The second ECNP Summit on the future of CNS drug research in Europe

14 October 2012

Notes

Participants

In alphabetical order:

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David Baldwin (ECNP)
Alastair Benbow (EBC)
Richard Bergström (EFPIA)
Claire Bithell (SMC)
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Michael Davidson (ECNP)
Gerry Dawson (P1Vital)
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Christine Gispen-de Wied (CBG)
Guy Goodwin (ECNP)
Michel Goldman (IMI)
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Paul Jenner (Novartis)
Shitij Kapur (NewMeds)
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Marc Laruelle (UCB)
Thomas Lönngren (NDA Group)
Ruth McKernan (Neusentis)
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Hans-Jürgen Möller (CINP)
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Sven Ove Ögren (ECNP)
Anders G. Pedersen (Lundbeck)
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Alexander Schubert (ECNP)
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Joseph Zohar (ECNP)

Apologies:
Philippe Cupers (DG Research)
Guido Rasi (EMA)

Background

In March 2011 ECNP hosted a summit to discuss concerns about the threat to science and patient care provoked by the pull-out of many “big pharma” companies from brain research and development. This led to a publication in *European Neuropsychopharmacology* (2011, 21:495-499) and a number of concrete developments aimed at helping to remedy the situation.

The Vienna meeting was called on the occasion of the 25th ECNP Congress to update parties on progress so far and to introduce new players into the discussions – specifically EFPIA and IMI. An invitation to the EMA was declined although they had attended the previous summit.

Format

The meeting was by invitation only. We heard presentations from a number of parties (agenda appended) and there was free and frank discussion under the Chatham House Rule. A number of current and future scenarios were discussed.

ECNP progress

This had occurred on several fronts.

1. The "Medicines Chest" initiative: David Nutt

One of the challenges facing drug discovery is that the understanding of human brain mechanisms lags a long way behind those in animals because there are few selective pharmacological agents available for the developing and testing of theories. The Medicines Chest has been set up to rectify this marked limitation by making available selective drugs to facilitate human research.

A survey of ECNP members had identified a wish-list of about 50 compounds that would be wanted for research. Discussions with industry personnel and a further poll of our members produced a top-ten list of compounds that already had sufficient safety data that they had been used in humans. This database with details of the compounds pharmacology clinical studies is now being put into a database on the ECNP website.

A test-case of this approach has been made whereby Lundbeck made available a compound no longer in development for human neuroscience research at Bristol University. The contract for this may serve as a template for other studies with compounds from other companies.

The current plan is to obtain as many investigational brochures for the top-ten compounds as possible and store these in a secure way at ECNP so that bone-fide researchers may access them to build research grants.

2. The Clinical Trials initiative: Guy Goodwin

The objective is to create a database for individual patient meta-analyses. The first target is clinical trials in major depression. The approach has been initially via Nefarma, the association for innovative medicines in the Netherlands (i.e. the industry association for the Dutch branches of innovative pharmaceutical companies). The initial responses have been positive but the availability of people and resources to develop the access to data is, as feared, quite limited and morale in the neuroscience area low. The intention is to persevere

EU progress

1. The Innovative Medicines Initiative (IMI): Michel Goldman

This is the largest public-private research partnership ever. It brings together a number of pharmaceutical companies with EU funding to explore pre-competitive research that may lead to new insights into disease mechanisms that can then give new treatment approaches. One major breakthrough is a mouse model of autism.

The approach has been successful with many thousands of researchers getting together in working groups. Outputs include hundreds of papers many in high-impact journals. However, a number of companies that pulled out of CNS research have reduced/stopped their work in this area of IMI. Efforts are being made to bring others in.

2. NEWMEDS: Shitij Kapur

NEWMEDS is one example of an IMI proposal particularly focused on schizophrenia and depression. The initiative is divided into several work packages that are focusing on better and more standardised animal models for cognition in schizophrenia, the use of imaging in early drug development (especially cross-species imaging), the use of fMRI at an experimental medicine Phase I/IIa stage to hone the indications, the use of pharmacogenetics in depression, and finally the use of modified trial designs.

To impact the last of these objectives NEWMEDS has brought together trial data on nearly 24,000 patients in antipsychotic trials from five companies. This has provided one of the largest placebo databases and is yielding new insights: proof of concept trials can be much shorter; women show a larger drug-placebo response than men; and those earlier in their episodes show a greater drug response. The program validates the model of collaborations and is yielding practical and open solutions to drug development problems – more details can be found at: http://www.newmeds-europe.com.

National Initiatives

1. UK – the MRC-AZ initiative

Recently AZ approached the UK MRC to offer them a number of compounds (28) that had failed in their primary indications for research and possible repurposing. About one third of the drugs had CNS indications. In return the MRC put up £10mill to fund research projects. This formed a specialised call for which there were about 90 outline applications across all areas of medicine. Initial selection was made by a panel on which AZ expertise was represented to ensure that projects were feasible given the known properties of the drugs. The competition was particularly well received because it had certain unique features: a) both the public, private and academic sector were making material investments; b) the IP framework was worked out right from the start; c) the companies were getting a 'second life' and a right of first-refusal for their compounds; d) the academics were getting a competitive advantage by accessing something novel; and e) finally, the project was co-developed by people in industry and academia who knew a lot about the compound and the subject at hand. Details available at: http://www.mrc.ac.uk/Fundingopportunities/Calls/MoD/MRC008389.

In the end 15 grants were funded, six of these in the neurosciences, of which one (on a novel antipsychotic approach) was in the mental health area. There is talk of a second round of grants, and this is to be welcomed if it comes to fruition. This is an innovative scheme and although it was disappointing that there was no ring-fence for CNS indications, it does offer a model for other companies to do similar schemes potentially as a CNS-only grant call.

2. USA – NIH NCATS scheme

www.ncats.nih.gov/research/reengineering/rescue-repurpose/therapeutic-uses/therapeutic-uses.html

This is similar to the AZ scheme but involves a consortium of eight companies that have donated 58 compounds to NIH for "repurposing". The NIH has made about $20mill available again as competitive grants, though only for USA applicants. Many of these compounds are originally for CNS indications such as ADHD, dementia and depression. It will be interesting to see if CNS researchers fare better in this competition than they did in the UK AZ one!

Biomarkers

Speakers from pharmaceutical industry noted that in others areas of medicine powerful and rapid advances have recently been made because of the discovery of new biomarkers, such as gene polymorphisms for some cancers. These have led to stratification of patients into drug sensitive and drug insensitive groups with much greater signal-to-noise ratios for drug treatment. This increase in trial power reduces the number of patients required for trials and so accelerates development. There is a pressing need for similar advances in CNS disorders.

Other ways forward

A number of other ideas were discussed. This ranged widely – from increasing lobbying to new research collaboration structures.

The EBC pointed out that their lobbying has increased EU spend on CNS research from € 180 million to 1,600 million over the past decade. This must therefore continue and ideally increase, particularly as the research settlement in the new budget is not as good as had been hoped.

Clinical trial designs need reviewing, with more emphasis on patient-reported outcomes. Also a faster registration scheme with more data collection in phase 4 would increase both the availability of new medicines and the better assessment of their clinical effectiveness.

Individual national payer systems are adding another hurdle – or rather 27 new hurdles; this now may be greater than that of current regulations in terms of dissuading companies from research in this area. This might be less onerous if the real benefits of drugs over the many decades they are used were taken into consideration in modelling cost-benefit relationships. The full societal value of drug research for psychiatry treatment needs computing.

Patients could also help research by donating useful information such as medical records and DNA samples in all trials to allow larger data-bases to be collected.

It seems inevitable that the current model of pharmaceutical business may need to be altered given the reducing likelihood of new “blockbuster” drugs. The industry needs to develop plans for this.

Better models are required in experimental medicine studies. For example we need to move away from drug models of illness, e.g. scopolamine for dementia, as they may predispose to certain drug activities that do not work in patients. One move in the right direction is that ECNP is now in the process of setting up a Europe-wide experimental medicine network for human CNS studies as part of their Networks initiative (www.ecnp.eu/projects-initiatives/ECNP-networks.aspx). This will identify and support expert centres working together using common imaging and other protocols to speed up research studies including those on patients and to ensure greater consistency and reproducibility of findings, so giving industry more confidence in this approach.

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Sunday, 14 October 2012
Austria, Vienna

Final programme

18.45 Dinner

19.00 Welcome – Joseph Zohar

19.05 Introduction – David Nutt and Guy Goodwin

19.10 Perspectives:
19.10 Industry – Anders Pedersen, Lundbeck A/S
19.20 Patients – Dolores Gauci, GAMIAN Europe

19.30 Strategies and approaches:
19.30 ECNP Medicines Chest and Clinical Database – David Nutt and Guy Goodwin
19.40 Innovative Medicines Initiative (IMI) – Michel Goldman
19.50 NewMeds/Medical Research Council (MRC) – Shitij Kapur
20.00 European Brain Council (EBC) – Alastair Benbow

20.10 Discussant responses:
20.10 Mary Baker, European Brain Council
20.15 Ruth McKernan, Neusentis
20.20 Marc Laruelle, UCB

20.25 General discussion – what have we achieved so far and finding new solutions

21.35 Wrap-up – David Nutt and Guy Goodwin

21.45 Dessert and Close