Timely Patient Access to Transformative Medicines: Early Access Strategy

ORPHA STRATEGY Consulting

David Schwicker, Principal

Early and Managed Access Programmes, London Pre-Conference Workshop B, October 24th, 2017
Agenda and Topics Overview

Early Access

Part 1: Strategy
- Shifting paradigms
- The “rare” challenge
- Early access objectives
- Key strategy elements
- Regulatory landscape
- State of play in Europe
- Interactive case study

Part 2: Value
- Hurdle to timely access
- Rapid effectiveness assessment
- Value demonstration with fewer data
- Real-world evidence
- OMPs/ATMPs value
- Interactive case study

Networking Break
Go Round #1

**Introductions, Interests, Objectives**

- Goal: create group agreement on workshop priorities
- Please give your name, where you are from, and one other fact of your choice, e.g. company, function
- State your interests and/or objectives for this workshop
- 30 seconds to one minute limit please
- No obligation, opting out is fine
Biomedical Innovation

Has Science Overtaken the System?

Empowered patients

Precision Medicine

“Need for Speed” – Adaptive Trials

Adaptive Pathways (PRIME/CMA)

Outcome and Value Uncertainties
Biomedical Innovation
The “Standard” Model

Pre-clinical | Phase I | Phase II | Phase III | HTA P&R | Phase IV

RWE | RWE

AIFFA
HAS
PATH TO FOCUS ON HEALTH
ORPHA
STRATEGY
Biomedical Innovation
New Paradigm – “Adaptive Pathways”

RWE – Life Cycle

- Pre-clinical
- Phase I
- POC (PII)
- Early MA
- PA (PIII/IV)
Serious Conditions
Focus on Unmet Need

- Life Threatening and Debilitating
- Major Impact on Patient Quality of Life
- Not Adequately Addressed by Current Standard of Care
Transformative Medicines

“Moving the Needle for Patients”

Promise of Substantial Benefit

Net Improvement of Outcomes

Meaningful to Patients & Carers
The Rarer the Disease, the Greater the Challenge

- Rare, yet not: 5-8,000 rare diseases, 6-8% affected, 36 million in the EU, children particularly vulnerable (hereditary component, early onset)
- Research bottlenecks: understanding of natural history, validated surrogate endpoints, scarcity of expertise, fragmented populations, limited patients
- EMA: 164 orphan products to treat 183 rare diseases (US 367/379)
- 2016: 16 OMPs, 2 ATMPs approved, 1/5 of all positive opinions (FDA ≈ half)
- Premiums incentivise investment: prices 8:1 vs. comparable non-orphans
- Sustainability debate with increasing budgetary impact
Early Access Strategy
The Science and Art of Creative Thinking
Early Access Strategy

A Definition

• Overriding goal: timely patient access to transformative medicines, mainly OMPs and ATMPs

• The science and art of creative, innovative thinking and discussion on the key elements of early access

• Iterative, interactive process that informs, enhances, and complements clinical development, value evidence generation, and market access planning from a uniquely “fast to market” perspective
Early Access Strategy Objectives

- **Innovative, accelerated pathways** to bring treatments to patients in the most timely manner
- Generating meaningful **patient-relevant outcomes** through early and sustained patient engagement
- **Early value demonstration** specifically addressing the challenges of early market access with fewer data
- Differentiated **value-based offerings** with the greatest net benefit for successful pricing and reimbursement
- **Maximising product value** from launch to LOE with a life-cycle full-spectrum evidence generation strategy
- Addressing burgeoning R&D expenses and competitive situations with a "fast to market" approach
Ideastorm #1

Key Elements of Early Access Strategy

- Call out ideas, concepts
- Fast, no censorship
- Crazy ideas welcome
- Leave comments and discussion for later
Early Access Strategy

Key Elements

- Early Product Promise
- Unmet Medical Need
- Patient Engagement
- Real-World Evidence
- Orphan Designation
- Compassionate Use
- Orphan, Specialty and Advanced Therapeutics with Potential for Accelerated Approval / CMA
- Early Value Demonstration
- Uncertainties

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## Overview of Early Access Regulation

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<td>Exceptional Circumstances (Rarity, ATMPs)</td>
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<td>Compassionate Use Opinion (CHMP, MS)</td>
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<td>Hospital Exemption (ATMPs, Named Patient, MS)</td>
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<td>• within 180 days (300 days standard)</td>
<td>• maximum 150 days (210 days standard)</td>
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Overview of PRIME scheme

- Early identification of therapeutic innovation in unmet medical needs.
- Iterative Scientific advice
- Enhanced regulatory guidance
- Incremental knowledge gain
- Proactive dialogue
- Promote use of existing tools

MAA review under accelerated assessment.

Nonclinical — Phase I — Exploratory — Confirmatory — Evaluation — Post-authorisation

- SA 1 (SAWP)
- SA 2 (SAWP)
- SA n (SAWP)
- Accelerated Assessment confirmation (CHMP)
- Early CHMP Rapporteur appointment

EU4 National Early Access Programmes

Eligibility for Adaptive Pathways

1. Is a conventional development pathway decided?
   - No, we have several options on the table
     - Are there iterative aspects to the development?
       - No
         - Scientific advice request
       - Yes
         - Do we need to discuss with HTAs?
           - No
             - EMA-HTA parallel scientific advice
           - Yes
             - Are we considering the use of RWD for regulatory purposes?
               - No
                 - EMA-HTA parallel scientific advice
               - Yes
                 - Adaptive Pathways EMA-HTA parallel scientific advice

Source: EMA guidance for companies considering the adaptive pathways approach, August 2016
One process, centrally coordinated through EUnetHTA EDWP (currently HAS and GBA coordinator and rapporteur)

Timeline 4 months from LOI to face-to-face meeting

Advice: 2 letters, one EMA, one consolidated from the HTAs; not legally binding, but need to justify deviations in MAA

Budget for 15 parallel consolidated consultations (PCC) in the first 2 years: EMA + EDWP + up to 3 HTAs

Parallel consultation individual (PCI) as before: EMA + HTA
Early Access - EU “State of Play”

- **Industry**
  - keen interest, 63 product applications for the Adaptive Pathways pilot in 2016; key benefit: safe harbour

- **Patient representatives**
  - enthusiastic, ready to embrace increased role early in development; but: access of even greater importance than availability – challenge to HTAs to accelerate value appraisals

- **Healthcare professionals**
  - interested; but: caution against softening of benefit/risk criteria; EMA: standards remain unchanged

- **Health technology assessment agencies (HTAs)**
  - viewpoints, resources, legal frameworks and methodological approaches differ considerably
  - diverging opinions on compassionate use, managed entry agreements, adaptive reimbursement
  - lack in predictability and divergent outcomes of HTA evaluations make value demonstration based on less complete data a crucial challenge

- **Real-world evidence (RWE)**
  - agreement that there is potential for an increased use of RWE, but still a long way to go
  - opinions on RWE remain diverse; concerns about the methodology, reliability and the usefulness in decision-making, particularly regarding treatment effects

- **General consensus**
  - progress in early access must be made in order to ensure that patients in the EU have access to safe, effective and affordable medicines – “collaboration is key”

Show of Hands

Interactive Case Study Selection

① EMA “Deep Dive”: Early Dialogues focus on PRIME (EMA)

② First Experiences with PRIME (Biogen)

③ Acromegaly: Patient-Centred Research and Regulatory Decision Making in Rare Diseases (Phase IV Programs)

④ AIFA “Deep Dive”: State of the art of EAP opportunities in Italy (Sanofi)