Patient input into benefit/risk issues during evaluation

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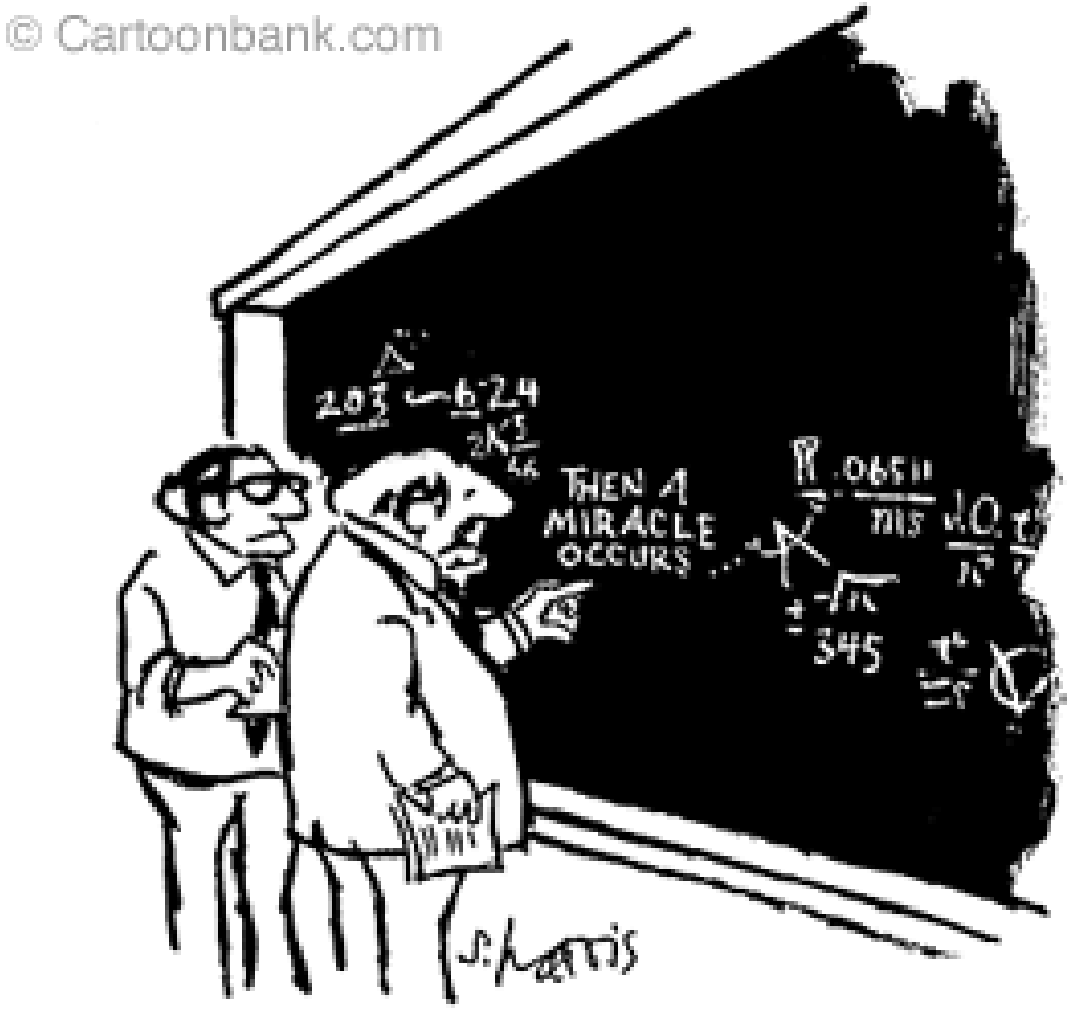
What is the problem?



"I think you should be more explicit here in step two."

What are the challenges we need to overcome?

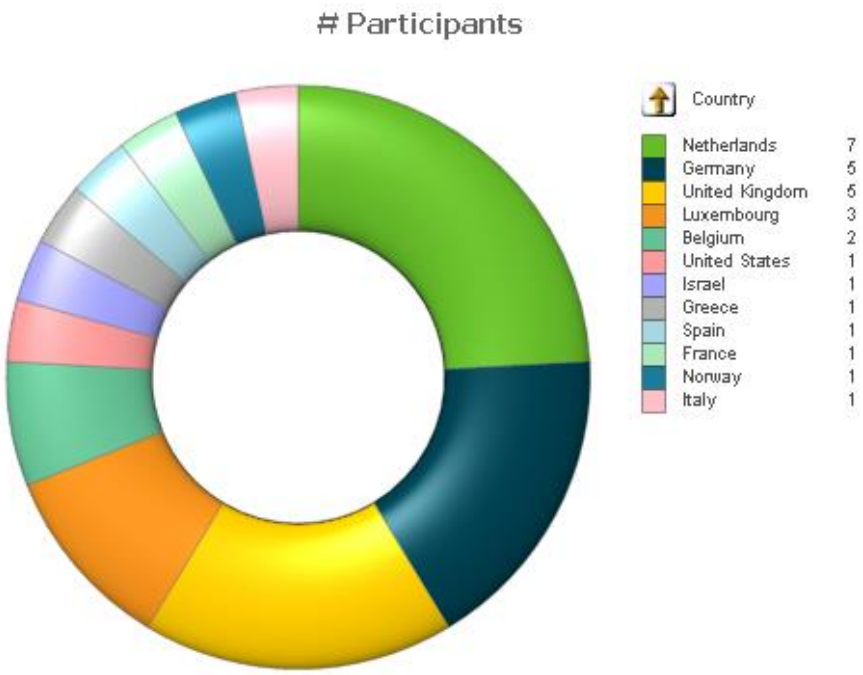
- Patients are all different and have different tolerance for risk: how to get a “representative view” and what does this mean?
- How do we manage potential conflict of interests?
- What tools/methodologies do we need to develop to improve patient input? When do we need their input?
- Patient disease knowledge and expertise is required : how do we manage this for all diseases?
- What is the role of Regulators to equip patients to input (eg Regulatory processes, confidentiality issues, etc)
- How does patient input actually impact the licensing decision? How should the patient voice be balanced with that of the regulators and other stakeholders?
- What is the involvement of patients in post-launch regulatory requirements?

Conclusions and next steps

- Strong and informed patients' voice should be a key input into Regulatory decisions
- Effective patient engagement continues to be an evolving science
- Mechanisms are needed to ensure the system delivers to patient needs
- Increased dialogue between Regulators, Patients, Industry and other stakeholders is needed to move constructively forward
  - We need a working party to address the key questions
  - We should explore opportunities under IMI

IMI: Patient involvement in collaborative research

- Input into scientific priorities: IMI Scientific Committee
- Idea generation: IMI scientific challenge workshops
- Participation in projects
  - Planning and execution
    - EUPATI – patient empowerment
    - U-Biopred – patient reported outcomes
    - PROACTIVE – patient voice in benefit/risk evaluation
  - Advisory and ethics boards
- Consultations on strategic priorities for IMI2: consultations since June 2012



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Examples of IMI PPP Patient-Centric Initiatives

PRO active

- **Development of Patient Reported Outcomes that**
  - measure aspects of physical activity relevant to patients and
  - are sensitive to changes due to treatment.
- 8 EFPIA companies; 7 Public organizations; 1 SME; 3 patient org;
- Total Budget: 16.7 Mi €

- Established diagnostic criteria on severe asthma
- Biomarkers for Predicting Severe Asthma Outcome
- 9 EFPIA companies; 21 Public organizations; 3 SME; 5 patient org;
- Total Budget: 20.1 Mi €

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Translate science into research, regulatory and medical practice

COMMENT

Priorities for improving drug research, development and regulation

Susan R. Forda, Richard Bergström, Magda Chlebus, Richard Barker and Peter Høngaard Andersen

Improved R&D models, supported by appropriate regulatory pathways, are needed to provide new drugs with greater efficiency, in a framework that is financially viable for all stakeholders. Here, we present the perspective of the European Federation of Pharmaceutical Industries and Associations on the key areas on which to focus to achieve this.

The standard model of drug research and development (R&D) is becoming less financially viable owing to factors such as the unsupportable growth in the cost of drug development, a regulatory environment that does not yet reflect the latest scientific advances and uncertainties over price and reimbursement. There has been much debate about these causes and possible solutions, and, indeed, many consortia and study groups have been formed. However, most have lacked the political legitimacy, integrated vision of reforms and/or long-term commitment to drive change. With this in mind, members of three of the European Federation of Pharmaceutical Industries and Associations (EFPIA) policy committees — the Scientific, Regulatory and Manufacturing Policy Committee, the Research Directors Group, and the Intellectual Property Policy Committee — held roundtable discussions on R&D models and regulatory pathways, the output of which forms the basis for this article. Although many ideas have been proposed to improve drug R&D and regulation, we contend that a concerted focus on the following seven themes would lead to the greatest advances.

Proposals

Redefine diseases by their underlying molecular mechanisms. One proposal that would improve R&D effectiveness, as well as reduce treatment costs, is to redefine diseases on the basis of their molecular characteristics rather than just symptoms[1]. Indeed, enhanced understanding of molecular defects in some diseases is gradually being translated into clinical advances; for example, in the diagnosis and treatment of breast cancer based on biomarkers such as positivity for the oestrogen receptor and the human epidermal growth factor receptor 2.

An example demonstrating the potential of applying such knowledge is the cancer diagnosis and treatment access programme operated in France by the National Cancer Institute (NCI) and the Ministry of Health. Since 2006, this programme has carried out molecular testing of patients with cancer to identify those who will benefit most from the latest targeted therapies. This has improved patient survival and quality of life, and resulted in cost savings (see a report from the NCI (20 May 2011) for more details). We propose to accelerate the process of disease redefinition through a targeted Innovative Medicines Initiative (IMI) programme.

Adapt regulatory frameworks to new science. In general, regulatory processes need to be adapted to scientific advances; for example, through improving the regulatory framework for companion diagnostics. It is particularly important to address this soon, as the lack of regulatory guidance is commonly cited by companies as a reason hampering the development of more personalized medicines. We propose that regulators, patients, and pharmaceutical and diagnostic industry representatives collaborate to develop a better framework for personalized or stratified medicine development and approval.

Develop new trial design and statistical methods. There is considerable interest in novel trial designs that could help reduce the high failure rate of late-stage clinical trials. An important aspect of these designs is the use of adaptive approaches, such as those based on Bayesian methodology, which can be used to more fully harness knowledge from outside the trial. Moreover, these designs can adapt an ongoing trial in response to information emerging from it (such as which doses might be more effective) while maintaining statistical rigour[2]. This can be especially useful if the sample size is limited, as may be the case if patient populations are increasingly stratified by various biological characteristics.

Reasons that adaptive designs are not currently used more widely include the complex methods and specialized software required, and we propose that further

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- Medicines Adaptive Pathways to patients
- Novel Clinical Trial Design
- Patient-centric Benefit/Risk evaluation
- Regulatory Science
- Operational excellence
- Global dimension

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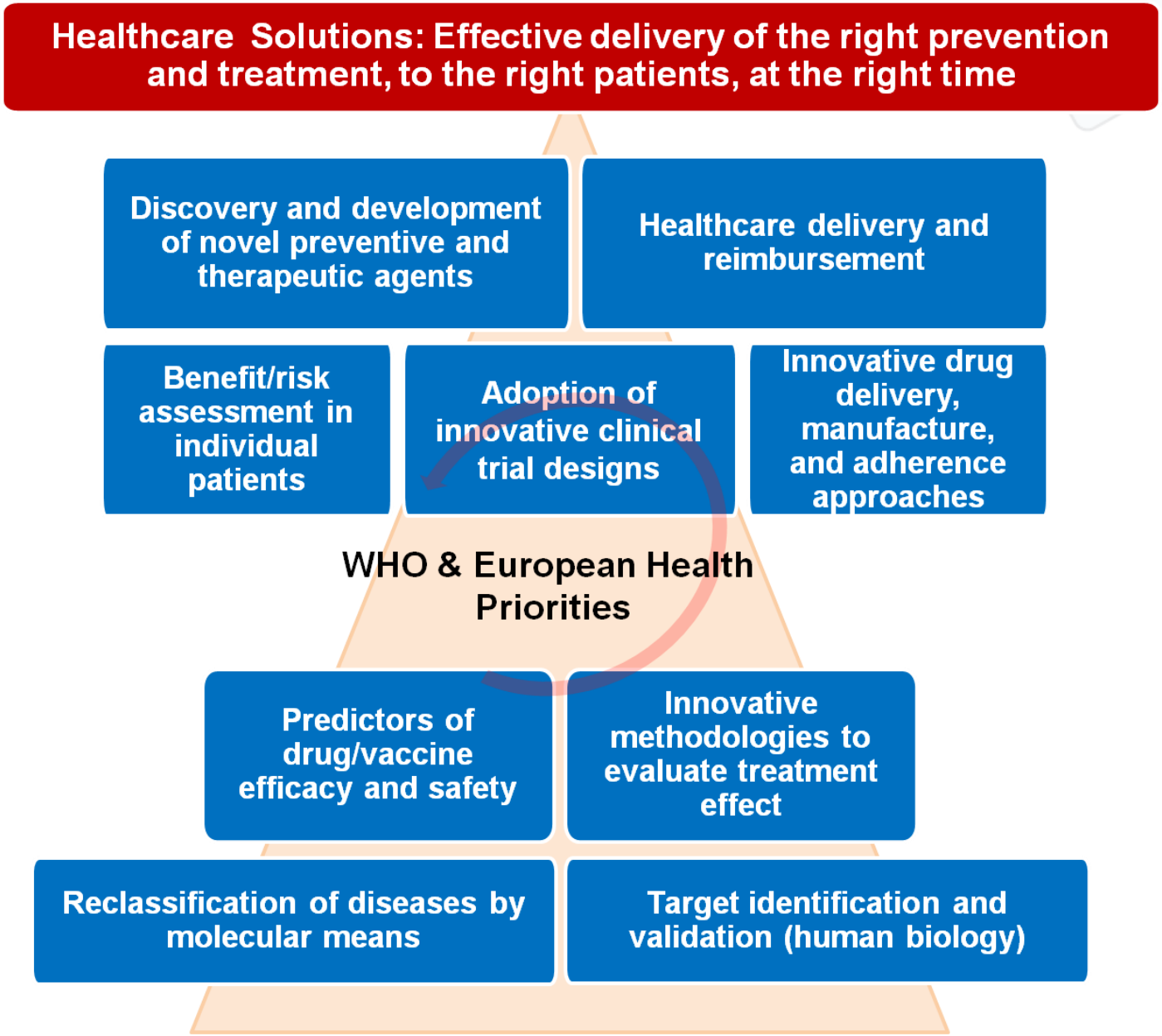
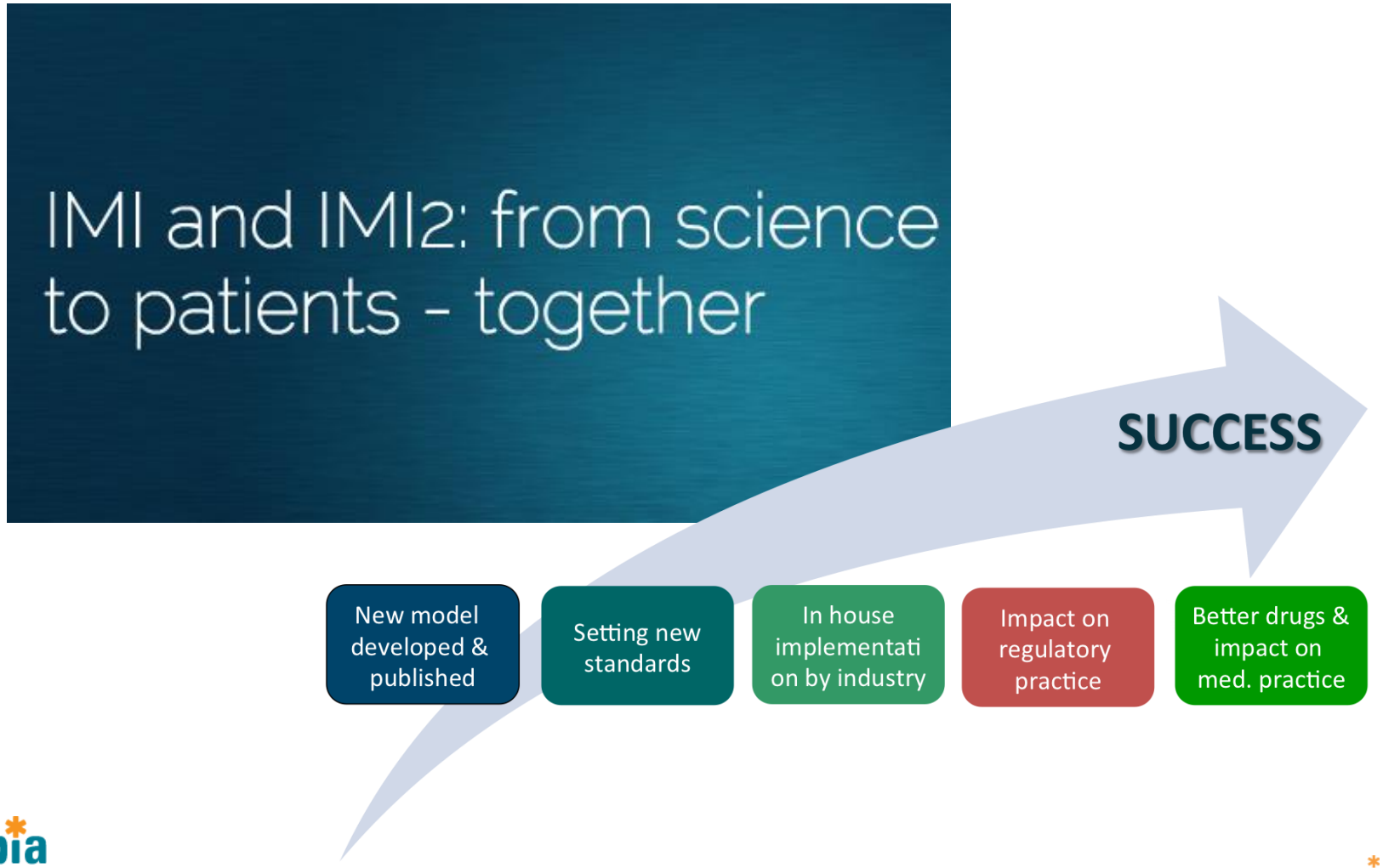

Healthcare Solutions: Effective delivery of the right prevention and treatment, to the right patients, at the right time
Discovery and development of novel preventive and therapeutic agents
Healthcare delivery and reimbursement
Benefit/risk assessment in individual patients
Adoption of innovative clinical trial designs
Innovative drug delivery, manufacture, and adherence approaches
WHO & European Health Priorities
Predictors of drug/vaccine efficacy and safety
Innovative methodologies to evaluate treatment effect
Reclassification of diseases by molecular means
Target identification and validation (human biology)

Right medicine, for the right patient, at the right time …



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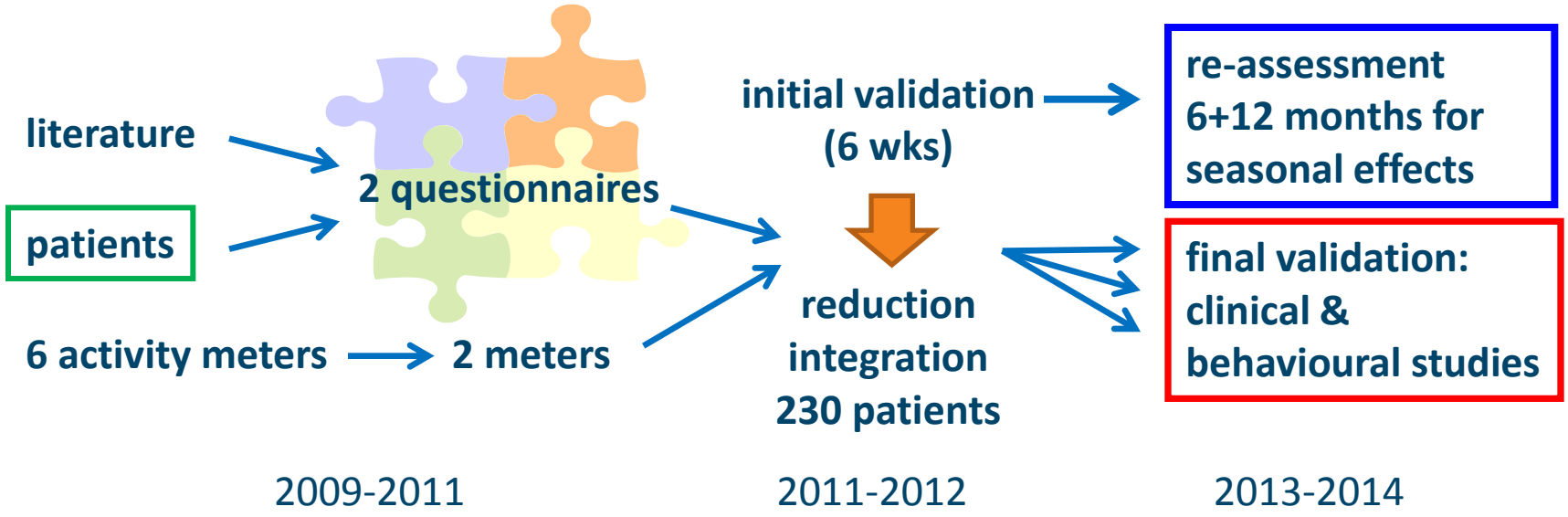
BACK-UP SLIDES

Development of tools to measure physical activity status in COPD

8 EFPIA companies; 7 Public organizations; 1 SME
3 patient org; Total Budget: 16.7 Mi €

Aim: development of Patient Reported Outcomes that

- measure aspects of physical activity relevant to patients and
- are sensitive to changes due to treatment.



PROactive: results and impact

- ✓ PROactive instruments to evaluate physical activity will be used in addition to existing scales

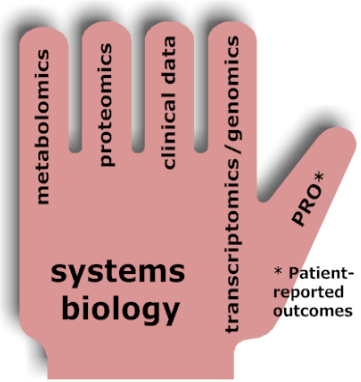
- ✓ PROactive instruments will allow patients to:
  - better describe their experience of physical activity to themselves and their treating physicians
  - help the assessment of novel therapies for COPD
  - and contribute to individualised treatments including self management

Biomarkers for Predicting Severe Asthma Outcome

U-BIOPRED

9 EFPIA companies; 21 Public organizations; 3 SME
5 patient org; Total Budget: 20.1 Mi €

- ✓ Established diagnostic criteria on severe asthma
- ✓ Developed various “omics” platforms based on genetic, proteomic, metabolomic, breathomic biomarkers
- ✓ Generated a preliminary phenotype ‘handprint’ by combining molecular, histological, clinical and patient-reported data
- ✓ **Patient cohort - 14 centres across Europe targeting 1025 subjects, to validate the handprints for their predictive efficacy in gold standard and experimental therapeutic intervention**



THORAX
An International Journal Of Respiratory Medicine

Diagnosis and definition of severe asthma: an international consensus; Bel et al., 2011

CHEST

An integrative system biology approach to understanding pulmonary diseases; Auffray et al., 2010