DGRA Annual Meeting

Adaptive Pathways
Experience and Perspective
of the Pharmaceutical Industry

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EMA/254350/2012: Pilot project on AL

- **“AL can be defined as a prospectively planned, adaptive approach to bringing drugs to market. Starting from an authorised indication (most likely a “niche” indication) for a given drug, through iterative phases of evidence gathering and progressive licensing adaptations concerning both the authorised indication and the potential further therapeutic uses of the drug concerned AL seeks to maximize the positive impact of new drugs on public health by balancing timely access for patients with the need to provide adequate evolving information on benefits and harms.”**

EMA/254350/2012: Pilot project on AL

EMA Case Study 1

- **Phase II: single arm study in previously treated patients with mutation and Stage IV melanoma shows outstanding efficacy.**
- **Traditional approach:**
  - **Phase III DBPC in untreated patients with same mutation**
- ***AL approach:***
  - **Conditional approval based on uncontrolled Phase II data**
  - **Condition: Phase III study in untreated patients.**
- **HTA bodies: Would they accept uncontrolled data?**

EMA/254350/2012: Pilot project on AL

EMA Case Study 2

- Novel antibiotic
- *Traditional approach:*
  - "Treatment of organ-specific infection"
  - 2 DBPC studies per organ specific infection
- *AL approach:*
  - "Treatment of bacterial infections due to aerobic Gram-negative pathogens in patients with very limited treatment options."

EMA/254350/2012: Pilot project on AL

EMA Case Study 2 cont.

- *AL approach:*
  - "Treatment of bacterial infections due to aerobic Gram-negative pathogens in patients with very limited treatment options." based on:
  - PK/PD modelling only (plus limited safety from PK study) or PK/PD + underpowered open label or PK/PD + one fully controlled and fully powered study (depends on PK/PD quality)
- Early HTA parallel scientific advice required!

AP is a discussion-platform:

- **EMA/CHMP advises on development/regulatory strategy,**
  - **no control from company perspective on selection of**
    - SAWP members
    - data protection, patents, US development
- **Discussion within Adaptive Pathway between stakeholders: Company, EMA (SAWP), selected HTAs and other potential stakeholders (e.g. patients).**
- **Only thereafter the formal existing procedures will be applied to discuss with the same stakeholders (SAWP, HTA, patients)**

Adaptive Pathway

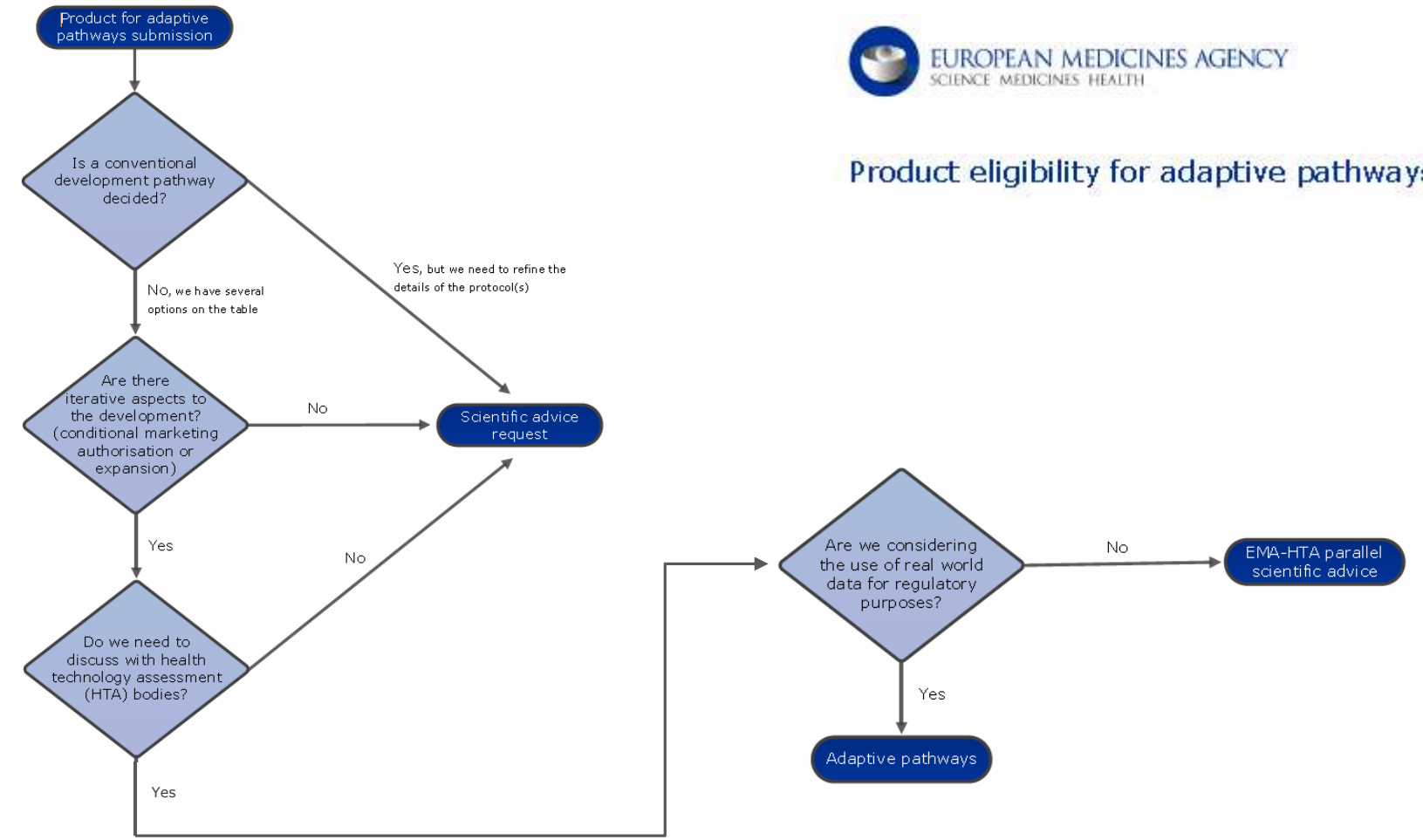
The approach builds on regulatory processes already in place within the existing EU legal framework:

- **Scientific advice**
- **Conditional/Accelerated approval,**
- **Compassionate use**
- **Pharmacovigilance tools (RMP including PASS, PAES, Registries)**

Adaptive Pathway

- Encourage developers of medicines to consider all regulatory tools and flexibilities within the existing EU legal framework
- Explore the extent to which regulatory demands for efficacy, safety, quality are compatible with e.g. HTA
- Investigate in a timely manner the hurdles that exist in realising the most efficient medicine development pathways, including the role and limitations of real-world data

Adaptive Pathway



EUROPEAN MEDICINES AGENCY
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Product eligibility for adaptive pathways

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Adaptive Pathway

The “Adaptive Pathway” is formalizing the existing practice - nothing truly new for those who are familiar with the processes

HTA involvement in the context of Adaptive Pathway meetings

HTAs will provide informal input only

- **Different HTAs provide different feedback**
- **Reimbursement systems in the EU not harmonized: more than 80 systems in place in EEA**

Adaptive Pathway leads to Adaptive Licensing (AL)

Summary

- AP has been developed to gain early approval in a first indication
- "Adaptation" of licence follows after initial approval
  - Further indications (Examples like Avastin)
  - Additional patient groups (cancer: late line followed by first line)
  - Additional dosages and treatment durations
  - "Loss of" contra-indications

THANK YOU !

Dr. Ulrich Granzer

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