4th EMA- EuropaBio Information Day
SUMMARY REPORT

22 November 2016, 10:00 - 17:00
De Vere Venues – Canary Wharf, 1 Westferry Circus, London

A. Introduction

Robin Evers (Novo Nordisk/EuropaBio), welcomed and thanked participants for attending the fourth EMA-EuropaBio Information Day. This forum provides an opportunity for members of EuropaBio and EMA officials to meet on an annual basis to share information and discuss topics of interest to the biopharmaceutical sector. He introduced the agenda, which covers a variety of topics in three main areas: 'International Cooperation with Medicines Agencies', 'Innovation and Development Support' and 'Evidence Generation during Medicinal Life-Cycle'.

Jordi Garcia Llinares (EMA), welcomed the participants on behalf of EMA. In his opening remarks he underlined the Agency's commitment to maintaining 'business as usual' and ensuring the protection of human and animal health, despite the uncertainty arising as a result of the UK referendum on EU membership. Furthermore, Dr Llinares touched upon EMA's ongoing work on the implementation of the Clinical Trial Regulation. He highlighted the pioneering role the EU is playing to ensure that every citizen now has access to clinical trial reports, with the publication of the first clinical data from marketing authorisation applications on 20 October 2016, pursuant to implementation of policy 0070. In addition, Dr Llinares highlighted the reinforcement of EMA's early access tools, with the launch of the PRIME scheme in March 2016. On Orphan Medicinal Products, he mentioned that the EMA will start implementing the Commission notice on the application of Article 3, 5 and 7 of Regulation (EC) No. 141/2000 on orphan medicinal products (2016/C 424/03) recently published by the EC. Finally, he concluded with the sentiment that since health does not have any barriers, interaction with other global regulatory bodies continues to be important for EMA.

B. Session I – International Cooperation with Medicines Agencies

Martin Harvey (EMA), opened the session with a presentation of the work carried out by the Agency and the HMA Network. He made reference to the EU Medicines Agencies Network Strategy to 2020 and outlined the four objectives contributing to the global regulatory environment: i) Assure product supply chain and data integrity, ii) Convergence of global standards and contribute to international fora, iii) Support training and capacity building and promote the EU regulatory model and iv) Ensure best use of resources through promoting mutual reliance & work sharing. A recent EMA report, entitled, 'Connecting the Dots', provides an overview of the various international initiatives that are ongoing. Mr Harvey concluded by stating that the EU regulatory system is based on work-sharing, mutual cooperation and efficiencies (more details can be found here).

During the panel discussion, **Colin McIff (FDA)**, informed the audience that the FDA interacts internationally via two main mechanisms, i.e. through multilateral organisations and bilateral engagements. One example of this, is the FDA and EMA liaison on site in each agency (more details can be found here). **Hideyuki Kondo (PMDA)**, highlighted that PMDA's International Strategic Plan 2015 was, i) to contribute to the world through regulatory innovation, ii) to maximize the common health benefits to other

countries/regions and iii) to share the wisdom with other countries/regions. More details can be found here. Furthermore, **Emma Du Four (AbbVie)**, stated that the recent EMA report, 'Connecting the Dots', is a good step for further transparency and showcases the need for enhanced cooperation. **Marie-Hélène Pinheiro (EMA)**, highlighted that the EMA like other international partners is very much in favour of enhancing transparency, and referred to the publication of exchanges of discussions of the various International Pharmaceutical Regulators Forum (IPRF) working groups. During the discussion, EMA's Martin Harvey clarified that the IPRF produces reflection papers rather than actual guidance which remain in the remit of the ICH or of regional and national bodies.

C. Session II – Innovation and Development Support

Rob Hemmings (MHRA), provided an overview of the early access tools developed by the EMA (i.e. conditional MA, Accelerated assessment and PRIME) and the experience building with the Adaptive Pathways concept of medicine development. For the PRIME scheme, he outlined the entry points for eligibility and required evidence. Dr Hemmings noted that if PRIME is not the right tool for a particular medicinal product then EMA can still provide support through other schemes such as scientific advice, SME office, Innovation Task Force, etc. More details can be found here.

James Kennard (Biogen), shared the company's first experience with PRIME for their product aducanumab (an investigational monoclonal antibody for patients with Alzheimer's Disease). Through PRIME, Biogen benefited from early rapporteur assignment, multi-stakeholder advice and eligibility for accelerated assessment (more details can be found here).

On the panel discussion, **Martina Schüßler-Lenz (Paul-Ehrlich Institute)**, said that 50% of PRIME scheme products are ATMPs, of which all have orphan designation. She also mentioned the importance of PRIME in helping support these innovative products. **Leeza Osipenko (NICE)**, stated that payers need to make sure that the benefit that they pay for truly exists. She stressed that when products enter the PRIME scheme they may look promising but it is unclear to what extent they will deliver as they can be at an early stage of development. HTA involvement at this early stage enables horizon scanning of promising candidates. **Nick Meade (Genetic Alliance UK)**, mentioned that PRIME is a positive development and more could be done to promote the scheme. He stated that the EMA is an excellent global example of involving patients' voice.

D. Session III – Evidence Generation During Medicinal Life-Cycle

Thorsten Vetter (EMA), presented the work of the Scientific Advice Working Party, which provides advice to sponsors on the scientific requirements for regulatory decision making throughout the life-cycle: before marketing authorisation (MA) and post-MA. He highlighted the role Scientific Advice can play as an important early platform to discuss and foster generation of Real World Evidence (RWE) to complement data arising from the randomized controlled trials. Dr Vetter concluded by saying that collaboration on RWE among different stakeholders is needed to realise its full potential. More details can be found here.

Francesca Cerreta (EMA), provided an update on the learnings from EMA's recent pilot of the Adaptive Pathways (AP). AP is a scientific concept of medicine development and evidence generation intended for medicines that address unmet needs. The focus is on evaluating the benefit/risk in a restricted population where unmet need is highest. EMA offers the opportunity to discuss whether the AP concept could apply to a particular development, e.g. eligibility for conditional MA , data requirements for potential additional data collection to facilitate pricing and reimbursement. The EMA has learned a lot from the pilot project on the practical implications of the AP concept with medicines

under development. Next steps include, i) integration in scientific advice and ii) consulting stakeholders at the December 8 workshop. More details can be found here.

Alison Cave (EMA), presented the role registries can play to generate RWE, such as, determining the clinical effectiveness of healthcare products and measuring the quality of care. It was noted that there are many challenges with current registries and sustainability is one of them. In order to facilitate the consistent use of registry data for post-marketing evaluation of medicines some solutions will require a concerted effort from all stakeholders, especially in the areas regarding funding and standardization of platform infrastructure. More details can be found here.

Maurille Feudjo Tepie (Amgen) provided a case study of blinatumomab versus standard therapy of adults with relapsed/refractory Acute Lymphoblastic Leukaemia (ALL) - a rare disease with a very poor prognosis. Amgen was faced with many challenges in conducting a Phase III RCT, and so RWE played a significant role in helping the product gain approval. He highlighted the importance for all relevant stakeholders to continue to explore the potential role of the RWE in drug regulatory process. More details can be found here.

Martine Zimmerman (Alexion), presented a case study of Soliris (eculizumab) approved in June 2007 for Paroxysmal Nocturnal Haemoglobinuria (PNH) and November 2011 for Atypical Haemolytic Uremic Syndrome (aHUS). She explained how registry data had been used to broaden the indication for PNH beyond transfusion dependent patients. Ms Zimmerman concluded that a registry is a good alternative when a prospective randomized study is not possible (when a no-treatment control group is considered impossible or unethical). More details can be found here.

Agathe Le Lay (Novo Nordisk), gave an account of the role of RWE to foster access to innovative diabetes medicine. She illustrated this with an example of insulin degludec which was evaluated in a large 3a clinical trial programme in adult patients with type 1 and type 2 diabetes (BEGIN®). This case study exemplified how the use of RWE helped local payers (e.g. local formulary committees) in getting additional insights into the clinical benefits of a novel intervention in addition to evidence from the initial RCT program. More details can be found here.

During the panel discussion, **Julian Isla (Dravet Syndrome Foundation)**, introduced Wacean which is an online platform created by the Dravet Syndrome Foundation, in order to have a database of patients diagnosed with Dravet Syndrome and other refractory epilepsies with comorbidities. **Rosa Giuliani (ESMO)**, emphasised that there is an enormous amount of data and stressed that the challenge that we face is in understanding how to navigate it and make it useful. **Leeza Osipenko (NICE)**, stated that there is no such thing as useless data and that NICE is willing to accept any kind of data available. She added that the challenge is to convert the data into something useful.

E. Conclusion

Robin Evers (Novo Nordisk/EuropaBio), thanked the EMA for sharing information during this 4th EMA-EuropaBio information Day. He also underlined that this annual meeting is an extremely productive platform and invited all participants to share this information with their respective organisations. Furthermore, he stressed that putting the patient at the centre of the treatment is key.

Marie-Hélène Pinheiro (EMA) thanked all participants for their contributions and valuable discussions. She noted how important it is to engage with all stakeholders (patients, industry, healthcare professionals, HTA bodies and industry) at an early stage of medicines development in view of science and healthcare ecosystems evolution and that the Agency looks forward to continuing the dialogue.