The SMR award 2016 and the December 2016 meeting

The 2016 SMR Award for Drug Discovery was awarded to the Bristol-Myers Squibb team responsible for OPDIVO® (nivolumab), a fully human anti-programmed death receptor-1 (PD-1) antibody approved to treat several cancers. Immunotherapies, such as nivolumab, are now widely recognized as a transformational opportunity that provides the potential for long-term survival for a meaningful proportion of cancer patients.

The SMR Award was presented to Dr Francis Cuss, Executive Vice President & CSO R&D, Bristol-Myers Squibb by Dr Wendy Alderton, SMR Chair, on 1st December 2016 at the ‘Recent Disclosures of Clinical Candidates’ meeting in London.

Dr Cuss delivered a fascinating SMR Award Lecture honouring the contribution of many key scientists and the team that discovered, developed and delivered Opdivo to market. Opdivo first entered clinical testing in 2006 and quickly showed potential in metastatic melanoma and other tumour types such as renal and lung cancers. Just two years after its first FDA approval in 2014 as monotherapy for unresectable melanoma, Opdivo has now been approved in more than 55 markets around the world after thirteen positive registrational trials, five of which were stopped early due to superior survival. To date, Opdivo has been approved in the United States in ten indications across five tumour types.

Beyond the award lecture, an international array of speakers presented work covering a range of therapeutic areas leading to clinical candidates. These included “Identifying high quality, potent and selective inhibitors of ATM kinase for oncology therapies: Discovery of AZD0156” by Dr Barnard Barlaam, (AstraZeneca, UK) which outlined the invention of AZD0156, now in Ph1 clinical trials in combination with Olaparib. Following the kinase theme and the interest in DNA repair mechanisms Dr Thomas Fuchs, (Merck KGaA, Germany) gave an account of the identification of “Highly potent and selective DNA-PK inhibitor M3814 with sustainable anti-

This year, for the first time, the SMR Presented a 3D-printed SMR Award representing a monoclonal antibody structure.

Check out our references section for a range of drug discovery topics highlighted by your committee.

Future SMR meetings

Gene therapy: right here, right now
Thursday 9th March 2017, London, UK
Innovative partnerships for medicines research: how is the landscape evolving?
15th June 2017
Cambridge Building, Babraham Research Campus, Cambridge CB22 3AT
Emerging paradigms of Drug Discovery
Joint SMR-BPS meeting
5th Oct 2017
Charles Darwin House London
Joint SMR/RSC meeting
7th December 2017

Welcome to the fourth edition of the SMR Newsletter, keeping you up to date with the activities of the Society. This newsletter includes announcements of our upcoming meetings, a precis of the SMR Award meeting from December 2016 and our October 2016 meeting a round-up of our 2017 meetings schedule and our gallery of recent literature and life science related highlights as highlighted by the SMR committee. We hope that you will find the diversity of topics covered valuable in your own work and in your continuing professional development.

Don't forget to follow us on LinkedIn and Twitter with all contributions welcome. Please do forward this newsletter to your network and make your colleagues aware of our 2017 meetings.

WWW.SMR.ORG.UK
tumour activity in combination with radiotherapy". Continuing in oncology but moving away from kinases Dr. David Edwards, (Cancer Research UK) described the development of a novel IgE-based antibody therapy in his talk "A Different Class of Oncology Therapeutics: Development of MOv18 - a novel IgE-based Therapeutic Targeting Folate Receptor".

In a discussion of the "Discovery of the clinical candidate JNJ-53718678, a potent and orally bioavailable fusion inhibitor of Respiratory Syncytial Virus", Dr. Sandrine Vendeville (Janssen IDV J&J Belgium) gave an intriguing insight into the issues involved in developing a compound targeted at a paediatric setting as a primary indication.

Dr John Liddle (GSK, Stevenage UK) highlighted the GSK Discovery Partnerships with Academia (DPac) model for sharing the risk and reward of academic collaborations in drug discovery (in this case seeking an i.v. kynurenine monoxygenase inhibitor) in his presentation "Recent disclosure of a development candidate to treat severe acute pancreatitis through a drug discovery collaboration between GlaxoSmithKline and The University of Edinburgh".

In earlier clinical trials for cognition PF-04447943, a PDE9 inhibitor, was shown to be safe but ineffective despite demonstrated target engagement. Dr Nick Clarke, (Pfizer Rare Diseases Unit, London, UK) in his presentation "Out with the old proposed indication, bring in the new clinical compound for the potential treatment of sickle cell disease" discussed the approach that led the team to identifying Sickle Cell Disease as a possible alternative disease target for PF-04447943.

This meeting was sponsored by Biogen, Liverpool Chirochem and supported by the EFMC.

The Society AGM

The Society's AGM was held at the December meeting in the presence of 30 Society members. The appointments of Dr. Simon Ward to Vice Chair and Dr. Gregor McDonald to Development Officer were approved by the meeting. The following Officers or Committee members were re-elected for a further term: Dr. Kate Brown, Dr. Rod Porter, Dr. Richard Davenport (Treasurer) and Dr. Ruth Lock (Honorary Secretary). The following new Committee members were elected: Dr. Stephen Wren (Oxford University), Dr. Andy Sykes (AstraZeneca) and Dr. John Overington (Benevolent AI). There is currently one vacant committee position which will be filled during 2017.

Dr. Steve Collingwood is retiring from the Committee after this meeting. He was thanked for all his contributions to the running of the Society as Committee member, Honorary Secretary and Chair over the last 12 years. Rod Porter is returning to Committee from Development Officer although will continue to edit the newsletter

The Society has a stable operating balance commensurate with its charitable status and scientific and educational remit. However, it is important that whilst the Society continues to secure meeting sponsorship, increased meeting registrations and increased membership rates, it must maintain low operating costs. The support of our sponsors The European Federation for Medicinal Chemistry, Pharmidex Pharmaceutical Services Ltd, Transpharmation Ltd, Astex Pharmaceuticals, Charles River Laboratories, GlaxoSmithKline, Vertex Pharmaceuticals, Liverpool Chirochem and Biogen is gratefully acknowledged. Janssen, Belgium are especially thanked for their hospitality in hosting the June meeting.

Meetings for 2017

Registration is open for our first meeting of 2017 Gene therapy: right here, right now - 9th March 2017, Charles Darwin House, London, WC1N 2JU

Whilst the concept, application and enormous potential of gene therapy to repair the direct cause of genetically driven diseases ‘at source’ has tantalised and fascinated the scientific community over recent years, the development of suitable treatments using this technology has encountered many challenges. Only a few gene therapy trials have reported clear clinical benefits and in some, severe adverse events including lethality were observed. Overall, concern and scepticism rose over the further deployment of these strategies. However these attitudes are changing with the introduction of new delivery approaches and gene technologies. Several trials in inherited diseases as well as cancers have demonstrated evidence of efficacy and safety. Additional precision gene editing technologies, in particular CRISPR, are now nearing the clinic, further increasing the possibilities of altering the human genome to treat serious diseases.

This meeting brings together experts from academia and industry to discuss the promise, challenges and reality of gene therapy as a therapeutic approach. This promises to be an exciting and interesting meeting with in depth discussion of how the drug discovery and development community has approached gene therapy in the past, how this will evolve in the future to benefit patients and provide an excellent networking environment for everyone interested in this important and rapidly emerging research.

Our second meeting of 2017 Innovative partnerships for medicines research: how is the landscape evolving? will be held on 15th June and is hosted by MedImmune at the Babraham Research Campus, CB22 3AT

The full programme and registration will be available on line shortly. The meeting is a follow-on from our June 2013
meeting "Partnerships: Future Models for Drug Discovery" which attracted a large audience and generated a lot of lively discussion. We anticipate the same levels of interest for this meeting addressing a topic that affects everyone working in the current life sciences environment - so book early.

A new meeting for young scientists

Planning for our Autumn meeting "Emerging Paradigms in Drug Discovery" - October 5th 2017, is now well underway. It will be a joint meeting with the British Pharmacological Society and will be of a different format to our usual meetings. It is strongly targeted at third year undergraduate through to post doctoral students and to industry workers in their early careers. There will be three keynote speakers who will be supporting talks by student and early career industry speakers accompanied by a poster session. While the focus will be on early career scientists the committee are hoping that some more "experienced" colleagues will also participate, as this will be a great networking opportunity for these young scientists with those who already have significant experience in drug discovery. Not of course forgetting the high quality talks and posters that delegates will also be able to enjoy. The meeting will be held at Charles Darwin House, London WC1N 2JU.

Please do keep an eye open for more information about this exciting new meeting and do let interested colleagues know about it. Remember we are able to offer limited numbers of travel bursaries to students - for more details see the side panel elsewhere in this newsletter.

Planning for our final meeting of the year 7th December is in progress and will be a joint meeting with the Royal Society of Chemistry focused on medicinal chemistry.

Please keep an eye on the website and our LinkedIn and Twitter feds for announcements about it.

A new venue for SMR meetings

Having read this far you will have noticed that the SMR is using a new venue for some of its meetings this year - Charles Darwin House in London WC1N 2JU. It is conveniently located within walking short walk of Chancery Lane, Holborn, Russell Square and Farringdon underground stations and Kings Cross/St. Pancras mainline stations. The venue hosts numerous scientific meetings and has excellent facilities for networking and for poster sessions which will be a feature of our October meeting.

Previous meetings

The October 2016 meeting 'Rare Disease, Extraordinary Aspirations', held on 13th October, brought together experts from academia, industry and disease advocacy organization’s to present their experiences and thoughts on tackling rare diseases through case studies and opinion pieces. The keynote speech was given by Dr. Alastair Kent OBE from the Genetic Alliance, who discussed the 'The Contribution of Patients and Families to Rare Disease Research and Development'. The focus of Dr Kent’s presentation was the important role that patients and families with life-limiting and chronic conditions can play in influencing the priority-setting agenda for innovative research and how novel therapies are developed against rare diseases. Dr. Chris Penland, Cystic Fibrosis Foundation, gave his perspective how drug discovery and development can be progressed for an orphan disease like cystic fibrosis (CF) and approaches to address challenges that success in a small disease population can bring. Prof. Bobby Gaspar from University College London, presented on the application of gene therapy for the treatment of immunodeficiencies in children in his talk ' Lentiviral Gene Therapy For Monogenic Diseases Of The Bone Marrow: Current Progress And Future Prospects" . . Prof. Matt Seymour from the NIHR Cancer Research Network in his presentation 'IRCI - Setting up an International Rare Cancers Initiative to Promote Global Research in a Difficult Field' discussed the unmet needs and challenges associated with the clinical development of new therapies for rare cancers. ; and Prof. Pam Kearns from the University of Birmingham looked at some of the barriers particularly in pediatric therapy working in rare diseases with 'Overcoming the 'Rare Disease' Hurdle in Developing Drugs for Childhood Cancer'. by Dr. Stephen James, from Swedish Orphan Biovitrum AB; Sobi reviewed the company's portfolio of drug discovery and development projects spanning a wide range of therapeutic areas before focusing on their MPSIIIA project Dr. Christine Bulawa of Pfizer speaking on 'Familial Amyloid Polyneuropathy: How a Genetic Disease Informs Drug Discovery' recounted the importance of insights from genetic studies in combination with biophysical studies of transthyretin amyloidosis variants in contributing to the identification of the only oral small molecule therapy for amyloid disease. John Tinsley from Summit Therapeutics plc discussed their approach to Duchenne Muscular Dystrophy by modulators of utrophin production focusing on Ezutromid (SMTC-1100). The SMR is grateful for the sponsorship of Vertex, GlaxoSmithKline, Charles River Laboratories and Pharmidex and the support of the EFMC.

Published meeting reports

The full meeting report of our October meeting has now published -
Drugs Fut. 2016, 41(11): 703

The meeting report for the December meeting will appear in the next few weeks.
As usual, meeting reports will be placed on the SMR website approximately 6 months after first publication.

**Published meeting reports on the SMR website**


These are now available on the SMR website.

**Meeting attendance**

Average attendance at meetings during 2016 (70) was down on 2015 (78) but was better than 2014 (65). Clearly increasing attendance at meetings remains a key area for the Society and the committee again urges all members to publicise meetings within their networks, Twitter, Linked-In and Facebook.

![Average attendance per meeting 2006 - 2016](image)

**Membership**

Membership renewal time is approaching fast so keep an eye out for this. Remember you can also take advantage of the new registration/membership option when booking your place for the March meeting which is proving a popular option for new members. Remember that renewing your membership will continue to give you early access to information about future meetings and this newsletter.

As a reminder membership fees can be offset against tax if paying yourself.

It is a great help to our Secretariat if, when moving between jobs, you can provide your new contact details to [secretariat@smr.org.uk](mailto:secretariat@smr.org.uk).

Following a decline in membership over a number of years the committee are pleased to report that numbers do appear to have stabilized. This is in part due to efforts to follow up lapsed members and in part the new registration/membership option for meeting registrations.

The members are the Society, so the committee encourage all members to promote the Society and its meetings to their networks.

We are particularly keen to encourage students and colleagues from the academic community to attend our meetings. As an incentive for students we have a number of student bursaries available, please see the panel that follows.

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**Student Bursaries**

Do you know a student who could benefit from attending one of our SMR conferences?

They can apply for a bursary.....

- Bursaries cover registration fee and can make a contribution towards travel costs.
- Applicants are eligible for one bursary per year.

How to apply:

- Visit the SMR website to download the application form.
- Complete form and appropriate registration document with a signature, confirm student status e.g. by head of department and send to [secretariat@smr.org.uk](mailto:secretariat@smr.org.uk) or post to the secretariat - details at the end of this newsletter.
- Decisions on student bursary eligibility are made by the SMR committee and are final
- Apply early - there are three available for each meeting
Some recent literature references highlighted by the SMR Committee


With the New Year comes the accounting for the previous year. Specifically numbers are in for the total number of approvals from 2016 which is down from 2015. With only 22 compared with 45 from 2015, the FDA rejection rate had increased relative to 2015 with twelve CRL’s compared with only two for 2015.

More details (L. M. Jarvis Chem & Eng News 30th Jan 2017, 28) suggest part of the problem was a rash of approvals in late 2015, which were expected in 2016.

U. Schulze et al
Market watch: Value of 2016 FDA drug approvals: reversion to the mean?
Considers putative market value of those drugs that have been approved and the view is values will be less than in previous years.

S. Robey & F. S. David
Drug launch curves in the modern era
The shape of the predicted sales launch curve can dramatically affect financial models of pre-commercial drugs. This article provides an update on a commonly used framework for modelling launch curves.

PMID: 27910876

For those plagued by “Dear highly-esteemed expert: how to cope with academic spam”, some tips on how to cope.
D. Cressey, Nature 2016 Dec 14th.

M. F. Rafferty
No Denying It: Medicinal Chemistry Training Is in Big Trouble
J. Med. Chem 2016, 59, 10859
Argues for creating/reinforcing academic industrial partnerships to support training of students in drug design concepts.
PMID: 27668824

A. M. Jordan and R. P. Grant
Communicating Our Science to Our Customers: The Vital Role of Passionate Public Advocacy
A particularly relevant topic for SMR members.
PMID: 27994724

D. L. Jardim, E. S. Groves, P. P. Breitfeld, R. Kurzrock.
Factors associated with failure of oncology drugs in late-stage clinical development: A systematic review
Cancer Treatment Reviews 2017, 52, 12.
Comprehensive analysis of the underlying reasons why cancer drugs have such a high failure rate in late stage clinical development.
PMID: 27883925

A. K. Ghose et al
Technically Extended MultiParameter Optimization (TEMPO): An Advanced Robust Scoring Scheme To Calculate Central Nervous System Druggability and Monitor Lead Optimization
ACS Chem. Neurosci., 2017, 8, 147
PMID: 27741392

R. Santos, et al.
A comprehensive map of molecular drug targets
Really interesting analysis where the authors have produced a map of molecular targets for approved drugs. They demonstrate a continued prevalence of privileged target families combined with a growth in the number of novel first-in-class mechanisms, particularly in oncology. The authors also note that only 5% of identified cancer driver genes are targeted by current cancer therapies.
As an aside, the drug-target data within ChEMBL is used in a number of other platforms such as Pharos (the portal for the NIH Illuminating the Druggable Genome project), Open Targets (a resource for pre-competitive target validation) and DrugCentral (a drug compendium from the University of New Mexico), all of which have papers in the 2017 Database Issue of Nucleic Acids Research, alongside ChEMBL:
Pharos: Collating protein information to shed light on the druggable genome
Open Targets: a platform for therapeutic target identification and validation
DrugCentral: online drug compendium
PMID: 27910877

K. M. Nelson et al
The Essential Medicinal Chemistry of Curcumin
J. Med. Chem., Article ASAP
Publication Date (Web): January 11, 2017 Copyright © 2017, American Chemical Society
A conclusion that curcumin is over rated in so many ways as a lead for drug discovery
PMID: 28074653

The recent draft FDA guidance for PBPK modelling is big news for Pharma:
PBPK modelling can be used to support decisions on whether, when, and how to conduct certain clinical pharmacology studies, and to support dosing recommendations in product labeling. Previously there was a lack of regulatory guidance regarding the format and content of PBPK analyses that are submitted to the FDA and packages would vary significantly across developers. The new draft guidance intends to help sponsors report physiologically based pharmacokinetic (PBPK) analyses to the agency in a standardized format and can facilitate FDA’s efficient assessment, consistent application, and timely decision making during regulatory review and is the goal of this guidance.
A good overview of an area where a lot of progress has been made. But there's still lots to do.

PMID: 28106067

M. E. Kennedy et al.
The BACE1 inhibitor verubecestat (MK-8931) reduces CNS b-amyloid in animal models and in Alzheimer's disease patients


With the compound in phase 3 is this the chance for the amyloid hypothesis to regain some traction.

PMID: 27807285

J. Sevigny et al.
The antibody aducanumab reduces Aβ plaques in Alzheimer's disease


Currently in PhII trials, PhII studies showed a dose dependent reduction in soluble and insoluble -amyloid in the brain and a slowing of clinical decline

PMID: 27582220

M. Matsui & D. R. Corey
Non-coding RNAs as drug targets

doi: 10.1038/nrd.2016.117

Non-coding RNAs (ncRNAs) may affect normal gene expression and disease progression, thereby representing potential drug targets. Here, Matsui and Corey assess the potential and challenges in therapeutically exploiting ncRNA species - including microRNA, intronic RNA, repetitive RNA and long ncRNA - highlighting key lessons learned during the development of technologies targeting mRNA.

PMID: 27444227

R. S. Wible and T. R. Sutter
Soft Cysteine Signaling Network: the functional significance of cysteine in protein function and the soft acid/base thiol chemistry that facilitates cysteine modification

Chem. Res. Toxicol., Just Accepted Manuscript DOI:10.1021/acs.chemrestox.6b00428
Publication Date (Web): January 25, 2017

Hypothesizes a signaling pathway governed by the chemistry of cysteine Sulphur.

PMID: 28122179

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