Timely Patient Access to Transformative Medicines: Early Access Strategy

ORPHA STRATEGY Consulting

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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*

Networking Break

Part 2: Value

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

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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

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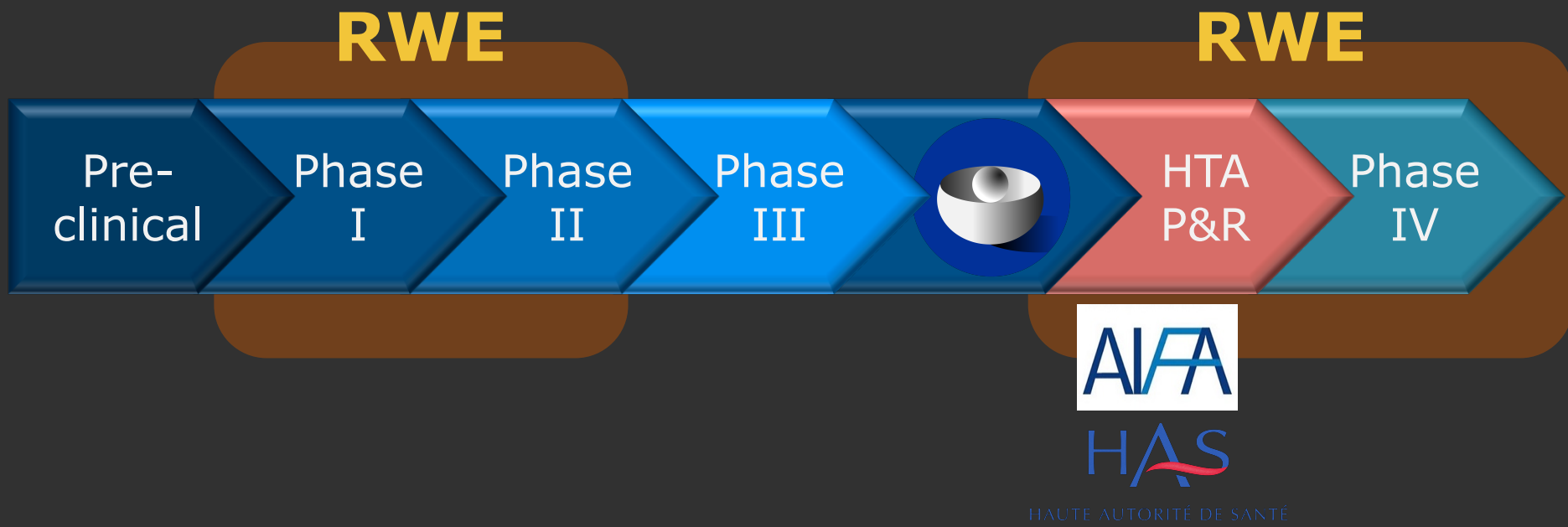
Biomedical Innovation
The "Standard" Model



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Biomedical Innovation
New Paradigm – "Adaptive Pathways"

RWE – *Life Cycle*

AIFA

HAS
HAUTE AUTORITÉ DE SANTÉ

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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

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Transformative Medicines
"Moving the Needle for Patients"

Promise of Substantial Benefit

Net Improvement of Outcomes

Meaningful to Patients & Carers

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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

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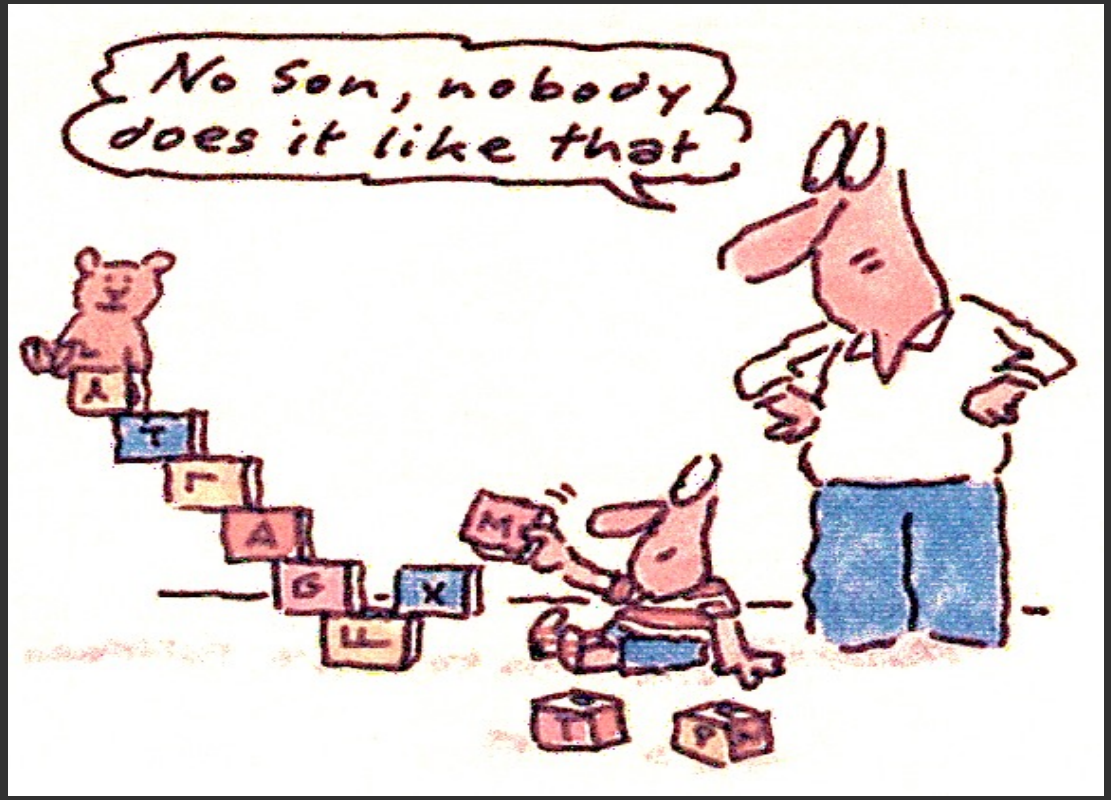
Early Access Strategy
The Science and Art of Creative Thinking



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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

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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**

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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

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Overview of Early Access Regulation

Key Features
Enhanced Early Agency Interaction
Dedicated Agency Resources
Earlier Market Authorisation and Access
Reinforced Scientific Advice
Accelerated Review of MAA
Orphan Drug Designation

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Overview of Early Access Regulation

Key Features	FDA Expedited Programs
Enhanced Early Agency Interaction	**Fast Track** Designation
Dedicated Agency Resources	**Breakthrough Therapy** Designation
Earlier Market Authorisation and Access	**Accelerated Approval** **Expanded Access**
Reinforced Scientific Advice	Fast Track Breakthrough Therapy Accelerated Approval Parallel EMA/FDA scientific advice (PSA)
Accelerated Review of MAA	**Priority Review** Designation • within 180 days (300 days standard)
Orphan Drug Designation	Affecting **< 200.000** people in the US • 7 years marketing exclusivity • tax credits/grants • common EMA/FDA application • Priority Review Voucher (paediatric)

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Overview of Early Access Regulation

Key Features	FDA Expedited Programs	EMA Support for Early Access
Enhanced Early Agency Interaction	**Fast Track** Designation	**PRIME** (Priority Medicines) **Adaptive Pathways** (AP)
Dedicated Agency Resources	**Breakthrough Therapy** Designation	**PRIME** early rapporteur
Earlier Market Authorisation and Access	**Accelerated Approval** **Expanded Access**	**Conditional Marketing Authorisation (CMA)** **Exceptional Circumstances** (Rarity, ATMPs) **Compassionate Use Opinion** (CHMP, MS) **Hospital Exemption** (ATMPs, Named Patient, MS)
Reinforced Scientific Advice	Fast Track Breakthrough Therapy Accelerated Approval Parallel EMA/FDA scientific advice (PSA)	PRIME and AP Parallel consultations EMA/HTA (EUnetHTA) Registries Initiative PSA
Accelerated Review of MAA	**Priority Review** Designation • within 180 days (300 days standard)	**Accelerated Assessment (AA)** • maximum 150 days (210 days standard)
Orphan Drug Designation	Affecting **< 200.000** people in the US • 7 years marketing exclusivity • tax credits/grants • common EMA/FDA application • Priority Review Voucher (paediatric)	Prevalence of not more than **5 in 10.000** • 10 years marketing exclusivity • centralised procedure • orphan specific scientific advice • reduced fees

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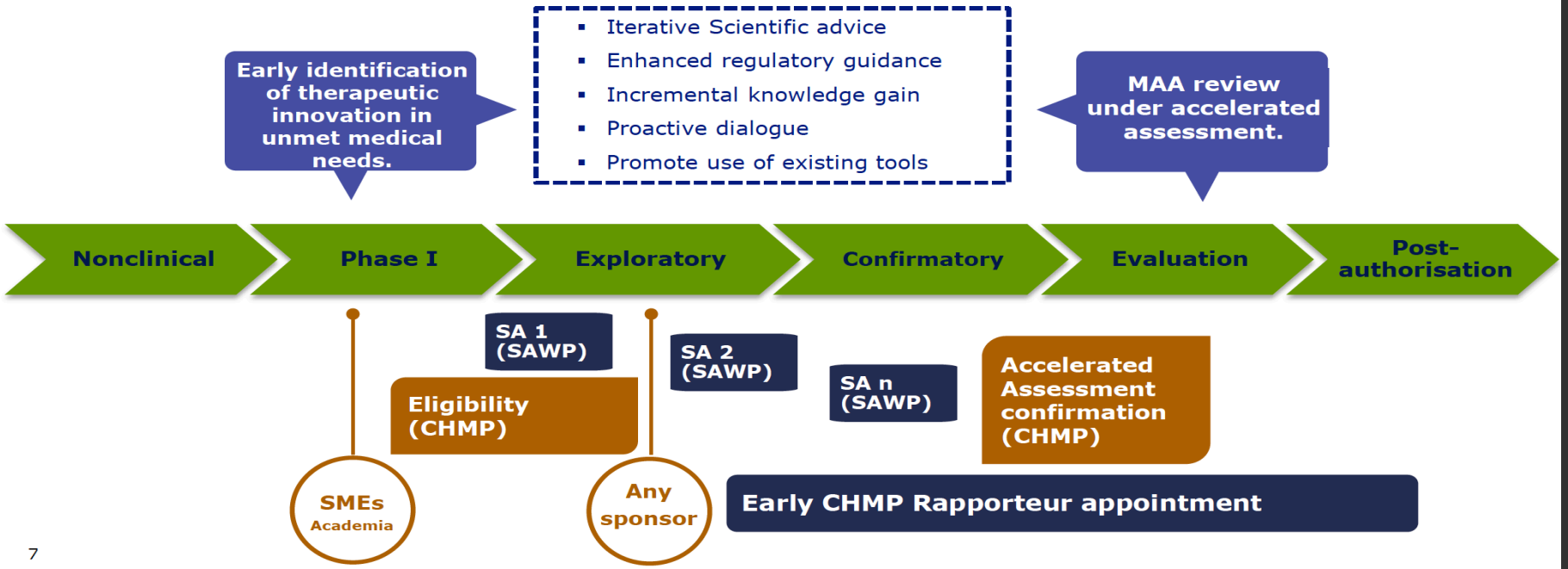
EMAs PRIME – Priority Medicines

EUROPEAN MEDICINES AGENCY

Overview of PRIME scheme



Source: Rob Hemmings, MHRA, SAWP chair, CHMP, Early Dialogue Presentation, 4th EMA-EuropaBio Information Day, 22 Nov. 2016

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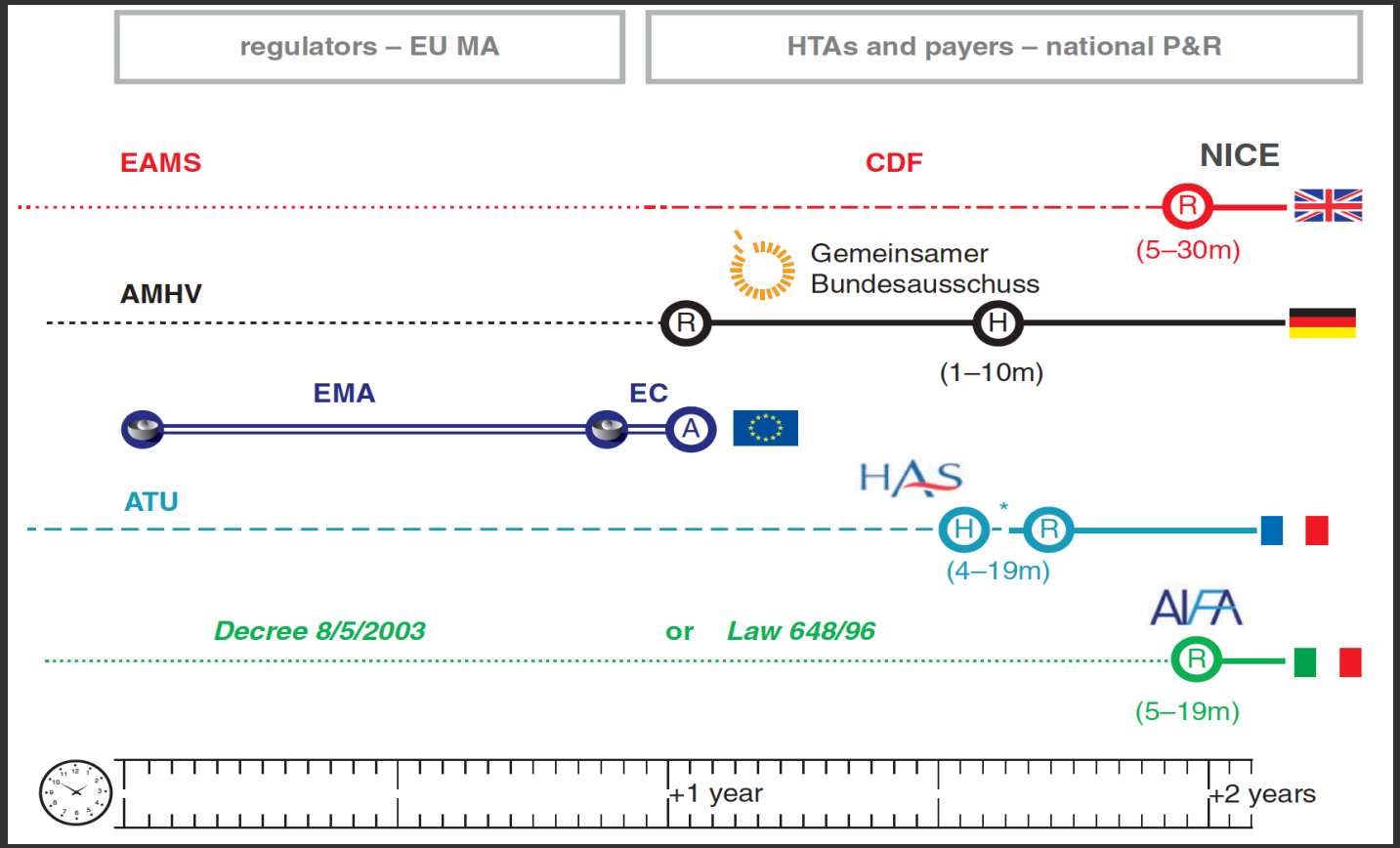
EU4 National Early Access Programmes



Source: Martinalbo J et al, Early market access of cancer drugs in the EU, Annals of Oncology 27: 96–105, 2016

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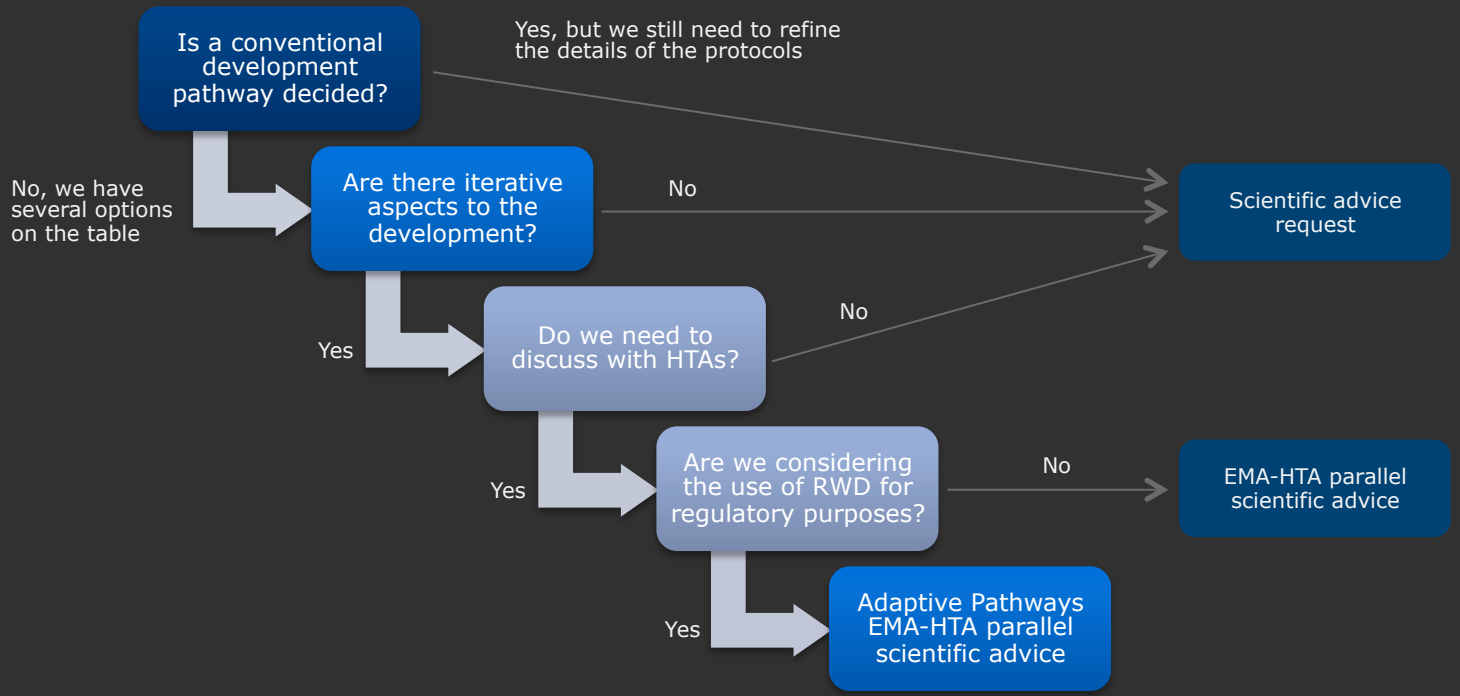
Eligibility for Adaptive Pathways



Source: EMA guidance for companies considering the adaptive pathways approach, August 2016

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EUnetHTA Forum, September 2017
Parallel EMA/multi-HTA Consultations

- One process, centrally coordinated trough 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

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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"

Source: the EMA's Adaptive Pathways Workshop, London, December 2016

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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)

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