PRIME First Experiences

EMA - EuropaBio Information Day, 22nd November 2016

James Kennard – Director, Regulatory Affairs, Biogen

Opinions expressed are solely my own and do not express the views or opinions of Biogen

KEEP
CALM
IT'S
PRIME
TIME

Background and pre-submission phase

Aducanumab is Biogen's investigational monoclonal antibody for patients with Alzheimer's Disease

- The potential for the inclusion of Aducanumab in the PRIME scheme was first considered by the company in 2015
    - Following informal discussions with regulators and publication of the draft reflection paper

- Application for inclusion in PRIME was prepared in advance of the formal launch of the scheme
    - Based on the adopted guideline 'Enhanced early dialogue to facilitate accelerated assessment of PRIority MEdicines (PRIME)'
    - Application for eligibility in accordance with annex 1

- EMA launched PRIME in early March 2016 → European Commission commented that PRIME is a major step forward for patients and their families for unmet medical needs, such as rare cancers, Alzheimer's disease and other dementias

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Progress so far….

- Submission of PRIME application
  - Biogen was one of the first companies to apply for PRIME in April 2016 and we wanted to share our early learnings from our experience
- Accepted as per guidance in May 2016
- Kick-off meeting in September 2016
  - EMA open to schedule very quickly
- Post-meeting EMA dialogue – extremely constructive

Acceptance into PRIME

Aducanumab accepted into PRIME on 26th May 2016 (4 out of 18 applications accepted) and is the only Alzheimer's product (still) to be accepted (only 22% of applications accepted to date);

- CHMP/SAWP agreed that there is a clear unmet medical need in Alzheimer's disease and that Aducanumab has the potential to significantly address this unmet need
- Quickly thereafter, centralised eligibility confirmed
- Rapporteur assigned one month later

Benefits of PRIME – early experience

Early Rapporteur assignment

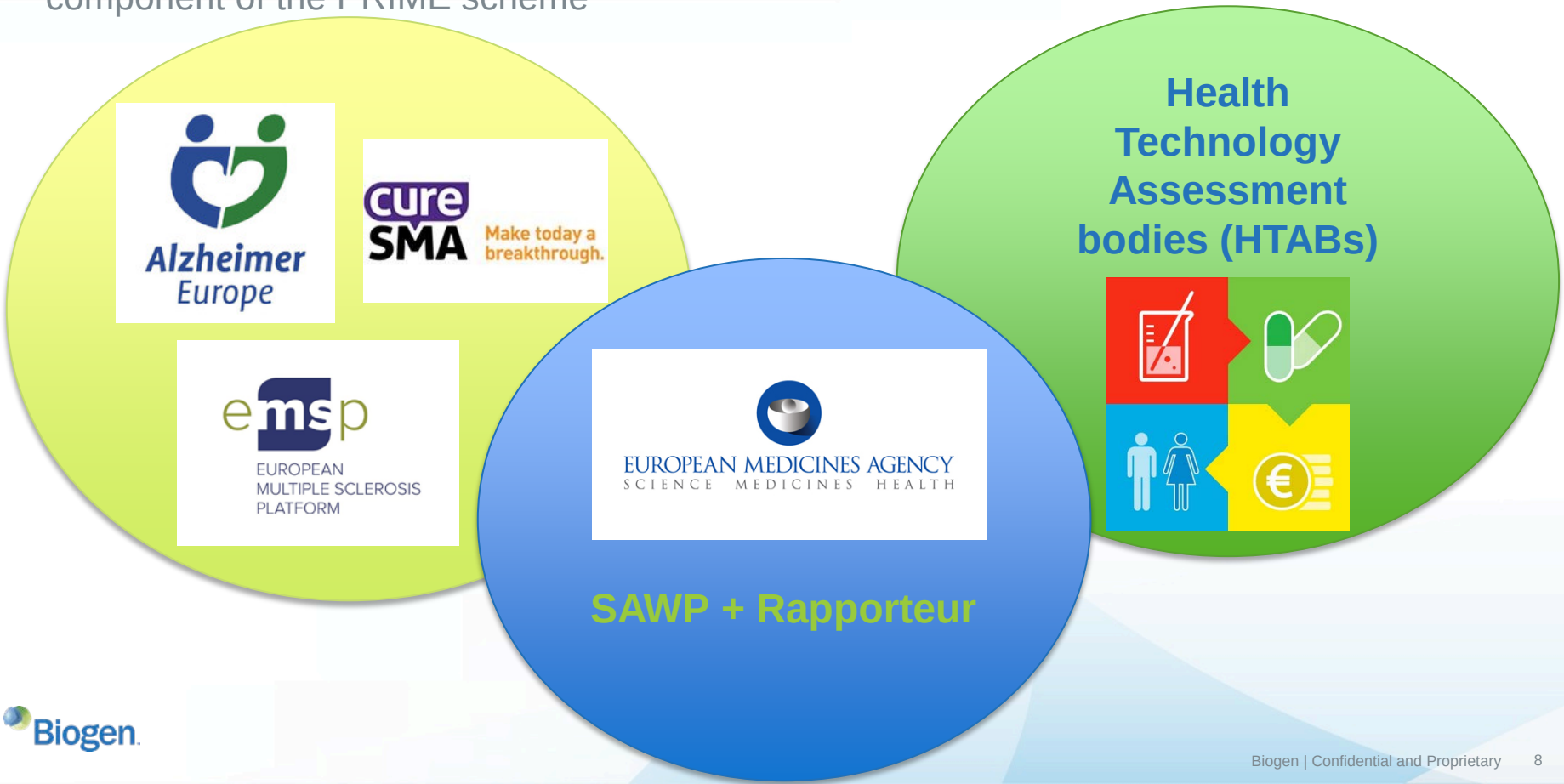
The Rapporteur (and their assessment team) normally assigned just prior to Marketing Authorisation Application (MAA) filing. Within PRIME, they are assigned much earlier in development…the advantage of which is they:

- Become more familiar with the product and strategy earlier in development
- Identify any potential issues/concerns in development that can be mitigated earlier
- Provide guidance throughout development and eventual MAA assessment

Benefits of PRIME – early experience

Multi-stakeholder advice is critical

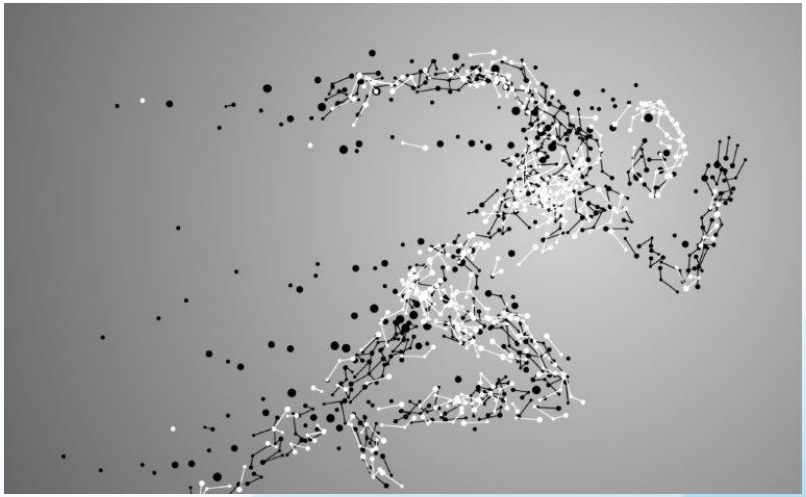
While the mechanism for multi-stakeholder advice already exists in Europe, the ability to bring these groups together with a Rapporteur, earlier in development is a critical component of the PRIME scheme



Benefits of PRIME – early experience

Potential accelerated assessment

- Reduces the review time within the centralised procedure for medicines designated by EMA to be of major public interest or a therapeutic innovation – saving ~ 4-6 months
- While this is an existing mechanism, early Rapporteur assignment allows continual dialogue to ensure that the development strategy continues to support a package acceptable for an accelerated procedure;
    - The opportunity for centralised advice within PRIME means that CHMP and the Rapporteur are engaged from an earlier stage, which increases the likelihood of keeping to an accelerated timetable



Biogen's experiences so far

Kick-off meeting briefing package

- Tailored to key topics for future engagement
  - Tabulated assessment of topics for future discussion and stakeholders to be involved, including timelines - well received and EMA request to update with major development timelines - living record of future engagement and development plans
- Substantial background to support key topics

Preparation for kick-off meeting

- Cannot stress enough the importance and value of dedicated EMA support/contact - many conversations on what to expect for the kick-off meeting and how best to prepare
- Approached the meeting in a multidisciplinary as all aspects of a development program are key to the potential success of an accelerated process

Importance of the agenda (received ~1 week prior to meeting)

- Agenda was structured with specific points raised by the Rapporteur for consideration
- Slide deck to be structured according to the agenda
- Change to normal preparation for EMA meeting – no expectation to get into scientific detail!

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Biogen's experiences so far

Very successful kick-off meeting with EMA, Rapporteur and CHMP/SAWP Chairs in September

- Rapporteur assessment team fully reviewed briefing package and gave very constructive feedback/considerations
- Clear that future scientific advice should be through centralised EMA advice and significant value in multi-stakeholder scientific advice
- EMA proposed to utilise shorter lead in time to centralised advice (40 days rather than 70) - in a 5-6 month procedure this is an advantage!
- Post-authorisation plans are key
- Recognition of need for HTAB engagement
- Further discussion with patient advocacy groups to ensure best involvement

During SAWP or CHMP weeks

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Key outcomes

EMA agreement on future engagement

- Aim for 40 day SA procedure and potential prioritisation
- EMA request to get on the books ASAP for scientific advice due to very busy schedule

Post meeting discussion with EMA: If contemplating parallel SA (PSA) consider the full 70 day procedure due to complexity of discussions and allowing HTABs to become completely familiar with data/strategy

Post authorisation strategy is key for EMA – reassurance around unanswered questions to be addressed and supportive of MAA submission strategy

If considering PSA, clear need for HTAB advocacy prior to first procedure – potential advocacy/scoping document in advance of centralised Letter of Intent (LoI) step

Further discussion with patient advocacy groups to ensure best involvement

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Potential improvements

Guidance on application and kick-off meeting clear and relatively straightforward to follow;

- One point to note on the briefing package for the kick-off meeting; on the one hand guidance asks for a short and focused package but the list of topics to cover in the annex is very long and requires detail!

Although centralised advice is preferred by EMA, it should be made clear to potential applicants that while national SA can continue to be sought, this may not always be possible and can be dependent upon the Rapporteur assigned

Key Takeaways from an Industry Perspective

- We support initiatives that facilitate multi-stakeholder engagement
- It is important to ensure scientific rigor to meet all stakeholders needs (patients, regulators and HTABs)
- With the ultimate aim of providing early access for innovative products that encompass robust data collection

We are excited as a company to be part of the PRIME scheme. If we can support in shaping the scheme and help to make it a success, then this can only be good for patients and other products

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