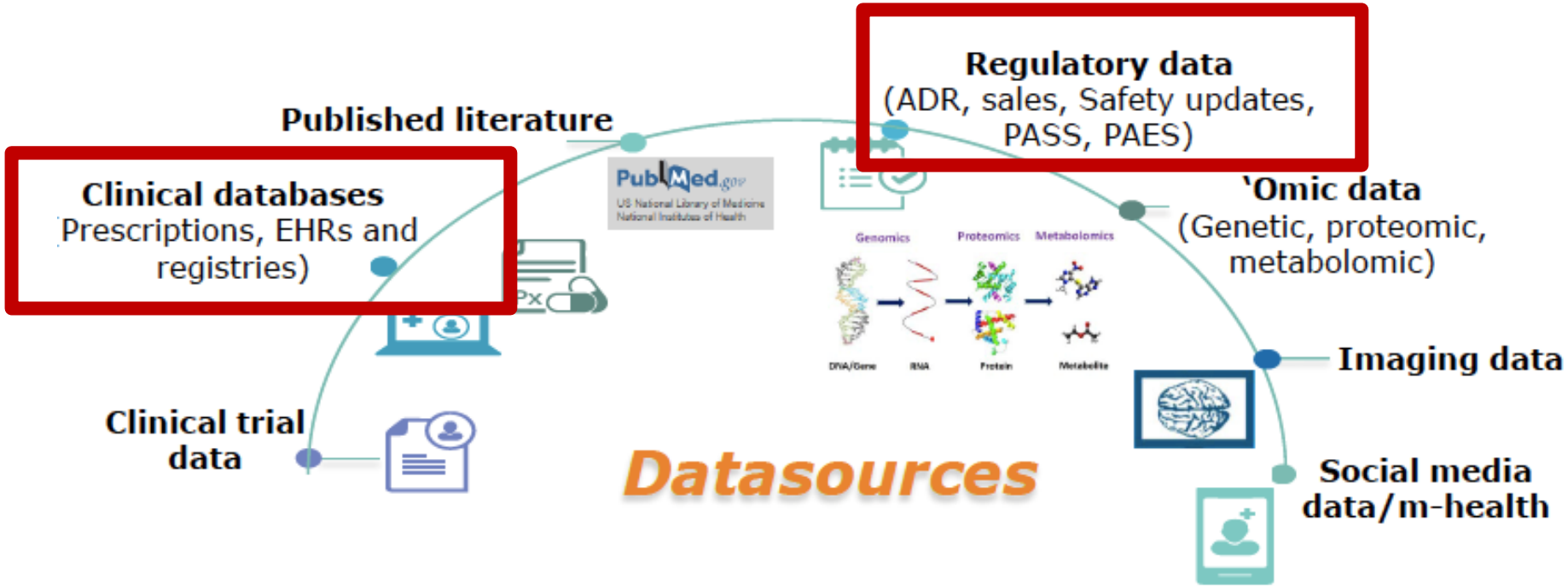
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Real world evidence (data) in CAT decision making

Kieran Breen
Committee for Advanced Therapies
Registries Working Group

The data landscape



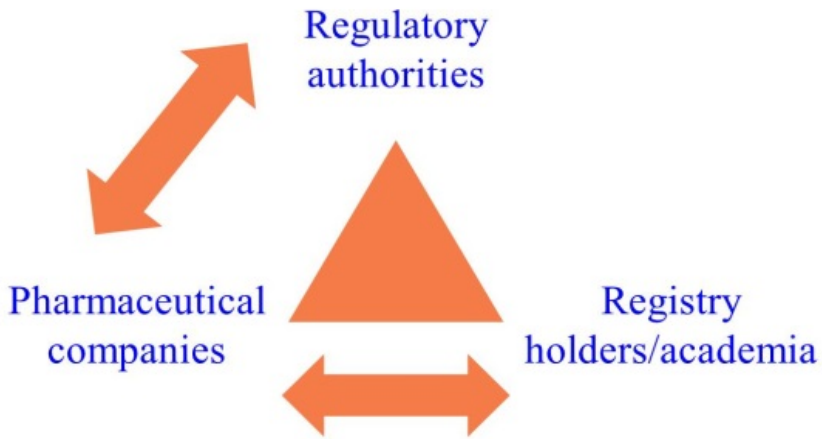
4

Patient registries

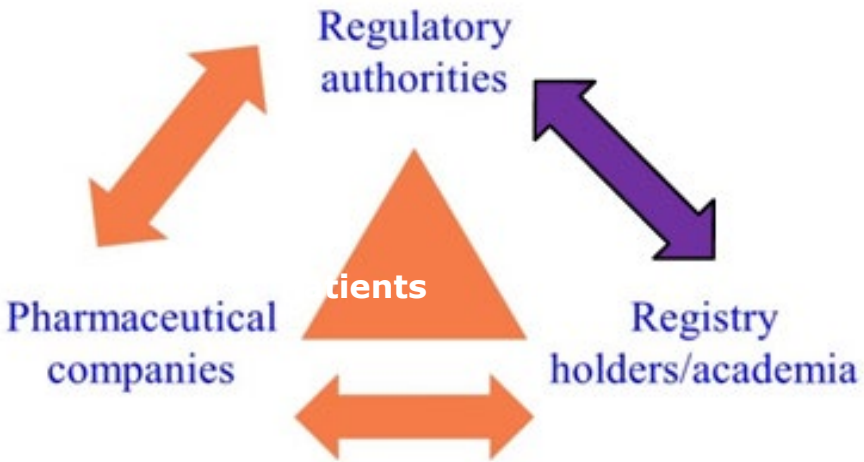
- Use observational methods to collect uniform data on a population **defined by a particular disease**, condition, or exposure followed over time.
- A patient registry is established primarily by a **clinician or a patient/consumer organisation**.
- Clinical **information is collected over time** and samples (e.g. blood specimens) may also be collected.
- Patients need to be aware of what information is being collected, **how it will be used and by whom**
- Make valuable contributions to the **evaluation and monitoring of medicines for public health benefit**, especially in relation to their safety

Interactions between regulators and registry holders

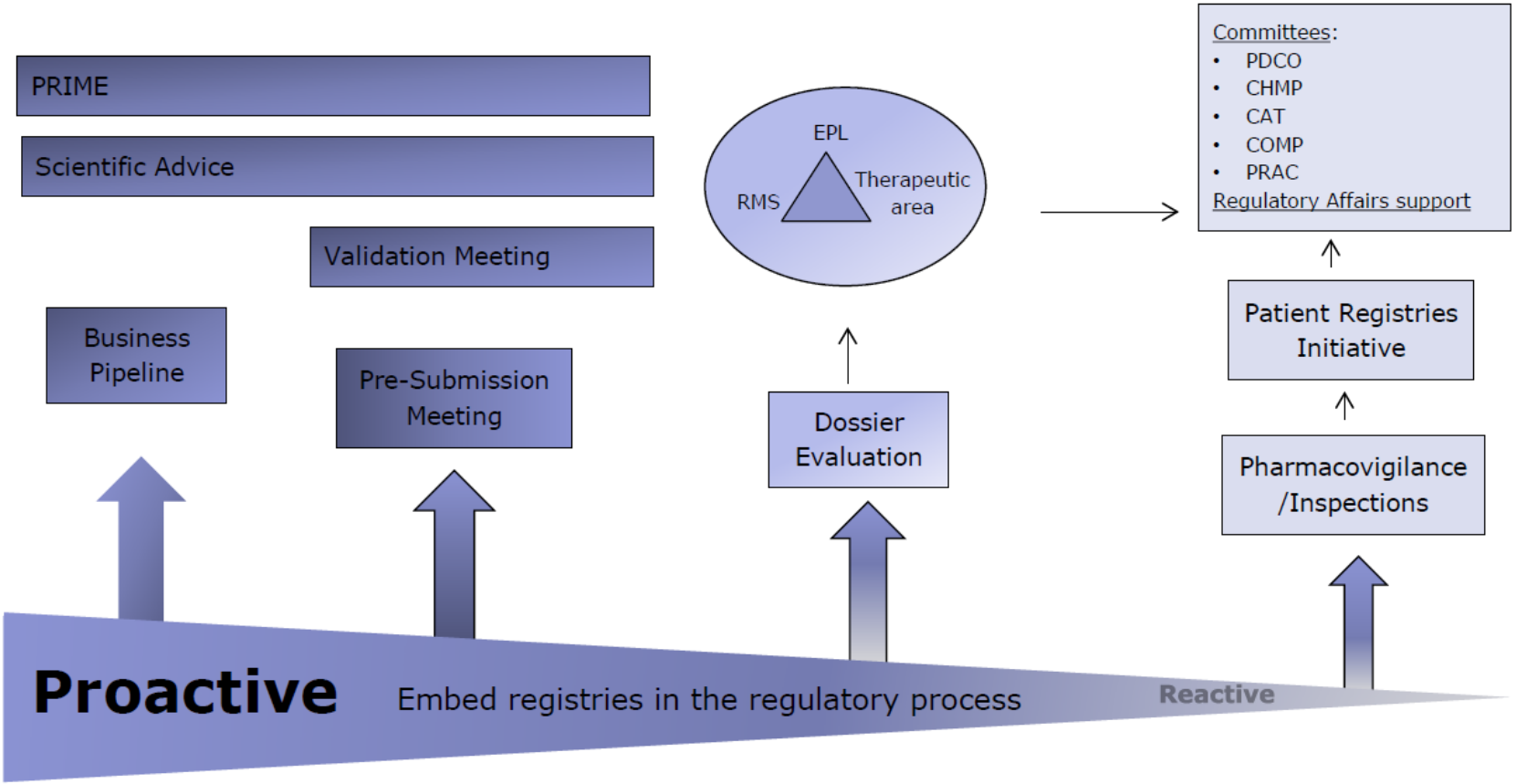
Previous…'the broken triangle'



Future…MORE COOPERATION



Registries in the regulatory process



Opportunities for Real World Evidence

Development

- Characterisation of **disease progression** or **natural history** (especially for rare/orphan diseases and areas of unmet need)
- Use of registries for **control population data in single-arm trials** with limited population numbers
- Understanding **current clinical practice**/standard of care
- Identification of **sub-populations** suitable for specific treatment approaches
- Validation of **surrogate endpoints**

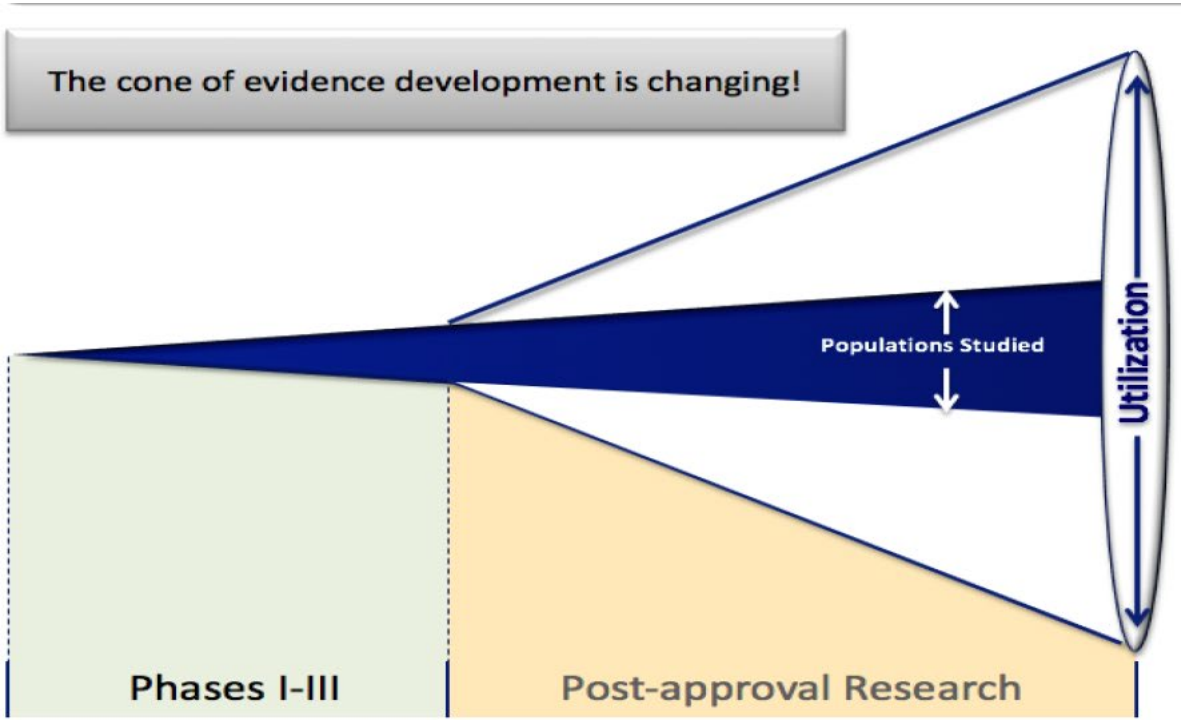
Authorisation

- Open label studies with existing registries
- Benefit/risk
- Design of PAES/PASS based on existing/new registries
- Risk management activities to address uncertainties
- Comparative effectiveness studies

Post-authorisation

- Assessing long-term efficacy and safety (ATMP regulations)
- Pragmatic clinical trial/registry studies
- Understanding patient subgroups
- Collecting patient-reported outcome including quality of life metrics
- Satisfy HTA and payers needs, outcomes-based reimbursement

Real world evidence – follow up



Variances in populations utilizing technology versus the populations studied

- Differing age groups (elderly, pediatrics)
- Race, ethnicity & gender variances
- Unstudied co-morbid conditions
- Differing concomitant drugs (including OTC)
- Lifestyle variances including smoking, dietary habits
- Differences in disease severity
- Varying levels of compliance

Use of Real World Data in ATMP Regulatory Decision Making 2018 - current

Pre-authorisation / submitted at marketing authorisation

- RWD were provided in 7/7 marketing authorisations
  - 6 of 7 single arm pivotal trials
  - 1 of 7 randomized controlled pivotal trial
  - Retrospective observational treatment data, or
  - Retro/prospective observational data to inform on natural course of disease
- Opportunity to support single arm trial data, provide context
  - Approach as outlined in ICH10 for external controls
  - Good quality patient level data, pre-specified matching, etc.
  - Same considerations as for non-ATMPs

Use of Real World Data in ATMP Regulatory Decision Making 2018 - current

Post-authorisation

- Prospective observational data acc. to agreed protocol, focus safety or efficacy, PASS or PAES imposed in 7/7 MA
- Disease registries are the most frequently used data source
  - 3 of 7 RWD -> existing EU wide disease registry
  - 1 RWD -> global disease registry supported by MAH
  - 1 RWD -> disease registry and a product registry
  - 1 RWD - > product registry
  - 1 -> "identification of a suitable registry" requested

The use of Real World Evidence for ATMPs

Registries

- Which registries are available for use by the company?
- What is the quality and suitability of these registries?
- Are the outcomes of interest when comparing with the single arm trial being validated?
- Would the same conclusions be reached using different registries?

Contextualise/evaluate representativeness of patients in the trial?

- Evaluate whether there is similar age distribution, gender, severity of underlying illness, comorbidities with the target population
- Evaluate whether patients in the registry are comparable with patient in the single arm trial

Real World Evidence for ATMPs

Clinical management

- Clinical management (standard of care and off-label) and the impact of the gene therapy and other treatments on course of disease, adverse events
- Evaluate the standard of care treatment outcome

Natural history of disease

- As diagnosis and treatments are changing quickly, new data on the disease and its progression are useful
- Incidence and influencing factors for disease outcomes

Operational

- Learn about doing studies on registries: how to engage them, how to assess data quality

Multiple existing registries e.g SMA

EUROPEAN MEDICINES AGENCY

	Numbers/countries	Data elements	Data collection
MDA US	Launched in 2013 4 diseases 2700 patients 26 centres in US	Wide range of clinical data from individuals seen in MDA Care Centers including diagnostic tests, clinical measures and interventions	Only by physicians or study coordinators
iSMAC	900 patients UK, Italy and US sites	Baseline characteristics and longitudinal data on treatment patterns, motor function, respiratory function, hospitalisations, and comorbid.	Physicians
Treat-NMD	Launched in 2007 5000 patients 26 national patient registries across 29 countries (20 countries in Europe)	SMA core dataset	Data self reported and/or provided by HCPs
SMArtCARE	2017 1000 patients 50 centres across Germany, Austria and Switzerland	Aligned with the international consensus for SMA registries (TREAT-NMD, iSMAC).	Physicians
Cure SMA	600+ patients 19 centres in US	Baseline characteristics, lab Test(s), Vital Signs, Procedures, Motor Function Scales…	Data self reported and provided by HCPs

Thank you!