**ECNP Targeted Expert Meetings (TEM)**
**11-12 September 2009, Istanbul, Turkey**

**Report on the TEM Affective Disorders and Antidepressants**
**Arne Mørk, Denmark, *coordinator***

The meeting, chaired by Arne Mørk and Eduard Vieta, Spain, focused on the importance of bridging the gap between drug discovery in animals and drug development in human patients when developing better treatments for affective disorders.

The first main lecturer, Mark Millan, France, discussed current issues in the development of new antidepressants. Due to the heterogeneous nature of depression and the high co-morbidity with other CNS disorders, it is a challenge to target this disease. Lack of valid animal models and efficacy/disease biomarkers and low current impact of genomics hamper the drug-discovery process. Translational research tools may be helpful in the future for predicting drug efficacy, doses and time of administration. The belated interest in multi-target compounds in drug development was discussed and concepts for novel exploitation of monoaminergic, non-monoaminergic and combined treatments were presented.

John F. Cryan, Ireland, acted as discussant and focused on the utility of current animal models. While numerous attempts have been made to create rodent models of depression, there are no satisfactory animal models available. There is currently a shift to more focused research dealing with an endophenotype-style approach, selective breeding programmes and incorporation of new findings from human neuroimaging and genetic studies. Additionally, emphasis has also been placed recently on developing mouse models of the early-life origins of stress-related psychiatric disorders as childhood trauma and neglect exert a profound and pervasive influence on risk for affective disorder.

The second discussant, Peter Riederer, Germany, focused on potential biological markers for major depression. However, according to the 'criteria of definitions,' currently proposed markers lack specificity, sensitivity and most of them have not been evaluated in postmortem studies. Peter Riederer pointed out that there seems to be a lessening of research into major depression subtypes and consequently a lessening of homogenous causality. Without the latter, it will not be possible to detect valid biomarkers for early diagnosis, differential diagnosis and follow-up of progression and treatment responses.

In the second session, Charles H. Large, Italy, presented current issues in developing drugs for bipolar disorder. Segregating bipolar disorder into symptom clusters to identify unmet clinical needs was addressed. The importance of understanding diseases to identify how to target the symptoms was also discussed. Moreover, the use of endophenotypes in translational medicine to answer issues on CNS penetration, target occupancy, required plasma levels and margins of safety was suggested. Finally, the possible use of influencing an abnormal circadian function for treatment of bipolar disorder was discussed. Haim Einat, Israel, presented the status of animal models of bipolar disorder. Modelling bipolar disorder is difficult due to the oscillating nature of the disease and the present behavioural models are limited to a very few domains of the disease. Ongoing research focuses on gene manipulation, which is challenging, since a complex interaction of a number of genes and effects of the environment may underlie the biology. Endeavours to model endophenotypes of bipolar disorder, the use of translational models and the identification of animal strains with innate behaviour were also addressed.

In the last session the main lecturer, Joseph R. Calabrese, USA, discussed the design of future clinical trials in drug development for bipolar disorder. To improve the generalisability of clinical trials fewer exclusion criteria would be needed. Exclusion of patients may inflate/deflate estimates of true population therapeutic effect sizes. Fewer exclusion criteria

could be managed by increasing sample size. Moreover, the value of enriched trial designs could be increased by using a metric to quantify the degree of enrichment. These suggestions were further elaborated on by the discussant, Eduard Vieta.

During the meeting the importance of a tight collaboration between preclinical and clinical research within this area was stressed. The challenge for cross-species translational research in psychiatry is to better understand the biological bases of affective disorders and, ultimately, to treat them more effectively.