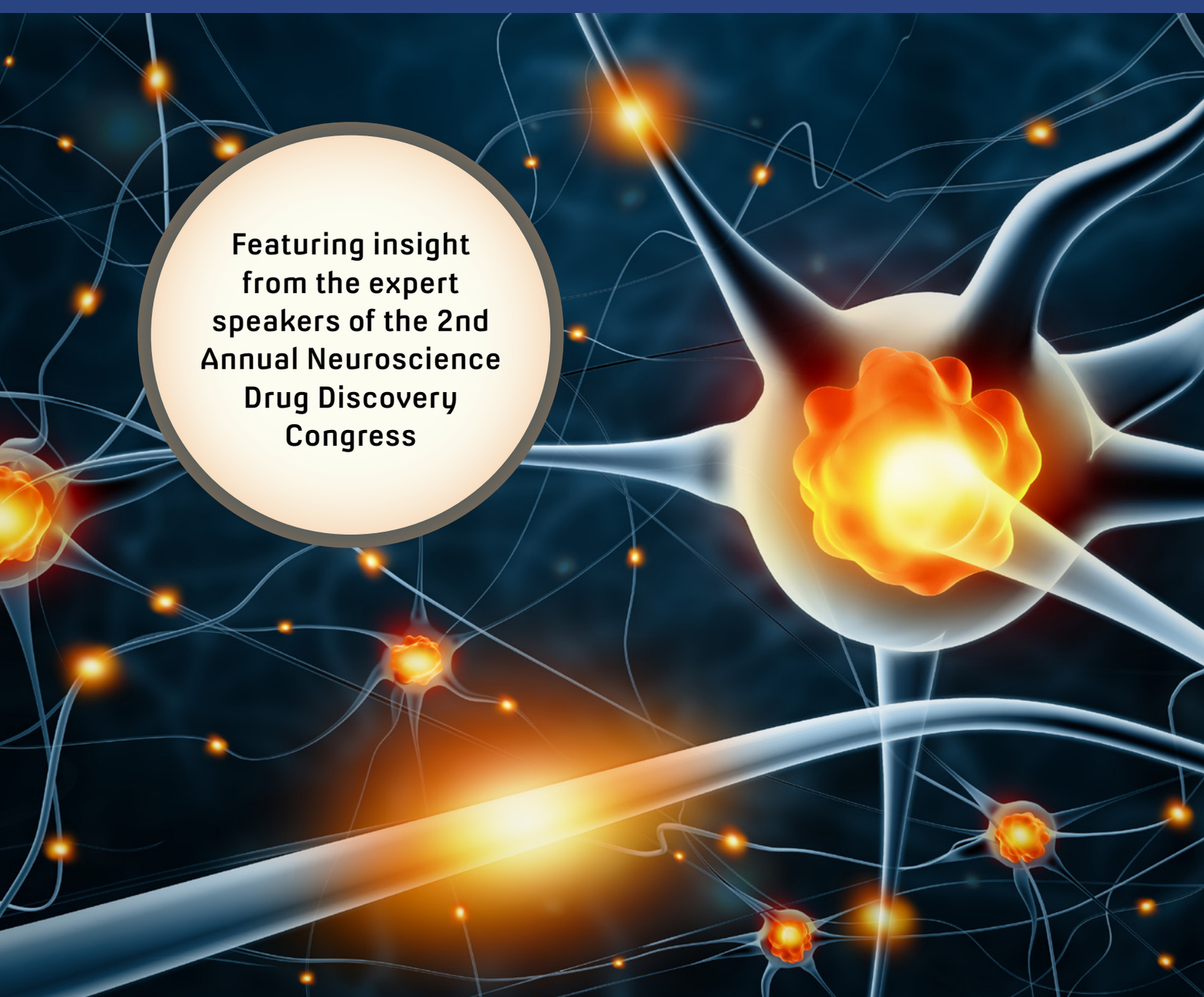
NEUROSCIENCE DRUG DISCOVERY

Newsletter March 2020



Featuring insight from the expert speakers of the 2nd Annual Neuroscience Drug Discovery Congress

2nd Annual Neuroscience Drug Discovery Congress
Part of the R&D Series 2020

OXFORD GLOBAL CONFERENCES

WELCOME TO THE NEUROSCIENCE DRUG DISCOVERY NEWSLETTER!

Oxford Global is proud to present our 2nd Annual Neuroscience Drug Discovery Congress, taking place in Berlin, Germany later this year 11 - 12 August. Ahead of the event, I am delighted to share with you an overview of the key features of the congress, as well as exclusive content from our industry-leading speakers.

The 2019 event saw over 315 delegates gather across the R&D Series EU to discuss the latest developments and critical approaches in drug discovery, alongside cutting-edge enabling tools and technologies for attaining advances in efficiency and pipeline productivity. With the launch of our event app providing attendees with instant agenda updates and our brand-new Innovation Showcase stream, inspiring industry growth and collaboration is at the core of our 2020 event.

This year's congress promises to be our most insightful and valuable congress yet, with a host of key leaders from global pharmaceutical organisations and pioneering academic research organisations presenting on the latest innovations in drug discovery and validation of novel targets. Our teams have worked incredibly hard over the past year to craft an event which addresses the foremost industry priorities in this field, inspiring positive steps forward in collaboration and partnership and highlighting essential solutions to the challenges in target discovery for Neurology, Oncology and Autoimmune Diseases. With over 100 unmissable presentations, the two-day R&D Series EU 2020 offers an intuitive platform for high level scientific and business discussions, ensuring valuable networking and interactive sessions with over 400 senior level delegates.

Driven by current industry focus, our Neuroscience Drug Discovery congress encompasses presentations on emerging trends and technological breakthroughs in drug discovery for Alzheimer's, Parkinson's, Huntington's and Schizophrenia. Experience high quality presentations on recent advancements in stem cell technologies to fuel drug discovery and on iPS cells in disease modelling. After a packed day of presentations, join us to unwind at our ever-popular networking drinks. On Day 2, we aim to emphasise the importance of targeted therapeutics and neuroimaging technologies in neurodegenerative disease, examining both the opportunities and challenges faced in the implementation of these strategies. Finally, our esteemed speakers will also present on the crucial roles of biomarker development for neurodegenerative disease and gene therapy in CNS drug discovery, leading on to translational approaches in neuroscience.

This newsletter provides a sneak peek into the exciting content that you can expect to see at the event. Enjoy thought-provoking interviews, in-depth speaker spotlights and industry analyses from our speakers.

We look forward to welcoming you to our series very soon!

- Chris Davies, COO and Portfolio Director of R&D Series

Neuroscience Drug Discovery Congress

Driven by an increased understanding of CNS disease biology and the emergence of new mechanisms and targets, pharma and biotech companies are striving to develop effective strategies for neurodegenerative drug discovery. Our 2nd Annual Neuroscience Drug Discovery Congress addresses the foremost industry priorities in this field, encompassing the emerging trends and technological breakthroughs in drug discovery for Alzheimer's, Parkinson's, Huntington's and Schizophrenia.

Building on the success of our inaugural event, the 2020 congress focuses on the latest developments and critical approaches in neuroscience discovery, with high quality presentations on recent advancements in stem cell technologies to fuel drug discovery and on iPS cells in disease modelling. On Day 2, we aim to emphasise the importance of targeted therapeutics and neuroimaging technologies in neurodegenerative disease, examining both the opportunities and challenges faced in the implementation of these strategies. Finally, our esteemed speakers will also present on the crucial roles of biomarker development for neurodegenerative disease and gene therapy in CNS drug discovery, leading on to translational approaches in neuroscience.

DAY ONE:	DAY TWO:
Strategies and Enabling Technologies	Neuroscience Translation To The Clinic

5 Reasons to Add to Your Calendar Now

11-12 AUG

1. **Current Industry Trends:** Hear case studies on industry priorities and recent advancements in the neurodegenerative drug discovery field.
2. **A Focus on Interactivity & Networking:** Interactive sessions on Imaging Enabling Technologies and Biomarker Development promote learning and knowledge-sharing among attendees.
3. **Promoting Collaboration & Partnerships:** Our R&D Innovation Showcase is designed to facilitate creation of new partnerships to enable collaborative solutions in neuroscience and drug discovery.
4. **Hear from Industry Leaders:** Engage with leading influencers from key companies in this space, including Executive Directors and Heads from Takeda, Novartis & Servier.
5. **Part of our R&D Series EU:** Experience three complementary events, where the co-located nature of the series encourages delegates to move between and interact with all streams.

Speaker Insight

STEM CELLS IN NEUROSCIENCE DISCOVERY

ROBERT MAYS

Robert Mays,
Vice President, Regenerative Medicine and Neuroscience Programme, Athersys

Dr. Mays is the Head of Neurosciences and Vice President of Regenerative Medicine at Athersys, Inc. He is focused on the company's novel adult human stem cell product, MultiStem®, and its applications in Regenerative Medicine and drug discovery, with a specific focus on injuries and diseases affecting the central nervous system. Dr. Mays was the Principal Investigator of the MASTERS (MultiStem Administration for Stroke Treatment and Enhanced Recovery Study) clinical trial assessing the safety and efficacy of MultiStem in treatment of ischemic stroke. He is also the Principal Investigator of the pivotal Phase III MASTERS-2 study, which has received RMAT, Fast Track and Special Protocol Assessment designations from the FDA. Dr. Mays is a member of the National Center for Regenerative Medicine, Center for Stem Cell and Regenerative Medicine, the American Heart Association and is an Adjunct Professor at the Case Western Reserve University School of Medicine. He has authored or co-authored >30 peer reviewed scientific papers or reviews and is the inventor of more than 10 patents relating to the use of stem cells for treating disease. Dr. Mays is on the Commercialization Committee and Co-chair of the Neuroscience Committee for the International Society for Cellular Therapy, and previously the Board of Directors for the United Cerebral Palsy Foundation of Cleveland and the scientific advisory board for the Children's Neurobiological Solutions Network in Los Angeles. He graduated from Carnegie Mellon in 1987 with a B.S. in Cell and Developmental Biology. In 1994, he received his Ph.D. in Molecular and Cellular Physiology at Stanford University. After doing Post-doctoral research at the University of Utrecht in the Netherlands, the Weizmann Institute in Rehovot, Israel and the University of California, San Francisco, Dr. Mays co-founded Athersys Inc., which focuses on developing novel and proprietary best-in-class therapies designed to extend and enhance the quality of human life.

What is your current focus within neuroscience drug discovery?

At Athersys, Inc., we have spent the last 15 years doing translationally relevant pre-clinical research, in vivo and in vitro, with our proprietary adult adherent cell product called MultiStem®. We have been focused on understanding the molecular mechanisms of action through which MultiStem administration improves outcomes across multiple animal models of CNS injury and disease.

Based on the data and information we obtained across multiple acute injury models of CNS injury (ischemic stroke, traumatic brain injury, spinal cord injury, hypoxic ischemic injury) as well as additional data derived from animal models of chronic neurological diseases (multiple sclerosis, ALS, Parkinson's Disease) we have moved in Phase 2 and Phase 3 clinical studies in ischemic stroke, with other clinical programs ready to initiate.

What are the advantages of utilising stem cells in neuroscience discovery? What are your main challenges in this area that you are working to overcome?

There are multiple advantages to using stem cells/cellular products to treat injury and disease when compared to single small molecule agents. Cells are dynamic therapies, with the ability to respond to different inflammatory/injury cues in different ways, depending on where and when you place them into the organism following initiation of the insult. Small molecule drugs and antibodies work through modulating one targeted pathway or physiological target. Cells can work through multiple mechanisms simultaneously.

Describe the main priorities for the neuroscience industry in stem cell research over the next year.

Many researchers believe that cellular therapeutics must be delivered directly into the CNS for the cells to provide meaningful benefit. The industry needs to understand the importance of the peripheral immune system and its involvement in exacerbating pathology of the CNS, and how cellular therapies can contribute to modulating this pathophysiology.

What keeps the life sciences industry so optimistic when it comes to drug approvals in neuroscience?

Recent advancements in understanding the initiators of disease and inflammation in many CNS disease models have provided optimism for new therapies. IPSC derived brain and tissue organoids and the development of CRISPR mediated gene editing has opened the door to more rapidly address many neuroscience related pathophysiology.

What is the biggest recent neuroscience discovery advancement that has affected your work?

Patient derived IPSC research. Allowing researchers the ability to take cells from patients with known diseases, and then recapitulate tissues and organs and look for dysfunction has been a huge step forward for neuroscience research ■

Speaker Insight

FUNCTIONAL MAGNETIC RESONANCE IMAGING WITHIN R&D

PRADEEP NATHAN

Pradeep Nathan, Vice President Clinical Development & Head of Experimental Medicine (Neuroscience), Sosei Heptares

Prof. Pradeep Nathan is Vice President and Head, CNS Clinical Development and Experimental Medicine at Sosei Heptares, a Japanese listed biotech with its core R&D activities based in Cambridge, United Kingdom. He is also Professor of Neuroscience at Monash University and an affiliated lecturer at the University of Cambridge. Pradeep trained as a pharmacologist and cognitive neuroscientist. His research focuses on the understanding of the neural substrates of cognition and psychiatric and neurological endophenotypes using behavioural and imaging methods and applying these approaches to drug discovery through development of molecular and functional biomarkers which might aid in the development of more refined and targeted treatment approaches for cognitive and emotional dysfunction in psychiatric and neurological disorders.

What are the main advantages of using functional imaging and drug development?

The main advantage is knowing which area in the brain the drug is having an effect and to determine if the drug is acting on brain circuits of interest to the drug (commonly called functional target engagement). The second advantage is that functional imaging could help compare pharmacodynamic effects of the drug in development with comparator drugs or standard of care to show that the drug has stronger effects. Finally, functional imaging may help determine if brain responses to the drug after a single dose or a few days of dosing could predict long term efficacy. This is however very challenging to show but if this can be demonstrated reliably, shorter and less expensive studies could be done in Phase 2 to make go/no-go decisions.

Are there different technologies, other than functional imaging? Is functional imaging different from functional magnetic resonance imaging?

Functional magnetic resonance imaging is sometimes called functional imaging. It is called "functional" because it measures brain activity (via changes in blood flow) usually when a person is doing a task (i.e. memory test or looking at pictures). As the person is doing the task, areas in the brain that are required to do the task become activated and there is increased blood flow to these areas which are detected with functional magnetic resonance imaging.

Are there any key challenges that you face?

One key challenge is knowing if the changes in brain activation you see are real (i.e. signal) and not noise. Knowing what is a real signal vs random noise can come down to how good your methods are and how big the study is. Larger studies that are statistically powered and methodologically sound would increase signal relative to noise. The second challenge is making sure that the task used in functional imaging studies (for example the memory test) shows good reproducibility in brain activation from week to week. A good task with high test-rest reliability is ideal for imaging studies.

Are there any key technological innovations that have helped with this?

Higher resolution scanners have been developed. MRI scanners have improved over the years from 1.5T to 7T and this has improved the resolution (i.e. you are able to image smaller areas more accurately). This will allow us to find small changes in brain activity in brain areas including areas that have relatively small (i.e. subregions of the amygdala for example). Technological advances have also been made in data acquisition and data analysis which has helped improve the quality of the data.

What are the next steps for your company in this work?

Sosei Heptares is a rapidly growing biopharmaceutical company. Our strategy is to develop new medicines by ourselves as well as in partnership with larger pharmaceutical companies. Our strength and expertise is our structure based drug discovery platform which uses an innovative way to stabilize drug receptor/targets (i.e. G-protein coupled receptors), image their structure and then make drugs that perfectly bind to the receptor in the way we want. This approach has attracted interest from a number of top pharmaceutical companies and we are collaborating with many of them to develop new drugs acting on novel receptors.

What are the top three takeaways from your presentation?

Functional imaging can be used quite effectively early in clinical development and be used in decision making. It can help determine if the drug modulates target systems in the brain. It could potentially be useful for comparing one drug to another to determine if the drug in development is superior to the current standard of care treatment. Finally, it may be used to potentially predict treatment response (i.e. work out which patient responds better to drug). However more work is needed to validate functional imaging as a biomarker in drug development, particularly around improving the reliability of the measurements and improving data analysis methods.

What do you hope to gain from attending this kind of conference?

The scientific program had some very good presentations on topics that were relevant to my area of interest. This made attending the conference worthwhile even though I was an invited speaker for the meeting. I met a number of people doing similar work and this has opened opportunities for collaborations. I thought the networking session useful in this regard.

Were there any specific areas that you are interested in, and would like to see again next year?

I think one or more sessions on digital technologies would have been nice to see given the increasing use of such technologies in clinical trials. It would be nice to see clinical trial data presented on this. I would also like to see more on patient stratification biomarkers in clinical trials for various indications including blood, CSF or brain imaging biomarkers ■

EARLY INTERVENTION WITHIN NEUROPSYCHIATRY

MORITZ VON HEIMENDAHL

Moritz Von Heimendahl,
Principle Scientist,
Boehringer Ingelheim Pharma GmbH & Co. KG

Moritz von Heimendahl trained in physics and did PhD and PostDoc work on neuronal coding in rats, using in vivo electrophysiology. In 2014, he joined the CNS discovery research department of Boehringer Ingelheim as a laboratory head, and has since worked on early drug discovery projects on the treatment of psychiatric symptoms. He has also led, since its inception two years ago, a working group that aims to identify novel targets for treatment of cognitive symptoms by investigating circuit dysfunctions underlying cognitive symptoms and back-translating these into preclinical research.

What is your company's translational approach in neuropsychiatry?

We follow several approaches. One can classify them into two major ideas. One is to say we haven't been particularly successful in pharma, in terms of treating the false syndromes. This may be because they are so heterogeneous that it's hard to identify the underlying neurobiology and for all approaches to focus on symptoms. This is an approach which has been promoted by the publication of our DOC research of the main criteria from the National Institute of Mental Health. The idea is not to treat depression, but rather to focus on anhedonia, for instance, as one of the constitute symptoms of depression, and try and understand the neurobiology underlying that. Only then would we move onto the treatment; particularly the brain circuitry that is dysregulated in anhedonia and trying to fix that pharmacologically. Most patients will not just have this one symptom, but several and then you can have a precision medicine approach where you treat the symptoms with polypharmacy. That is one approach. The hope is that that would allow you to have a precision medicine approach in the clinic. In terms of translation, it is probably much more realistic to generate an animal model off a motivational deficit, meaning anhedonia, but we'll never have a depressed mouse. It's essentially an approach that will make translation better, and eventually lead to more successful treatments. This is the approach which we call circuit symptoms - focus on the symptoms and try to identify the circuits that underlie them. We recently also became interested in early intervention, particularly schizophrenia - viewing it as a neurodevelopmental disorder and trying to identify teenagers who are on the road to schizophrenia, which is not to say we don't also treat chronically-ill adults, but we also try to catch the symptoms early.

Are there any technological innovations that have furthered your ability for early intervention?

There are neurodevelopmental models, but I don't think they're particularly new or really technology-driven. It's more obvious for the circuit symptom story, where we have the progress in neuroimaging in humans, which has helped to begin to understand which circuits are impaired in patients. Then we have techniques and rodents, which allow you to either monitor or influence circuits. What is also very helpful in this is the recent development of translational tasks. In particular, tasks that don't just look translational but have a good construct validity. Even if an animal doesn't do something that looks the same as what humans do, a lot of work has gone into really making sure that the process going on in the animal is comparable, like a specific cognitive process.

What are the models that you use for target identification and validation?

In the circuit symptom approach, there are circuit models. It's a loop; we start with a patient and we try to understand which circuit is wrong in the patient. For example, we know that in schizophrenic patients we've got a deficit in the excitation inhibition balance. It's a micro circuit between a pyramidal neuron and an inhibitory neuron. The balance between the two is off, and there's an impairment in the subtype of interneurons, which are the Parvalbumin-expressing interneurons. This has been described in patients and postmortem studies. We take this and translate it back into rodents. Using optogenetics, we impair the Parvalbumin interneurons in mice. We hope to observe deficits, both in terms of behaviour and physiology that resemble what's observed in the patient. If we see the deficit, then that tells us this circuit is relevant. In terms of target identification, one could just start looking for targets right in that circuit, so in this case, targets in Parvalbumin interneurons. Once you've established such a model with a circuit impairment, that's manifested in both the behavioral and physiological consequence, then, of course, you can try and reverse these deficits, and that would give us high confidence that this will be translated into benefits in humans.

What are the main challenges in the translational approach that you take, and what translational challenges have you overcome?

The main challenge is that it's the brain and it is incredibly complex. It's a no brainer to say, but I think one hurdle is that you find a circuit in humans, and then you're going to find the same circuit in rodents. It's not always obvious or even possible, because the brain is different. So many structures are evolutionarily conserved, but others are not. In particular, the most interesting ones like in the prefrontal cortex, it gets difficult to pinpoint, e.g. the medial orbital frontal cortex, what is that exactly in a mouse? In terms of the behavioral tests, you can't ask the mice how they feel. You always have to get your answer in a very indirect way. There's always the risk of measuring something but not what you think you're measuring.

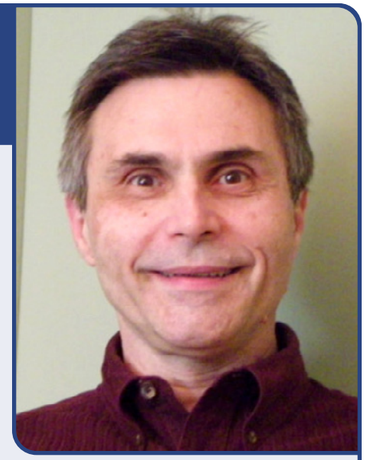
What are the top three takeaways that you hope the delegates will take from your presentation?

This general approach of saying, we want to treat specific symptoms rather than the syndromes. That is one important message. As I previously said, I don't think this is an idea our company invented. This is an idea that is out there. We believe in this approach and we'd like to promote it. I think an important message is also for the animal models. Animal models have been criticized a lot and an important message is if you can't have an animal model of a disease, you can still have an animal model of a more restricted deficit and that then still makes sense. We have to keep justifying why we use animal experiments and that is a very clear and concrete way to justify this ■

THE FUTURE OF BLOOD BIOMARKERS

THOMAS MISKO

Thomas Misko,
Lead Scientist & Senior Scientific Director, Translational Neuroscience,
Abbvie Neuroscience Development



Thomas Misko has had over 25 years of experience in pharmaceutical R&D. His expertise includes both small molecules and biologics and spans from early Discovery to Phase 2 POC. After receiving his Bachelor of Science degree in Biological Sciences from Indiana University, he received his doctorate in Biochemistry from Johns Hopkins University. As a postdoctoral fellow (Stanford) in the laboratory of Dr. Eric Shooter, he purified and cloned the low affinity NGFR (p75). Joining Searle-Monsanto (St. Louis), he contributed to/led several projects to discover/develop potential therapeutics for Inflammation and Neuroinflammation. During his tenure in St. Louis (Pharmacia, Pfizer), Tom co-discovered the activation of cyclooxygenase by NO and led a group that developed sensitive assays to monitor iNOS (inducible nitric oxide synthase) activity in vivo and in vitro by quantifying nitrites/nitrates as well as nitrated proteins. These assays were instrumental in the discovery and clinical development of selective inhibitors for iNOS through enabling the monitoring of target engagement in the clinic. Tom's collaborations with academia (e.g., Drs. Anne Cross, David Holtzman, L.S. Lohmander) helped to characterize the role of iNOS in diseases such as MS, AD and arthritis (RA, OA) in which free radical-mediated injury appears to contribute to disease pathology. His work in neuroscience, inflammation and neuroinflammation has resulted in over 60 peer-reviewed publications. As a Scientific Director in Translational Medicine at Takeda, Tom led teams monitoring biomarkers in CSF and in plasma to assess target engagement and coverage for potential disease-modifying and symptomatic therapies in schizophrenia, epilepsy and AD. Dr. Misko is currently a Senior Scientific Director in Translational Neuroscience at AbbVie where he has devoted his efforts to advancing AbbVie's growing portfolio in Neurology focused on disease-modifying therapeutics and neurorestorative therapies in MS, AD, Stroke and PD.

Could you tell us more about your use of blood biomarkers?

They fall into a couple of categories. One is looking at neurodegeneration markers like neurofilament light in plasma, because the reason for looking at plasma and serum is that you can take more time points, you can define a patient's trajectory much more easily than trying to get CSF. Patients often don't even want to give you one CSF, let alone two. The other approach is using and developing exosomal cargoes to monitor the disease, which basically translates into cells that are alive that will secrete small membrane vessels that have either good proteins or bad proteins in them. You can monitor the disease state by measuring them, isolating them, and measuring their cargoes in the periphery.

What would you say are the key benefits of using blood biomarkers?

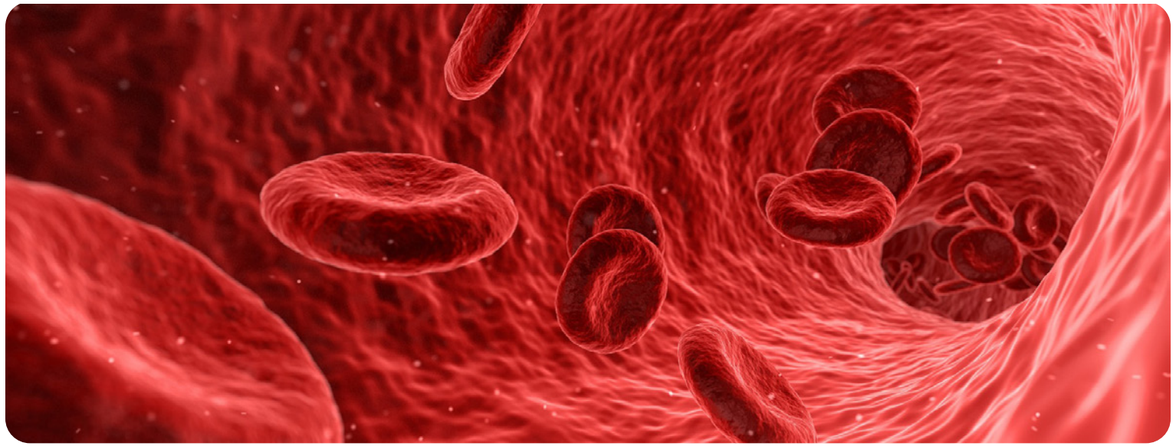
You're able to define an individual patient's trajectory, because everyone is at a different stage of disease – even though we'd like to try to place everyone into a certain phase, everyone progresses at different rates. If you have a treatment, you can better understand how that treatment's affecting that individual as opposed to trying to clump everyone together. You might not end up understanding the response very well, because you might have seven that responded, and three that didn't. The three that didn't balance out the seven that did, so you end up with nothing.

Am I correct in saying that you're in the clinical stage in some of your work?

As a translational neuroscientist, what I do is I bridge between discovery and clinical, and I am in the clinical group. The objective is to identify biomarkers where you can monitor targets in the clinic. Either you've defined that you've now engaged the target by changing something that the target drives or like with things like NFL or neurofilament light, ensure that you're getting disease modification.

What are the main challenges that you face in the biomarker development?

It's getting clinically well-characterized samples. There are a few companies that can deliver them, like Precision Medicine in San Diego. Being able to get longitudinal samples is not always that easy. There are some companies that can get those for you. However, once again, you might not have some of the cognitive readouts from the individual patient, they might go to the patient at home like Sanguine does. If you don't know what their cognitive status is, it's a little hard to understand how the biomarker changes that you're looking at relate to their cognitive deficit.



How are recent innovations and new technologies benefiting the identification of biomarkers?

The availability of the digital ELISAs for proteins and immunoassays have been fantastic. Being able to measure different micro-RNAs and RNA species in the blood and cells. That's become more easily done than it used to be in the past. We're at a stage where, after 30 years of many failures, even though there was great science, we still haven't found anything for Alzheimer's; we're at the point where we are going to shoot up quickly, and we'll be able to identify treatments more easily.

Would you say that's the next steps for your company's work in this field?

It's to gain acceptance for different markers and that's really building the data set. That's the other challenge - you can't use certain markers as decision making markers. You have to build enough data to know that it really works and it's not just an aberration or a very small group of the population. That's where collecting the data, and being able to analyze it, is so important.

Are you partnering with any other companies to further the development of blood biomarkers?

Not at this point. I work with some people at Quanterix that do the digital ELISA. We're looking into some other approaches. I've talked to Abcam, and I'm interested in some of their approaches, but we're not closely linked with anyone at this point.

What are the top three takeaways from your presentation?

That plasma markers are real, that you can monitor CNS by looking at them. That each patient should be looked at as an individual case instead of looking at the bucket and saying they all need to cluster together, which they're not going to do ■

Speaker Insight

FRAGMENT-BASED DRUG DISCOVERY IN NEUROSCIENCE

MARKUS SCHADE

Markus Schade, Scientific Director, Grünenthal GmbH

Dr Markus Schade has worked for over 18 years in the pharmaceutical industry. He started his career as a co-founder of the biotech company Combinature Biopharm AG. Next Markus worked for the global Pharma-CRO Evotec AG before he joined the BigPharma companies Pfizer and thereafter AstraZeneca in the UK. Since 2012 Markus does pre-clinical drug discovery with the pain specialist Grunenthal GmbH in Germany. He has specialized in the field of Fragment-based Drug Discovery (FBDD), where he has successfully led many projects and published several peer-reviewed articles and patents. Markus studied biochemistry at the University of Hannover, Germany, and the Massachusetts Institute of Technology, USA, and holds a Ph.D. in structural biology from the Free University Berlin, Germany. Presently he holds the position of a scientific director at Grunenthal.

What are the main advantages of fragment-based drug discovery in neuroscience?

The main advantage is it delivers low molecule-weight starting points for chemistry. That's a requirement for CNS exposure. With other technologies, the average molecular weight will already be at, or exceeding, what is allowed to passively permeate the blood-brain barrier.

Could you explain a bit more about your work with fragment-based drug discovery?

We apply FBDD in parallel to other small molecule discovery technologies and are virtually always successful in identifying novel starting points for synthetic chemistry, even for tough drug targets, such as protein-protein-interactions. That's a strong plus to begin with. If crystallography is enabled as well fragments can often be merged with chemical series from other sources to quickly arrive at novel and potent interventions.

What are the challenges that you face coming up with clinical molecules?

It includes getting sufficient exposure in the CNS, which can vary between rodent disease models and human patients. Often you can't predict, and there is some literature hypothesis on "leaky" blood-brain-barrier in rodent models, meaning that CNS exposure in such rodents could be substantially elevated as compared with human patients. Insufficient exposure in humans leads to insufficient efficacy, and a failed clinical trial. You're never entirely sure with regards to what is the reason for failure; insufficient exposure to the target tissue might be one, but of course, it could also be the mechanism of action not working in your patient group.

Have there been any recent innovations or technologies that have helped you to overcome or solve these challenges?

What is new in the industry, and quite interesting, is antisense-RNA and gene therapy, and you can intrathecally administer those. In the old days, daily or even weekly intrathecal administration wasn't really accepted and didn't sell very well, because it was hard on the patients. Nowadays, with those long duration of action RNA therapies, you only have to dose every two or three months, promising a much better patient compliance. You basically have a new window that opens up, and interventions for historically intractable CNS diseases can be designed.

What are the key priorities of the industry in this area?

We are specialized for moderate to severe pain medications. There, it is promising to focus on targets and mechanisms where we have robust human genetic validation data, rather than merely efficacy in rodents, which has often led to clinical failure. Human genetic data, especially from pain patients, provide us with a head start, where you're much closer to getting validation for analgesic efficacy but also some preliminary evidence for the safety in those patients.

Does that relate to the next steps of your company in this field?

We are investigating, among others, exactly those targets and trying to enrich our portfolio with the most promising new analgesics.

What would you say are the top three takeaways that you would hope delegates will take from your presentation?

Begin with a patient genetically-validated target. Use the smartest technologies, such as fragment-based discovery for small molecules, or siRNA or antibodies, or gene therapy interventions. Finally, try to go for druggable, feasible targets, don't embark on blue sky,hope and pray interventions; that's usually not giving a good return on your hard work and investment.

What do you hope to see in the future of fragment-based drug discovery in neuroscience?

The whole workflow could be a bit more automated. It could do with more integrated cheminformatic tools, better databases that will speed up and facilitate testing analogous chemicals, as well as smartly learning from prior art. Cryo-EM of CNS targets will certainly have a positive impact, too.

Would you like to see more talks on automation and new tools in neuroscience?

The cheminformatics field does get some good coverage, and machine learning and artificial intelligence is everywhere on the front pages; it just has to be intelligently implemented, and tools need to be user friendly for non-IT experts. But yes, every new tool is most welcomed and may help developing new medicines for the patients in need ■