EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Overview of one-year experience of PRIME eligibility assessment

First anniversary of PRIME: experience so far, 19 May 2017

Presented by Robert Hemmings
SAWP chair

Eligibility to PRIME scheme

Based on Accelerated Assessment criteria

Medicinal products of major public health interest and in particular from the viewpoint of therapeutic innovation.

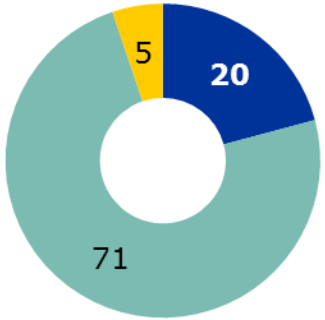
- Potential to address to a significant extent **an unmet medical need**
- Scientific justification, based on data and evidence available from nonclinical and clinical development

No satisfactory method or if method exists, bring a major therapeutic advantage

Introducing new methods or improving existing ones

Meaningful improvement of efficacy (impact on onset, duration, improving morbidity, mortality)

One year of PRIME



■ Granted ■ Denied ■ Out of scope*

22% success rate

108 requests received

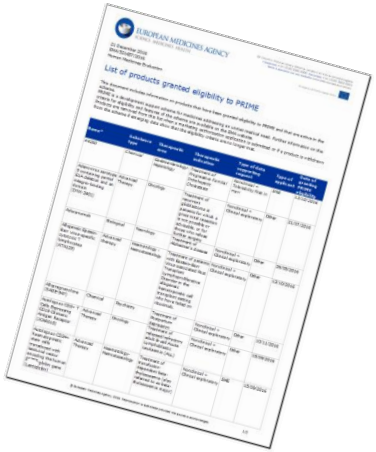
> 90 eligibility requests assessed

> 50% from SMEs

20 granted*

+

Publication of report and list of products on EMA website



PRIME over time

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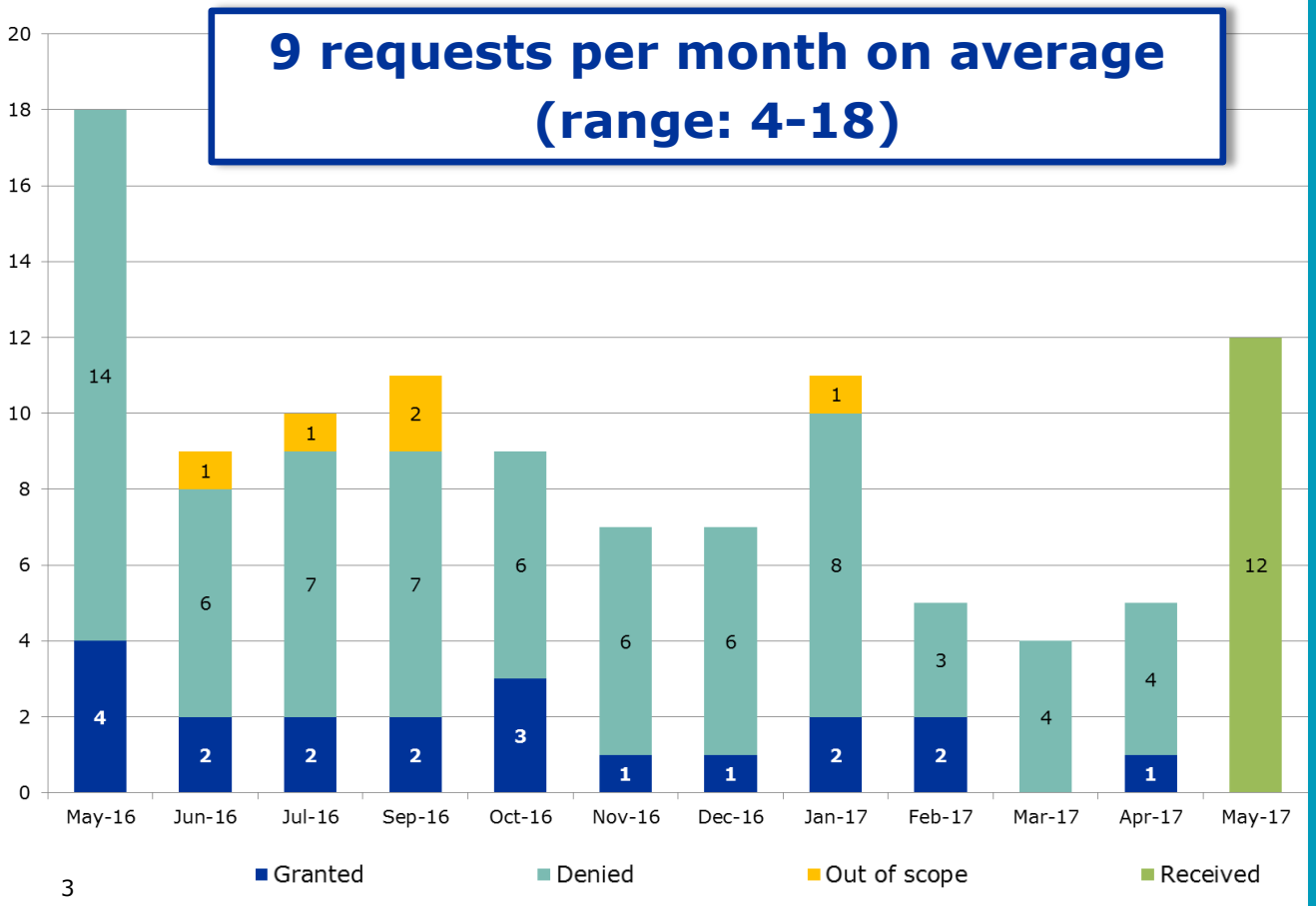
9 requests per month on average (range: 4-18)



Good quality of applications

Few 'out of scope' applications

- Academic or SME with no FIM data
- Non-SME with no exploratory data
- Issue with definition as medicinal product
- Resubmission with no new data

Requests covering wide range of therapeutic areas and product type

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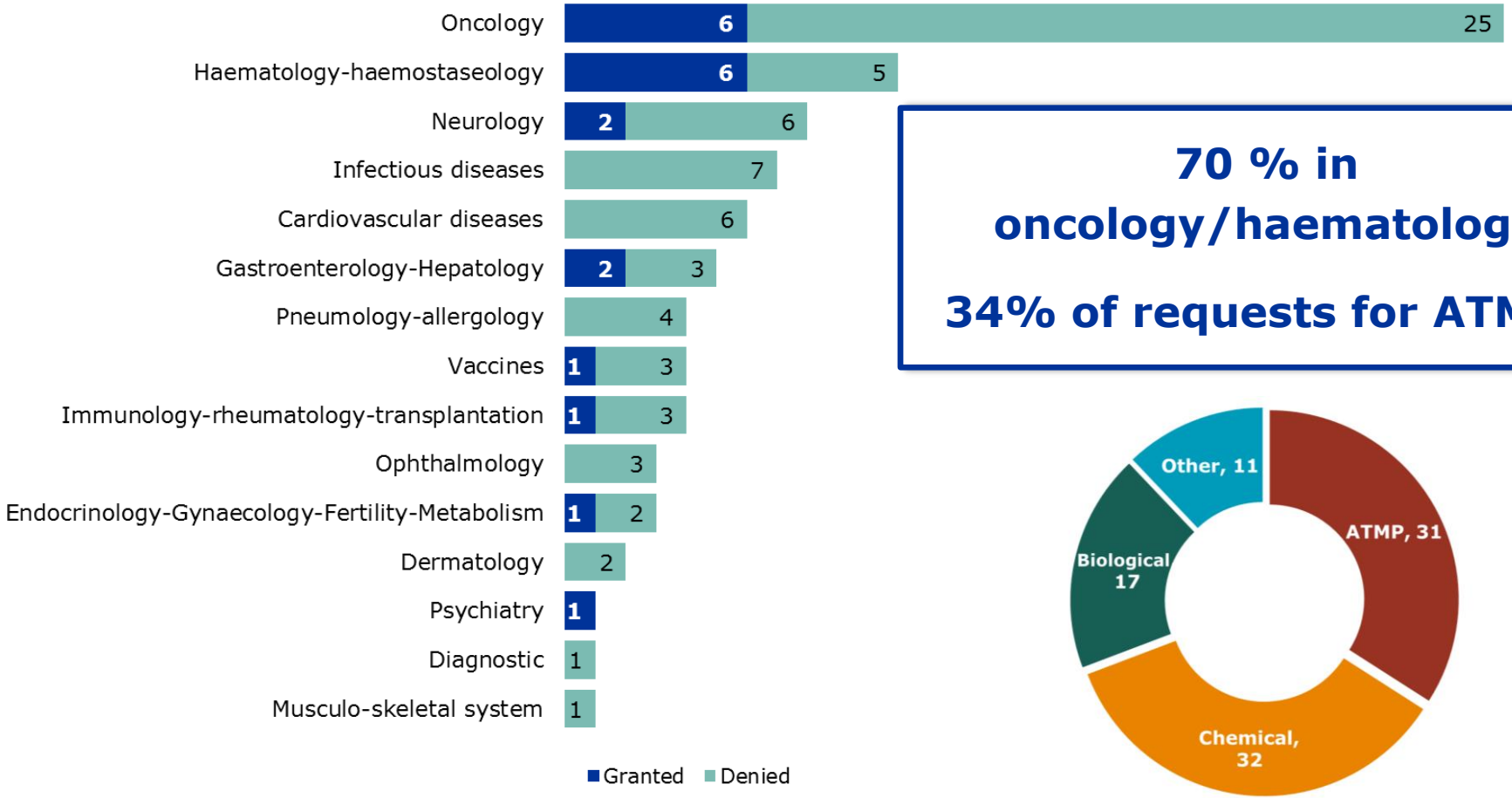
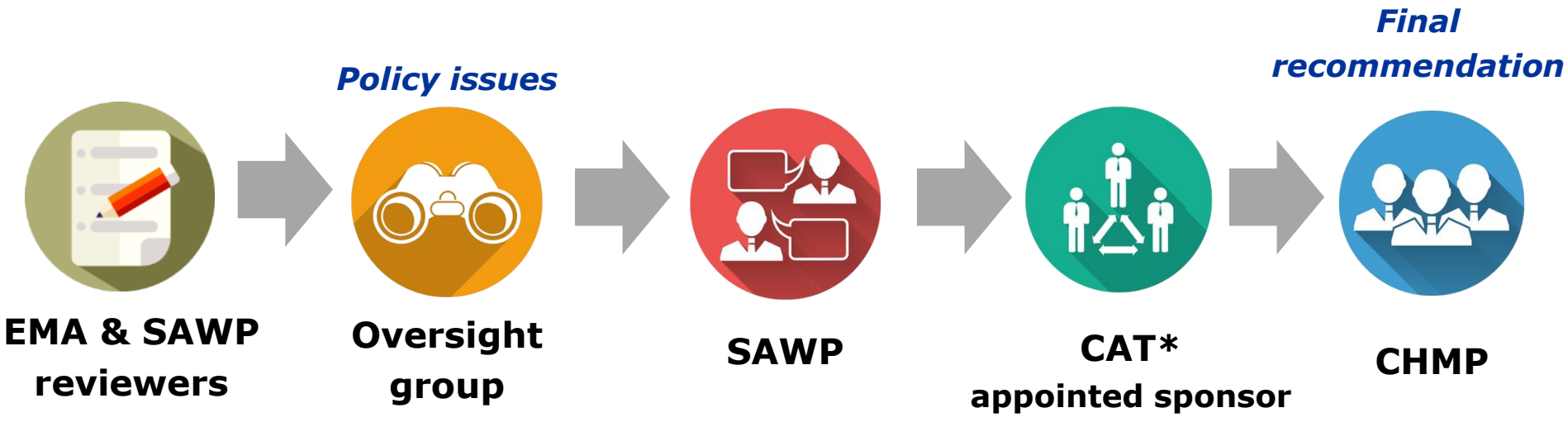


70 % in oncology/haematology

34% of requests for ATMPs

Assessment of eligibility requests: 40-day procedure



Short, lean process, involving multiple committees for robust assessment

*For advanced therapies

Examples of Oversight group policy discussions

Products in late stage of development

Examples of Oversight group policy discussions

Products in late stage of development

Main focus of PRIME is to support early in development

Before denying, consider additional benefits of PRIME for the concerned development and type of product

Examples of Oversight group policy discussions

Products in late stage of development

Comparison to products under development or evaluation

Examples of Oversight group policy discussions

Products in late stage of development

Comparison to products under development or evaluation

Other products under development or evaluation do not yet fulfil the unmet medical need

Examples of Oversight group policy discussions

Products in late stage of development

Comparison to products under development or evaluation

Unmet medical need

Examples of Oversight group policy discussions

Unmet medical need

Can be agreed:

in *subgroup*, if clearly defined, with mechanistic rationale for use vs entire population

in *prevention* setting and prevention of clinical complication if relevance duly justified.

in *non-life threatening condition*

Examples of Oversight group policy discussions

Products in late stage of development

Comparison to products under development or evaluation

Unmet medical need

Requests based on literature

Examples of Oversight group policy discussions

More acceptable at proof of principle

Use of literature may not be applicable similarly between chemicals, biologicals and ATMPs

Need reliable, trustworthy, high quality literature

Applicant planning further studies

Requests based on literature

Examples of Oversight group policy discussions

Products in late stage of development

Comparison to products under development or evaluation

Unmet medical need

Requests based on literature

Extrapolation of data from other products

Examples of Oversight group policy discussions

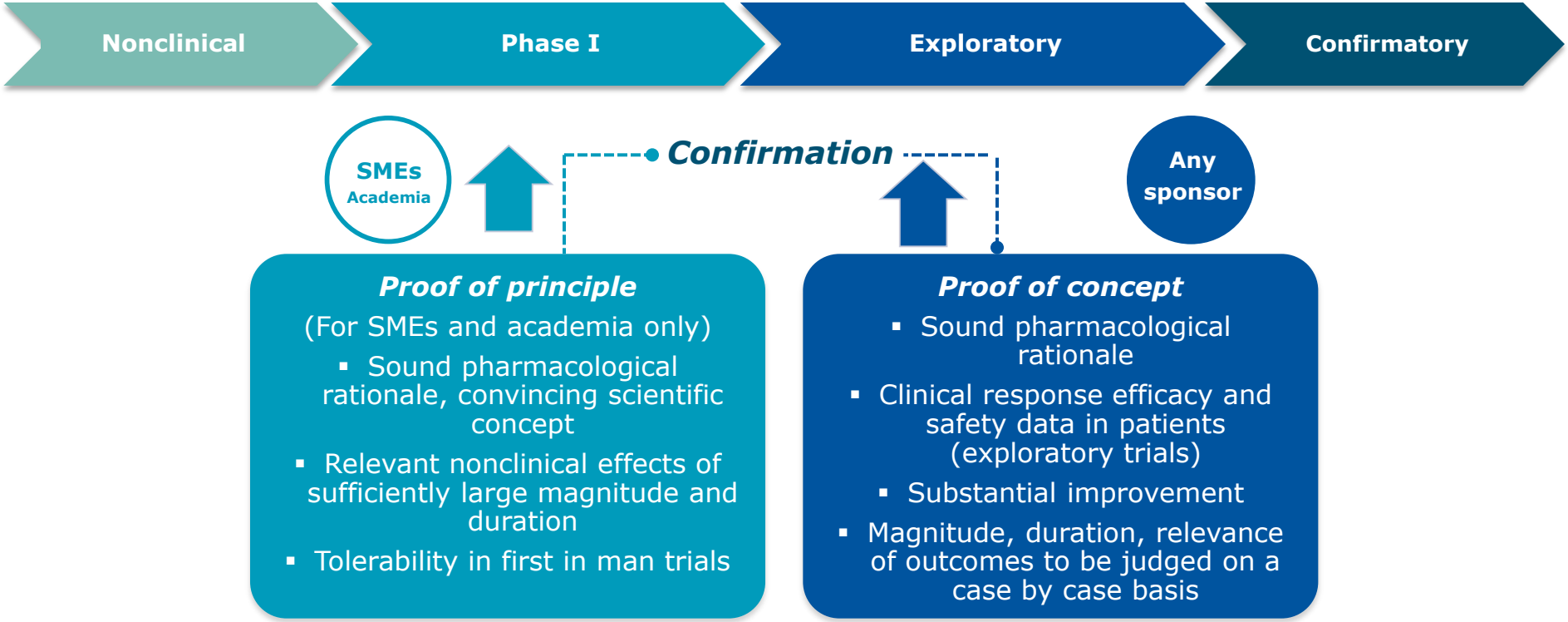
Expect data generated with the product itself

Acknowledge possibility for other products' data to be supportive (e.g. in cases with surrogate marker validated)

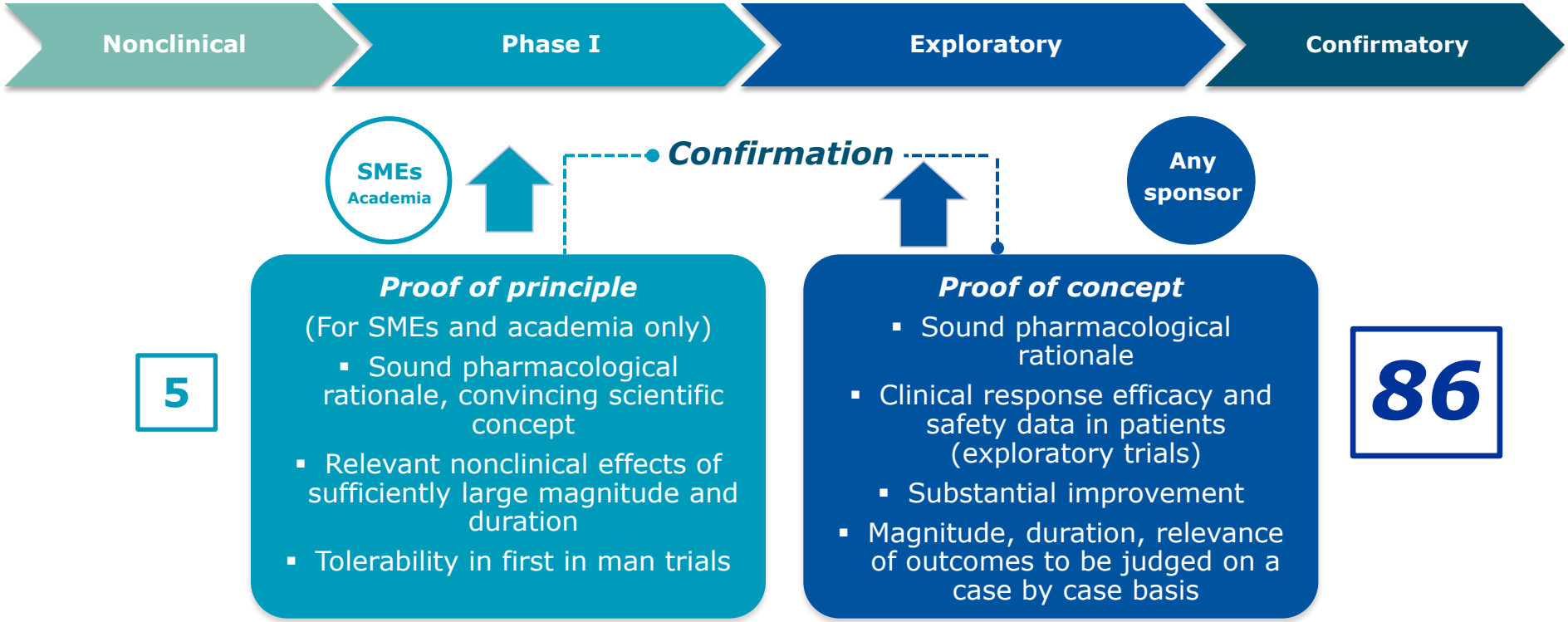
Requests based on literature

Extrapolation of data from other products

Entry points of PRIME eligibility requests



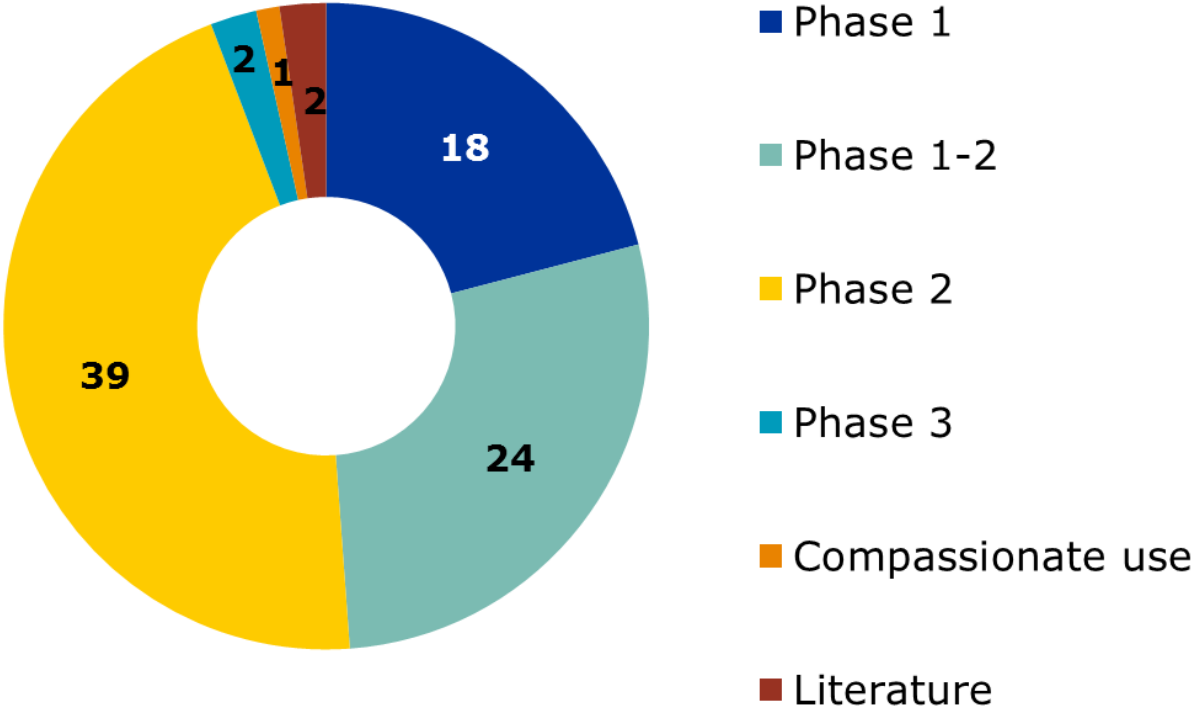
Entry points of PRIME eligibility requests



Proof of concept: phase of supportive studies

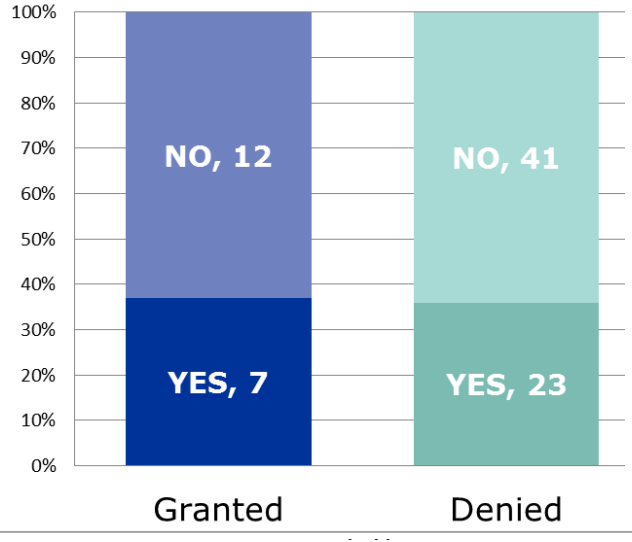
Mostly data from phase 1-2

> 50% with supportive data from only 1 study

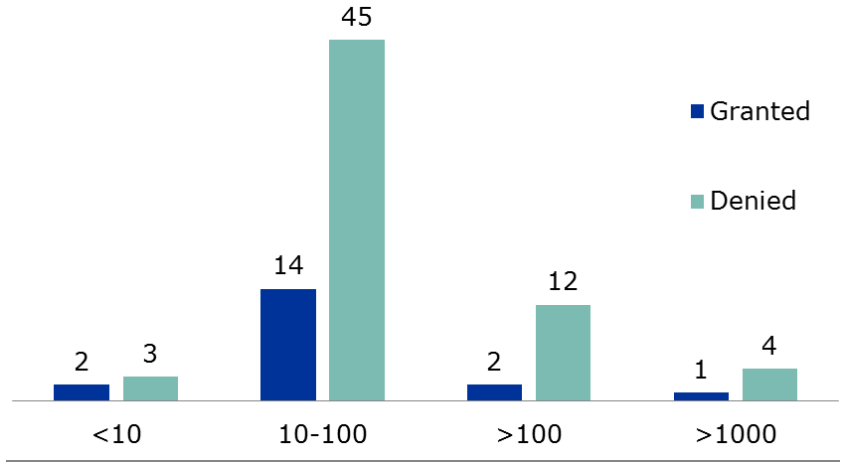


Proof of concept: study data and number of patients

Data from randomised and controlled trial



Number of patients in target population



No correlation between study type, number of patients and success rate

Proof of principle ‘early’ stage: only 1/5 request granted

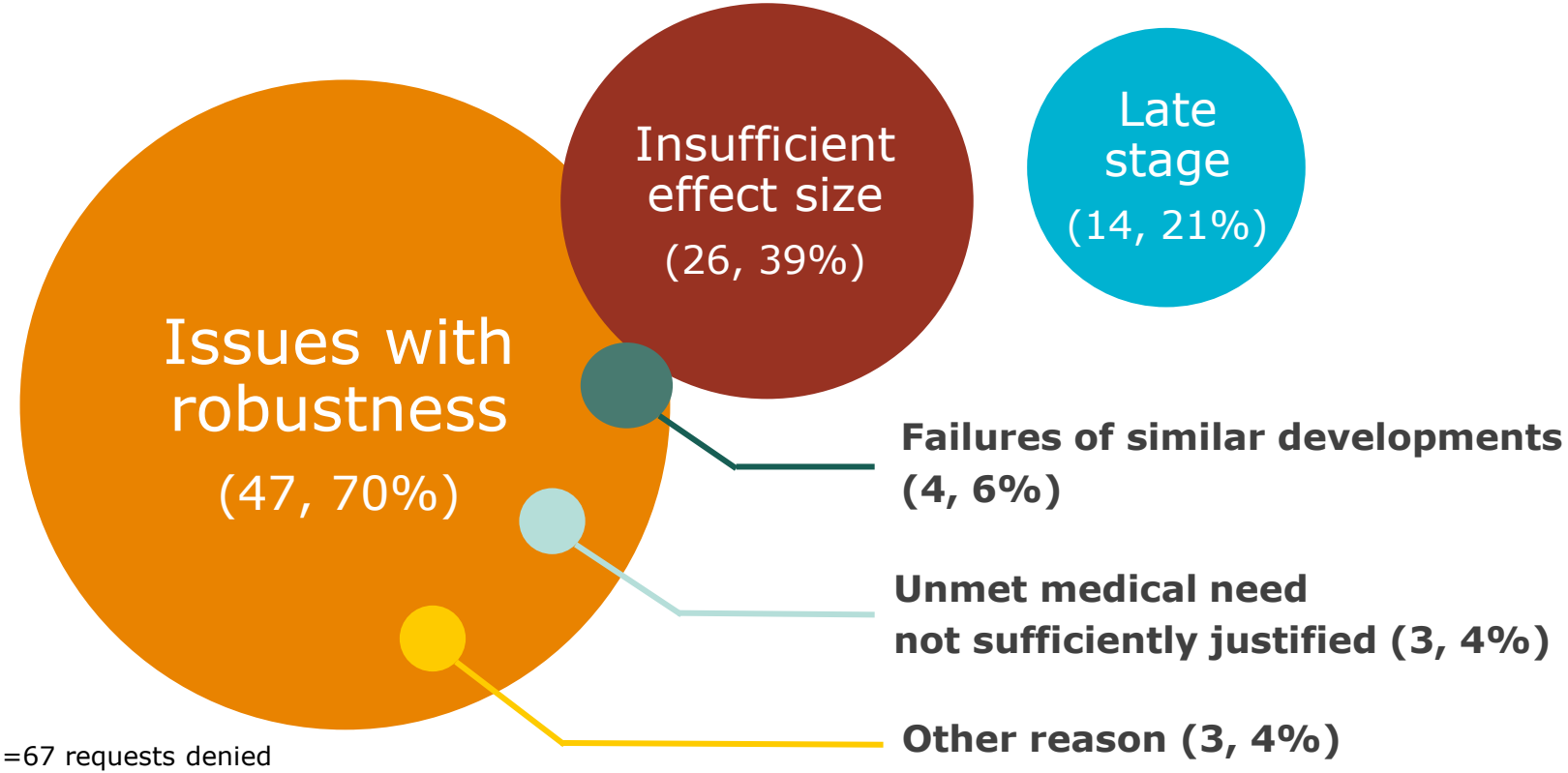
Main reasons for denial

Weak pharmacological rationale, insufficient nonclinical evidence on the claimed mechanism of action

Limited relevance of animal models presented

Insufficient PK exposure data to support expected clinical outcome

Reasons for denial at proof of concept stage



N=67 requests denied

Reasons for denial at proof of concept stage: Examples of robustness issues

Trial design issues eg treatment effect not isolated from other factors, use of concomitant treatments

Failed study

Inconsistency of results
across studies, study groups or endpoints

Claim in subgroup insufficiently justified

Sample issues
size, heterogeneity, insufficient information on baseline

Comparison to inadequate historical control data

What do we expect to grant eligibility?

Unmet medical need
No treatment, or clear limitations of existing therapies (e.g. Alzheimer's disease)

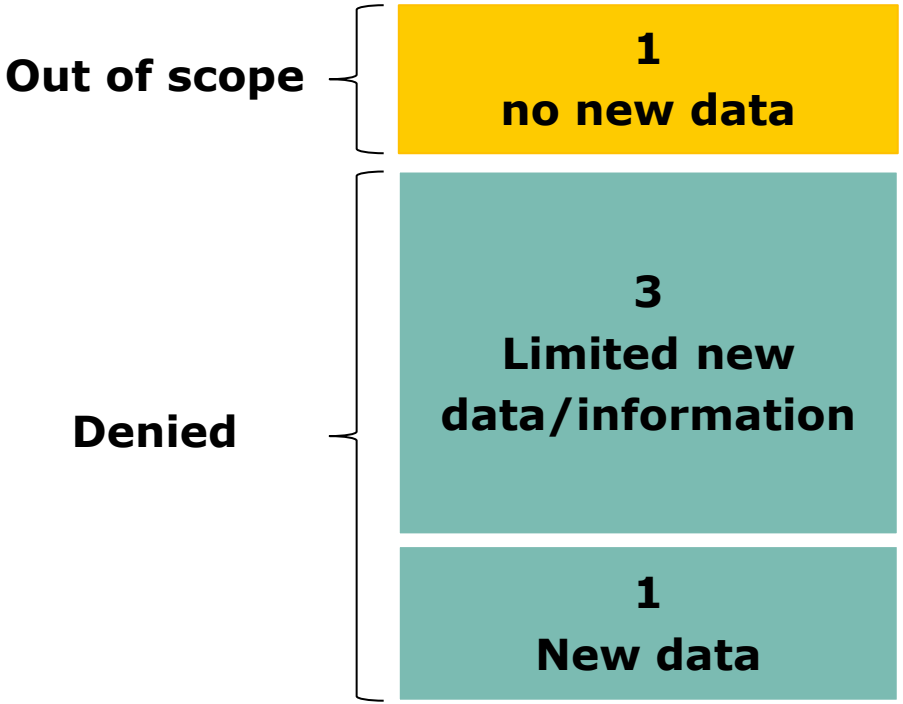
Nonclinical data supporting pharmacological rationale (e.g. gene therapy)

Clinical exploratory data on **relevant endpoint**

If uncontrolled, use **comparable historical control**
i.e. need sufficient information on baseline characteristics

Magnitude of the effect size supporting major therapeutic advantage

5 re-submissions following denied eligibility



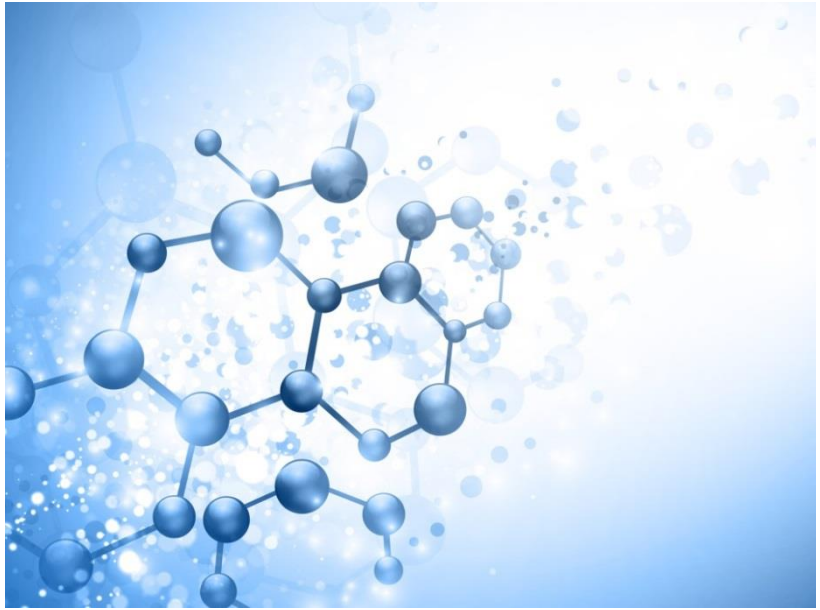
If unclear outcome, applicants can **contact EMA** for further clarification

Different reviewers appointed to resubmission

Important to **bring new evidence** and not just re-discussion

If new data, should **not** be **too late in development**

In summary,



Eligibility review: robust, short time, in writing

Quality of applications received is generally high

Substantiate the reliability of comparisons to external control

Proof of concept data and policy considerations determine timing for eligibility request

Resubmission should include new elements

Thank you for your attention

Further information

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