



Innovative Medicines Initiative

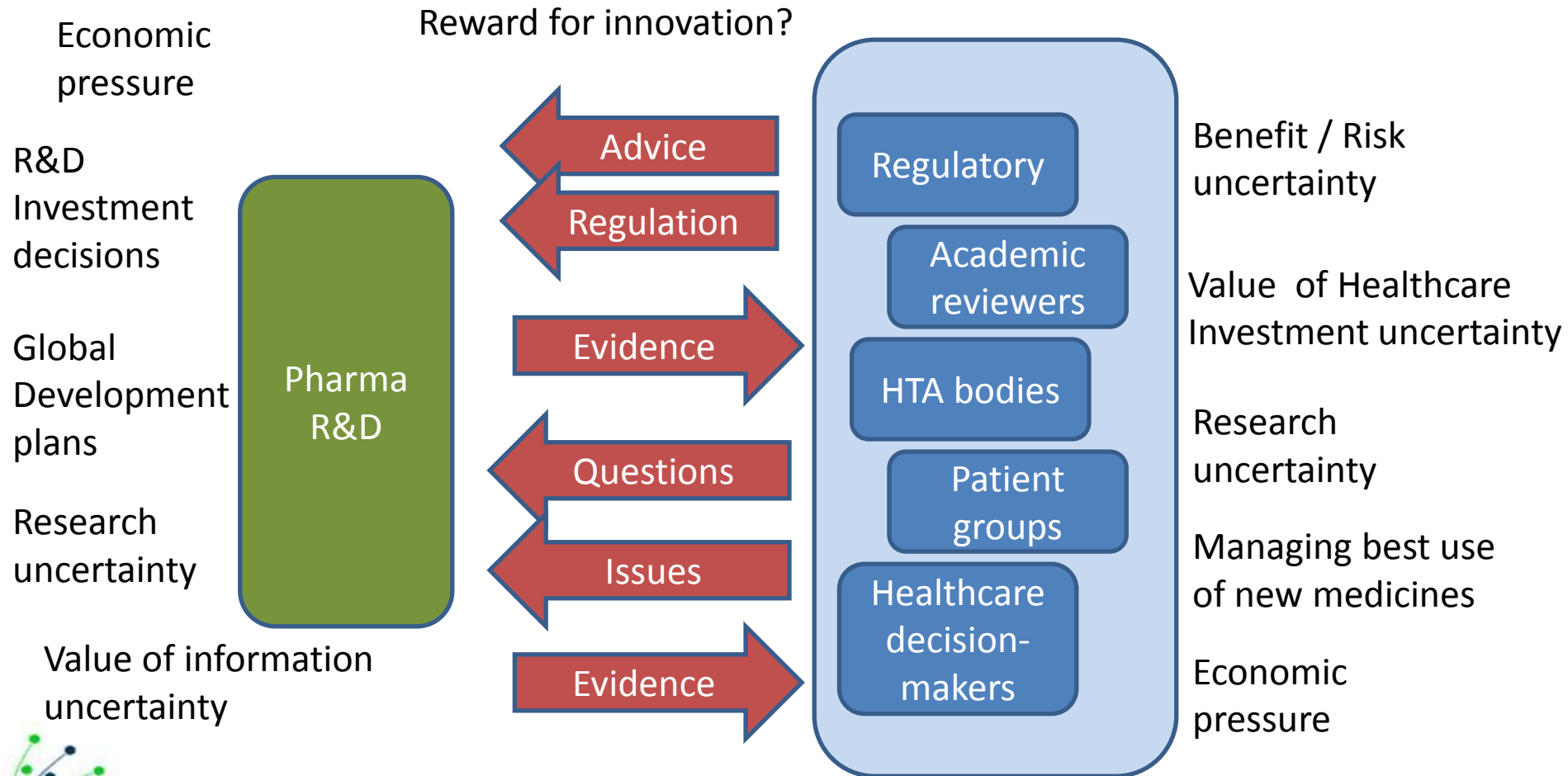
INCORPORATING REAL-LIFE CLINICAL DATA INTO DEVELOPMENT STRATEGIES

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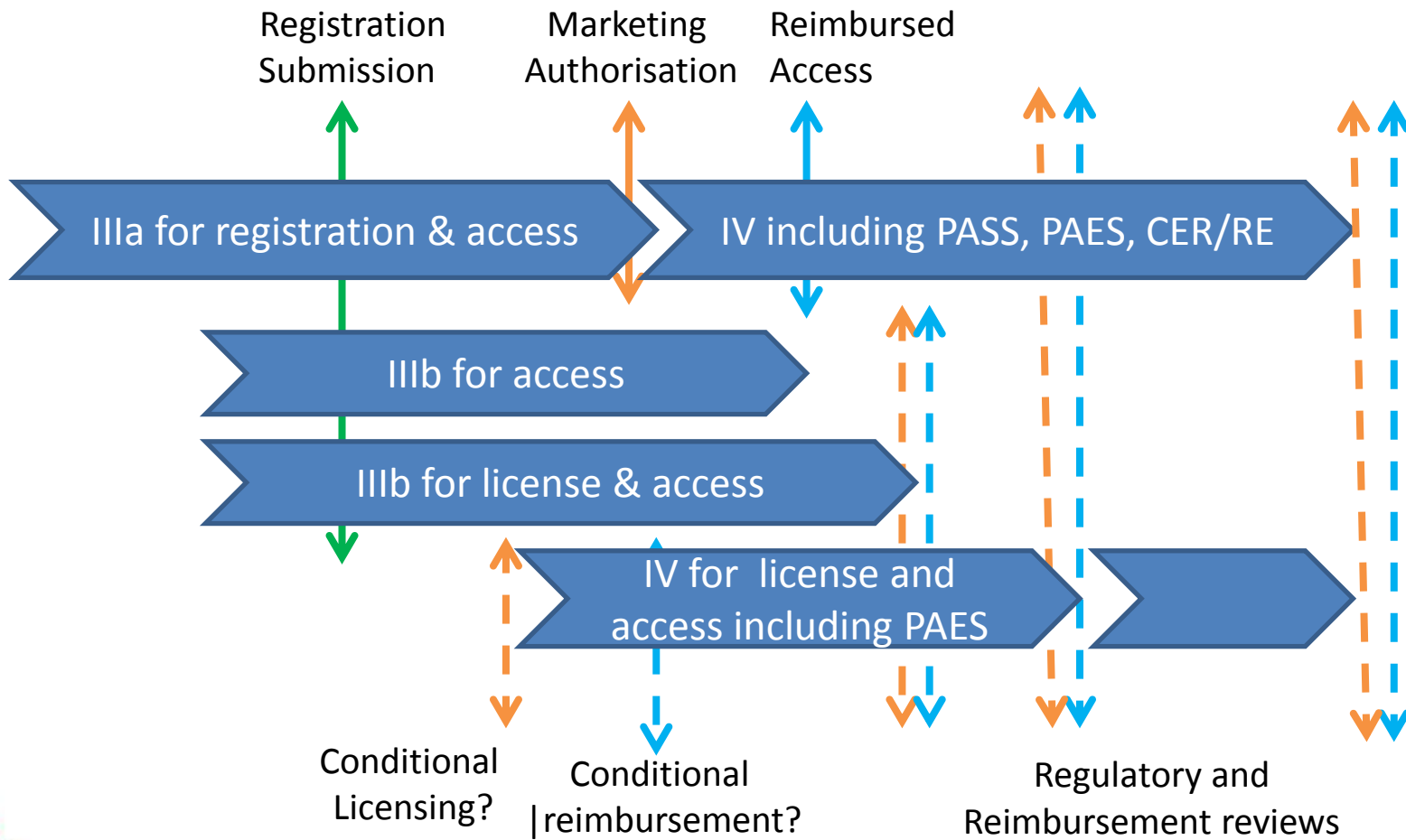


efpia*

Need for public-private collaboration



Continuum of evidence generation



Case Study: COPD

Uncertainty in IIIb pragmatic study



Strategic need:

The value of a new ICS LABA will be driven by effectiveness vs. existing drugs

Strategic uncertainty:

Required as Phase IIIb or phase IV?
How far to go in pragmatic design?
UK study acceptability in other EU countries?
Results for HTA and for promotion?
UK study impact on US launch?
Liability risks
Complication of EMA discussions?
Primary vs secondary endpoints?

Strategic Insight:

Joint scientific advice from NICE and MHRA confirms value to HTA

Operational uncertainty:

Finding high quality EHR
Primary / secondary / pharmacy linkage
Regulatory permission
Large study – safety and equipoise
Safety monitoring
Estimating size and power
Sufficient patients available / enrolled?
Quality control of data
Study drug supply
Training on new device
Consents

Analytical uncertainty:

Mixed comparator arm
Appropriate analysis plan
Transfer from UK to other countries
Integration with IIIa study results
Incorporation into c/e models

Objectives of the full project



- Assess existing methodologies and develop new research methodologies to improve the **quality of information** available to inform both benefit-risk and real world effectiveness at critical points in the assessments of medicines.
- Research **how and when** Relative Effectiveness research can be incorporated into R&D drug development plans
- **Identify research options**, including trial designs, endpoints and outcome measures that may be used in both clinical trials and observational studies
- Develop open tools to assess the value of new medicines which would **increase the confidence and consistency** of decisions that HTA bodies and other decision makers may take, affecting patient access and the ability for patients to benefit from new medicines



Objectives of the full project



- Develop **training activities** on relative effectiveness research, in particular on the value of new medicines to patients and providers, for a **better understanding and awareness** in R&D
- Identify research issues and develop pragmatic designs to **address difficulties** associated with generating evidence of relative effectiveness before launch
- Develop and pilot approaches to **analyse and incorporate the results of effectiveness studies** in evidence reviews to foster discussions/decisions between industry, regulatory authorities, HTA and reimbursement agencies on
 - **reasonable expectations for evidence available at launch,**
 - **the robustness of predictive models**
 - **the value of further evidence collected after launch.**



Pre-competitive nature



- The EFPIA companies recognise that a single set of standards and guidance is required for their collective interactions with the regulatory, HTA and reimbursement authorities.
- Work on specific case studies and disease areas may be used by all companies with development programmes in those disease areas, but will also be used to establish general principles that can be applied to other disease areas



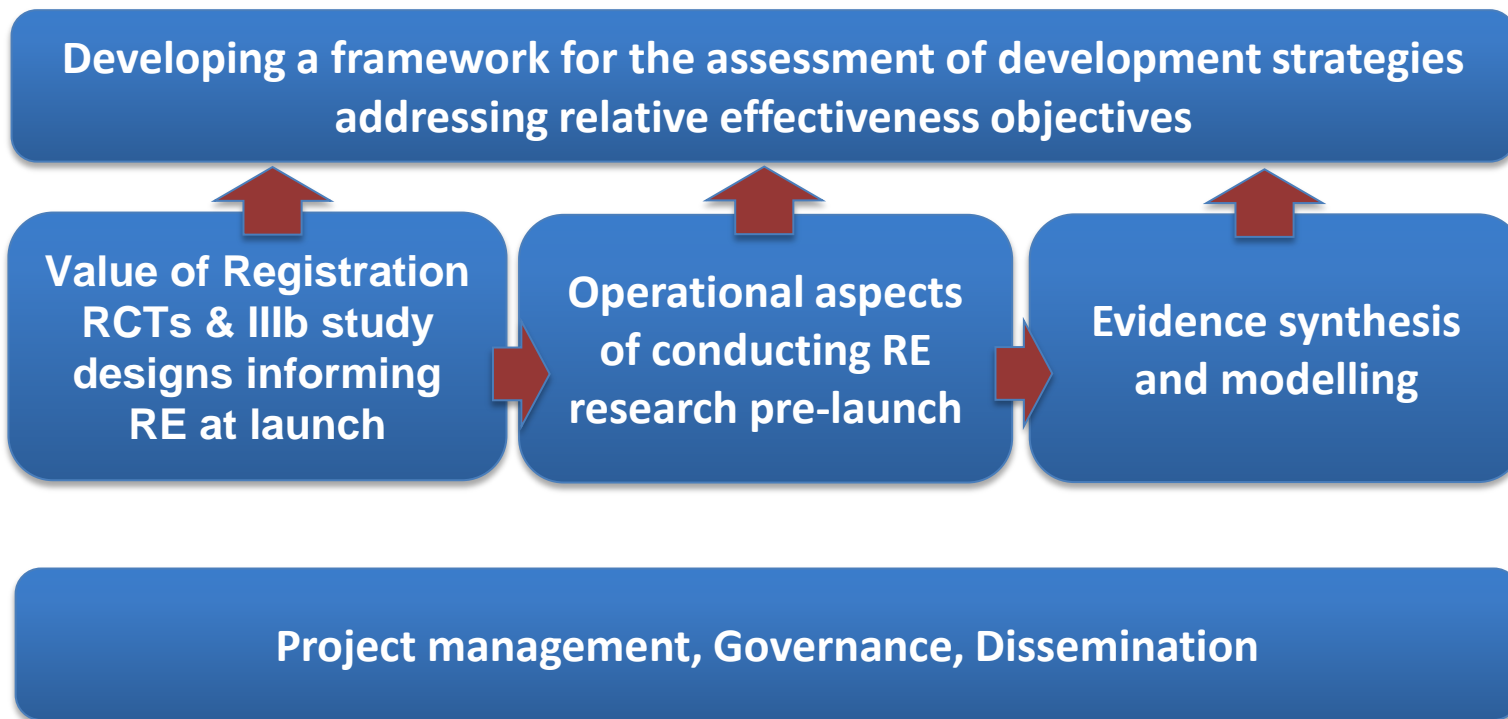
Expected impact on the R&D process



- Consistent scientific advice from multi-stakeholder interactions
- More certainty in R&D decision making when considering alternative development strategies / regulatory approval options
- More effective investment in evidence of value to regulatory and HTA assessments; with a balance between pre and post-launch research
- No intention to increase the cost and burden of evidence required for the initial **regulatory** approvals; any increase in research cost for **access** approval is an investment decision.



Suggested architecture of the project



Expected contributions of the applicants



- A multi-disciplinary grouping, enabling effective communication between key stakeholder groups (international academia, regulatory agencies, HTA bodies, reimbursement agencies, healthcare budget holders, and patient groups).
- Pan-European in nature to ensure frameworks and procedures developed through the course of the project are relevant for a broad range of European countries.
- Expertise in
 - Clinical trial design, health economics, modelling, regulatory affairs, HTA, disease management, patient and carer experience, medical ethics, strategic decision making
- Access to local effectiveness databases in their countries (e.g. from sickness funds, primary care consortia, registries)



Expected (in kind) contributions of EFPIA members



- Dedicated time from the following expert groups:
 - Health Economics / HTA policy
 - Regulatory Affairs
 - Bio-statistics
 - Epidemiology
 - Clinical Trial Operations
 - Clinical specialists
- Clinical trial datasets
- Observational / Epidemiology datasets
- Insights from previous regulatory and HTA interactions



What's in it for you?



- Regulatory and HTA agencies would benefit from the increased quality and relevance of evidence provided to them by Pharma R&D at initial assessments, and from an increased alignment of expectations for evidence generation before and after marketing authorisation.
- Academic researchers and SMEs would benefit from being able to work with both evidence providers and evidence users; from collaboration with a network of experts; and from access to research datasets
- Patients would benefit from any improvement in access to new medicines; from the improved relevance of evidence to their actual clinical experience; and from the opportunity to engage and influence developers and assessors of new medicines.
- Healthcare providers would benefit from the increased relevance of clinical evidence to everyday clinical practice and decision making, and from the opportunity to influence both evidence providers and assessment bodies.



Key deliverables of the full project



- Analysis of the “relative effectiveness questions” relevant to different stakeholders; and of relevant comparators chosen by HTA agencies in different countries and the reasons for these choices
- Development of a decision-making framework for the systematic identification and assessment of different development strategies; considering:
 - The incremental value of information from a study programme in the estimation of relative effectiveness at launch and after launch
 - Technical and practical issues related to different designs
 - Interaction with regulatory, HTA and other review processes.
- a “toolbox” of study designs in specific disease areas classified according to their best fit in the drug development timeline:
 - Clinical trials that meet regulatory requirements for IIIa evidence and also address relative effectiveness questions;
 - Clinical trials that would not be suitable to address regulatory requirements, but would inform relative effectiveness questions and are feasible pre-launch IIIb studies
 - Clinical trials that are not feasible pre-launch but could address relative effectiveness questions as post launch studies including HTA and regulatory commitments (eg PAES)



Key deliverables of the full project



- A “hierarchy of evidence” for relative effectiveness (including trials and models) to indicate the robustness of the evidence in assessing a medicine’s value in real world use.
 - Clinical trial designs that address factors most responsible for differences between efficacy and effectiveness; characterised in terms of their internal/external validity and transferability
 - Analyses predicting RE from phase II and III RCT efficacy studies alone
 - Analyses integrating RCTs, additional relative effectiveness studies and observational data
 - Analyses that predict relative effectiveness in one country from data on relative effectiveness derived in another
 - Development and validation of tools for assessing and choosing comparators
 - Development of guidance in specific disease areas on the operational & practical implementation of real world research methods and modelling techniques pre-launch (with input from regulatory and HTA agency endorsement)
 - White papers, results of pilot studies and scientific publications
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Questions?



- Contact the **IMI Executive Office**

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