - 4th October - Elrig, Liverpool
- 8th - 19th October - 7th Annual Orphan Drugs and Rare Diseases Conference, London
- 24th - 26th October - CPhI Worldwide, Frankfurt

- 31st October - Findacure Rare Disease Showcase, Newcastle
- 6 - 8th November - BIO-Europe, Berlin
- 30th November - Bionow Awards Dinner, Cheshire
- 14th December - Genesis, London



Rare Disease Showcase to visit Newcastle sponsored by HFR!

On the 31st October, Newcastle's Centre for Life will host the Rare Disease Showcase, a day-long event aimed at celebrating and highlighting the rare disease projects and research being undertaken in the city and across the North East of England.

Organised by the charity Findacure and part-sponsored by HFR, the event aims to provide a friendly forum for patient groups, researchers, clinicians and life science professionals to come together to encourage collaborations within the rare disease community and improve the future of rare disease science and healthcare.

The event will:

- Provide a forum to share rare disease projects taking place in Newcastle and the North East
- Showcase Newcastle as a European hub for rare disease research
- Feature talks highlighting progress in rare bone disorders, neuromuscular disorders and rare skin cancer
- Include an afternoon networking session with lightning talks proposed by delegates
- Allow networking between all major rare disease stakeholders

With our 30 year heritage of providing development and scale up services to the pharmaceutical industry and increasing focus on orphan drug manufacture for the treatment of rare diseases, we're delighted to be supporting Findacure as sponsors of the Newcastle event.

The charity works to promote collaboration between patients, clinicians, the pharmaceutical industry, medical professionals, and other interest groups,

to facilitate treatment development and drug repurposing for rare diseases.

In particular, Findacure believes that patient groups have a fundamental role to play in addressing patient needs and representing the patient voice in research. It actively works to empower patients with rare diseases to form patient groups and develop as a charity, so as to help drive treatment development.

To find out more about the charity and its work, please visit <http://www.findacure.org.uk/>

Tickets for the Newcastle Rare Disease Showcase can be purchased at www.findacure.org.uk/newcastle-rare-showcase and early bird tickets are on sale until Monday 11th September. If you're unable to attend but would like to find out more, do keep your eyes peeled for our next newsletter and on our website for updates on the event and a roundup of the day's discussions.

High Force Research will be attending the Rare Disease Showcase and we're keen to meet with any contacts who may be there on the day. If you would be interested in arranging a meeting at the event, please contact stellajames@highforceresearch.com



HFR launches new services

Over the last year, we've been busy working away on launching a number of new services, including:

- **Diagnostics:** Using our 'traceable manufacture' process (see overleaf), the principles of which are firmly based on GMP manufacture, High Force Research is able to assist in the development of reagents for Life Science research, point-of-care testing devices and high-throughput analysers for hospitals and commercial diagnostics laboratories
- **Imaging:** We have extensive expertise in the synthesis and development of fluorescent molecules for use as cell-specific imaging agents. In addition, working in collaboration with Durham University we have developed a range of novel fluorescent retinoids based on the natural retinoid ATRA (All-Trans Retinoic Acid). Our retinoid derivatives are stable and also intrinsically fluorescent. They can function as both a biologically active retinoid and at the same time act as a visual probe. Imaging applications for the use of these novel compounds in cell biology range from visualisation and localisation to monitoring real-time concentration and local environments
- **Orphan drug manufacture:** Building on our track-record of offering development and scale-up services for the pharmaceutical industry, High Force Research is ideally placed to provide orphan drug manufacture for the treatment of rare diseases. Our facilities include two segregated ISO Class 8 laboratories in which multi-stage synthesis to cGMP standards is carried out. Each facility operates at a 30 litre scale, typically enabling production in batches of up to multi kilo quantities

The above services are already proving a big hit. If you'd like to find out more about any of High Force Research's products or discuss our work in more detail, please contact stellajames@highforceresearch.com

HFR Chemist Celebrates PhD Success!

High Force Research team member David Chisholm, is celebrating completing his Biological Chemistry PhD from Durham University.

David has spent the last four years studying synthetic retinoids and their potential uses for treating Alzheimer's and Parkinson's disease. His postgraduate research, undertaken with Ph.D. supervisor Professor Andrew Whiting from Durham University's School of Chemistry, was sponsored by High Force Research.

David, who recently joined the High Force Research team will continue his post-doctoral research, which is being co-funded by the Biotechnology and Biological Sciences Research Council (BBSRC) and High Force Research from his new base at High Force Research's Wilton Centre laboratory in Teesside.

It is part of a new two year project, funded by the BBRSC and led by a team

of scientists at the University of Aberdeen in conjunction with Durham University and High Force Research, that is researching a synthetic version of retinoic acid usually created from vitamin A that interacts with the body's natural receptors in the brain in an even more powerful way than regular retinoic acid. It is hoped the research will contribute towards the development of therapeutics – primarily for Alzheimer's but potentially Parkinson's disease and other neurodegenerative diseases.

Commenting on the news, David said: "I'm very pleased to have completed my PhD and that all the hard work paid off in the end. It has been a great experience and I have particularly enjoyed being able to collaborate with scientists from different disciplines and institutions. I am now looking forward to carrying on the project at the Wilton Centre with High Force Research."



Caption: High Force Research Wilton Centre team member, David Chisholm

High Force Research's Dr Neil Sim said: "We're delighted that David has completed his PhD – it's testament to his skill as a chemist and the outstanding work he has been undertaking on the joint synthetic retinoid research project with Durham University and the University of Aberdeen. David recently joined our Wilton Centre team and we're looking forward to observing how his research progresses in the coming months."



High Force Research's Roy Valentine has joined forces with scientists from Durham University, Newcastle University and Helwan University on latest research paper.

Regular readers of our newsletter may remember that in our last issue, we mentioned High Force Research had hit the headlines over Christmas, thanks to a new research project.

The work, which is being led by a team of scientists at the University of Aberdeen in conjunction with Durham University and High Force Research, is exploring a synthetic version of retinoic acid usually created from vitamin A – a vitamin most commonly found in a number of vegetables, including carrots and sprout – which it is hoped may be used to treat neurological disorders. The synthetic design interacts with the body's natural receptors in a more powerful way than its

regular counterparts, benefitting the brain and central nervous system.

More recently, High Force Research's Roy Valentine has joined forces with Durham University's Professor Andrew Whiting, Dr David Chisholm, and Dr Ehmke Pohl, Newcastle University's Dr Christopher Redfern, and Helwan University's Dr Hesham Hafez, to publish a research paper entitled 'The molecular basis of the interactions between synthetic retinoic acid analogues and the retinoic acid receptors'.

The study arose from the need for a deeper understanding of receptor and ligand flexibility, and conformational freedom, with a view to aid the development of more stable and effective ATRA analogues for clinical use.

The team used molecular modelling techniques to define retinoic acid receptor interactions with the natural all-trans-retinoic acid (ATRA), and two synthetic analogues. They compared their predicted biochemical activities to experimental measurements of relative ligand affinity and recruitment of coactivator proteins.

The findings were then used to inform docking studies of the synthetic retinoids.

Synthetic analogue, EC23, was found to be an excellent mimic for ATRA and was observed to have a higher binding affinity, due to an increased rigidity and linear structure. This synthetic analogue was also seen to be more potent than its natural ligand counterpart, even in lower concentrations. In addition, the research concluded that the biological activity of natural and synthetic retinoids depends on the different retinoic acid receptor types, cell-type variation, and the expression of coactivators which may determine the role of different receptor types in driving particular biological responses.

It is hoped that the research will provide improved design qualities not only in new synthetic retinoids, but also more widely in the drug industry, through a deeper understanding of the molecular interactions that create strong binding with receptors.

For more information or to receive a copy of the research paper, please contact stellajames@highforceresearch.com

Shining a light on new research

Product Focus: Traceable Manufacture

In our upcoming issues, we're going to be taking a closer look at some of High Force Research's services. In this issue we're taking a look at High Force Research's Traceable Manufacture.

What is Traceable Manufacture?

Traceable Manufacture is defined by HFR as a bespoke quality standard based in principle on GMP manufacture. Traceable manufacture allows clients to tailor their own quality standard using HFR's GMP procedures to control only high-risk processes. This approach allows HFR to provide clients with cost effective manufacture without any compromise to quality

What is involved?

Typically we work with clients to construct a bespoke technical agreement that is fit for purpose for the product's end use within the appropriate industry sector.

Traceability from raw materials through manufacture, analysis and delivery is at the core of this quality standard. Other systems may be altered, for example:

- Facilities: Synthesis will be carried out in an isolated laboratory or a segregated area of HFR's laboratories instead of a clean room

- Batch Records: Batch record information is recorded on a defined production record designed to provide batch traceability. Savings are often made by reducing the requirement for non-essential witness controls. Equipment cleaning controls may be conducted by visual checks made by the project chemist to reduce costs further
- Equipment: Contact equipment used can be logged for use if required or project dedicated contact equipment can be assigned, should the client prefer this. There is an option of using general laboratory glassware if no controls are required
- Analysis: Selected key raw materials will be identified/analysed by QC prior to use, not all raw materials. Intermediates and product/s will be analysed by QC. Retention samples will be kept
- Documentation: Risk assessment, deviation and out of specification investigations are not typically documented for traceable manufacture campaigns. All other documentation such as analytical methods, master production records, change notification controls and CAPA reports are generally reported

All material is accompanied by a certificate of conformity, a certificate of analysis and a TSE statement (if required). Documentation will be completed and shared in real-time with the customer to allow traceability of each batch of material.

What sort of projects is Traceable Manufacture suited to?

Traceable manufacture is ideal for new or established products that require high quality, cost effective, small scale manufacture.

Do you have examples of previous work?

High Force Research has worked with numerous clients on Traceable Manufacture projects, such as the manufacture of API starting materials; API for pre-clinical proof of concept studies or toxicology; medical devices; materials used for clinical diagnostics; monomers used for high performance polymers; and Organic electronics (OLEDs).

How can I find out more?

If you would like to find out more or believe High Force Research's Traceable Manufacture process may be relevant to a project you are aware of, please contact Dr Stella James at stellajames@highforcerearch.com

HFR STEM Co-ordinator leading the way in schools outreach!

High Force Research's STEM Co-ordinator, Iain Lawson, had a busy few months during the summer term visiting local schools and colleges to help encourage pupils to consider careers in STEM.

Iain has visited a number of schools and colleges across the region. The visits have focused on a wide variety of topics - from speaking to AS Level students at Bede Sixth Form College about how you take a drug from 'bench to market', through to demonstrating chemistry in action in everyday life to pupils at Wallsend St Peter's Church of England Primary School!

Speaking about the visits, Iain said: "It's great to be able to visit so many of our local schools and colleges and I always find the visits so rewarding. There are so many different roles and specialisms for young people to consider, but often career routes within the industry aren't obvious and young people are surrounded by so many negative perceptions of science.

"I always try to make the visits as fun and informative as possible as I really believe that Science should be fun. After all it's messy and lots of things go bang! But best of all you get to spend your time discovering things.

"We've had a lot of interest in HFR's STEM outreach visits and

we're keen to reach out to as many schools as possible during the new school year."

If you work at or know of a school or college that may be interested in arranging a visit over the next term, please contact Iain on info@highforcerearch.com



Caption: High Force Research STEM Co-ordinator Iain Lawson speaking to AS Level students about taking a drug from 'bench to market'

HFR Employee Treads the Boards Once Again in Bishop Auckland's Kynren

High Force Research employee James Masters has once again been treading the boards in Bishop Auckland's Kynren production – the UK's most spectacular open-air live show.

After completing a Chemistry for Europe degree at Surrey University (involving a year's industrial placement in Paris), and getting married, southern-born James moved up north with his wife, and has now been working at our Bowburn laboratory for 16 years.

After starting in the lab, James moved through various roles including Good Manufacturing Practice and Quality Control before taking on his current position as Project Co-Ordinator in which he oversees the dispatching of material for HFR's main client accounts.

Outside of work, James (with his wife and two children!), has once again been involved in Bishop Auckland's epic Kynren production. The production involves 1,500 volunteers (aged 5-80 years old) making up the cast, tech team, pyrotechnics, costume department and 'experience team'. The show is headed up by renowned live event director, Steve Boyd who has contributed to 13 consecutive Summer and Winter Olympic ceremonies spanning Barcelona '92 to Rio 2016.

We caught up with James to find out how he got involved, how he fits it into his busy schedule and whether or not he would do it again...

How did you get involved in Kynren?

I heard about the production when I was volunteering as a room steward at Auckland Castle and was immediately intrigued so looked into it further. In the end myself, my wife and two children got involved! We were part of the first production last year and volunteer this year too.

Did you have any previous experience of acting or theatre?

No, not really! Only through school, and Primary School at that!

As one of 1,500 volunteers, what's your role in the show?

My role is always changing, everyone's role is mixed and matched. We're put into teams and each have at least four roles, so I've been Joseph of Aramathea, a Roman Centurion, English soldier, Georgian harvester and a miner to name a few. I fight with a sword, shoot flaming arrows and walk on water! Luckily there is no speaking – everything is done to a soundtrack which makes it a bit easier.



Caption: James as Joseph of Arimathea – © Eleven Arches

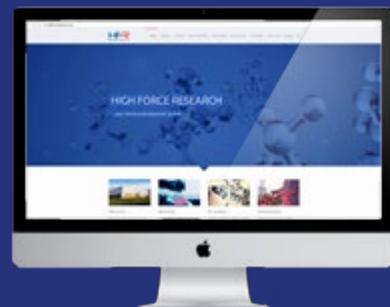
How often did you have to rehearse for the show?

We started rehearsals before Easter, and they were full on – to start with they're around 4 nights per week, with rehearsals going on till 10pm but then nearer to the live shows we start rehearsing at weekends as well.

Would you do it again?

I would definitely do it again – every year! I'm considering acting more too, I'm looking to get involved in a play with my local church – a passion play – which we're hoping will be repeated yearly.

New HFR website launched



Those observant readers among you may have spotted that the High Force Research website has recently undergone a bit of a transformation!

Please do let us know what you think of the new site – we would really like to hear your thoughts - and don't forget to keep an eye on our News & Events page to find out more about the events that High Force Research will be attending in coming months.

Fluorescent Retinoids Sample Test Kits

Special sample test kits containing three Fluorescent Retinoid derivatives produced by High Force Research and Durham University are being offered free to research institutions.

If you would like to receive a free Fluorescent Retinoid sample kit, please contact Dr Stella James at stellajames@highforcerearch.com



High Force Research Limited,

Bowburn North Industrial Estate, Bowburn, Durham, DH6 5PF, UK

www.highforcerearch.com Tel: +44 (0)191 377 9098 Fax: +44 (0)191 377 9099

Registered in England No. 02248615