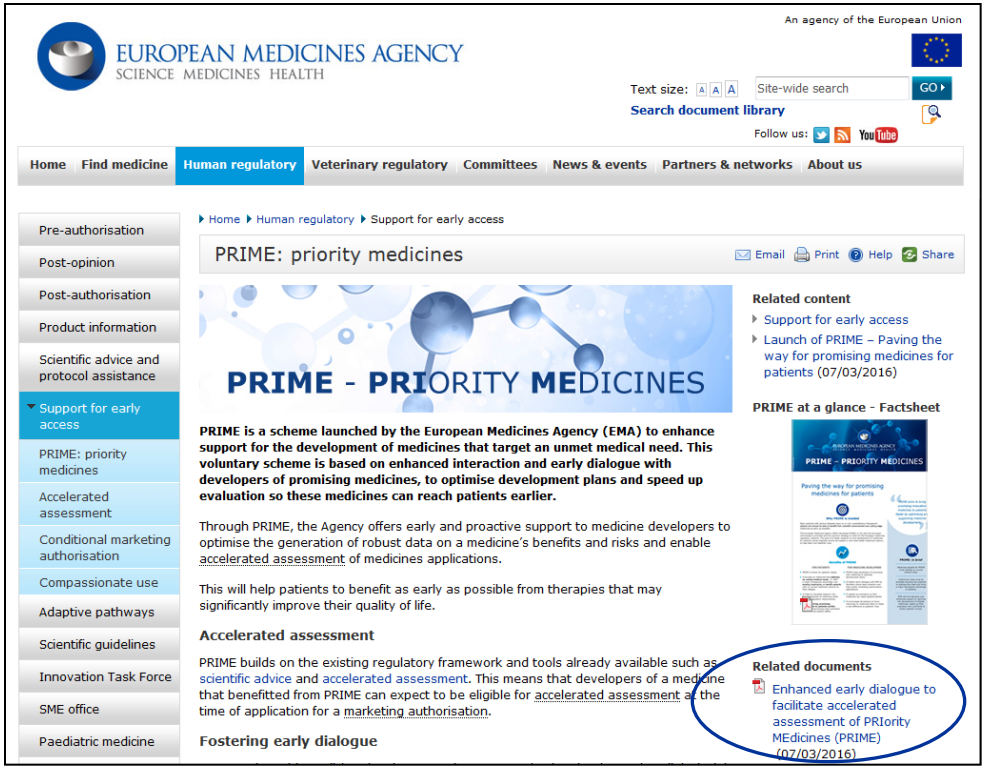
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

The PRIME scheme: experience one year on

Jordi Llinares Garcia, Head of Scientific & Regulatory Management Department

SME info day Supporting innovative medicines' development and early access, 17 November 2017

PRIME was launched in March 2016



Factsheet in lay language

Q&A, templates, application form for applicants

prime@ema.europa.eu

PRIME scheme - Goal & Scope

To foster the development of ***medicines with major public health interest.***

Reinforce scientific and regulatory advice

- Foster and facilitate early interaction
- Raise awareness of requirements earlier in development

Optimise development for robust data generation

- Focus efficient development
- Promote generation of robust and high quality data

Enable accelerated assessment

- Promote generation of high quality data
- Facilitated by knowledge gained throughout development

Building on existing framework;

Eligibility according to existing 'Accelerated Assessment criteria'

Eligibility to PRIME scheme

Based on Accelerated Assessment criteria
For products under development yet to be placed on the EU market

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

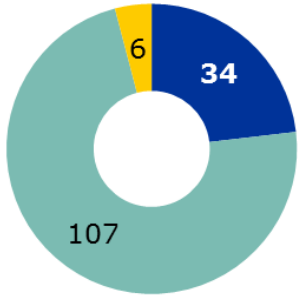
- Potential to address to a significant extent **an unmet medical need**
- Scientific justification, based on data and evidence available from nonclinical and clinical development

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)

PRIME eligibility recommendations adopted by 9 November 2017



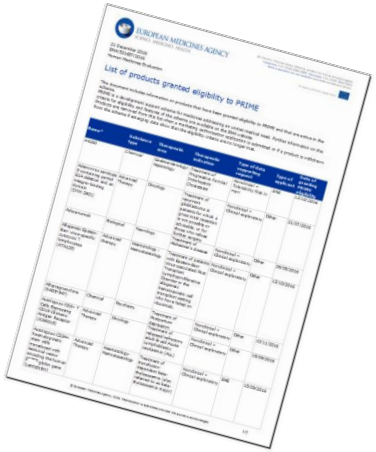
23% success rate

147 eligibility requests

34 granted*

+

Publication of report and list of products on EMA website



SMEs in PRIME

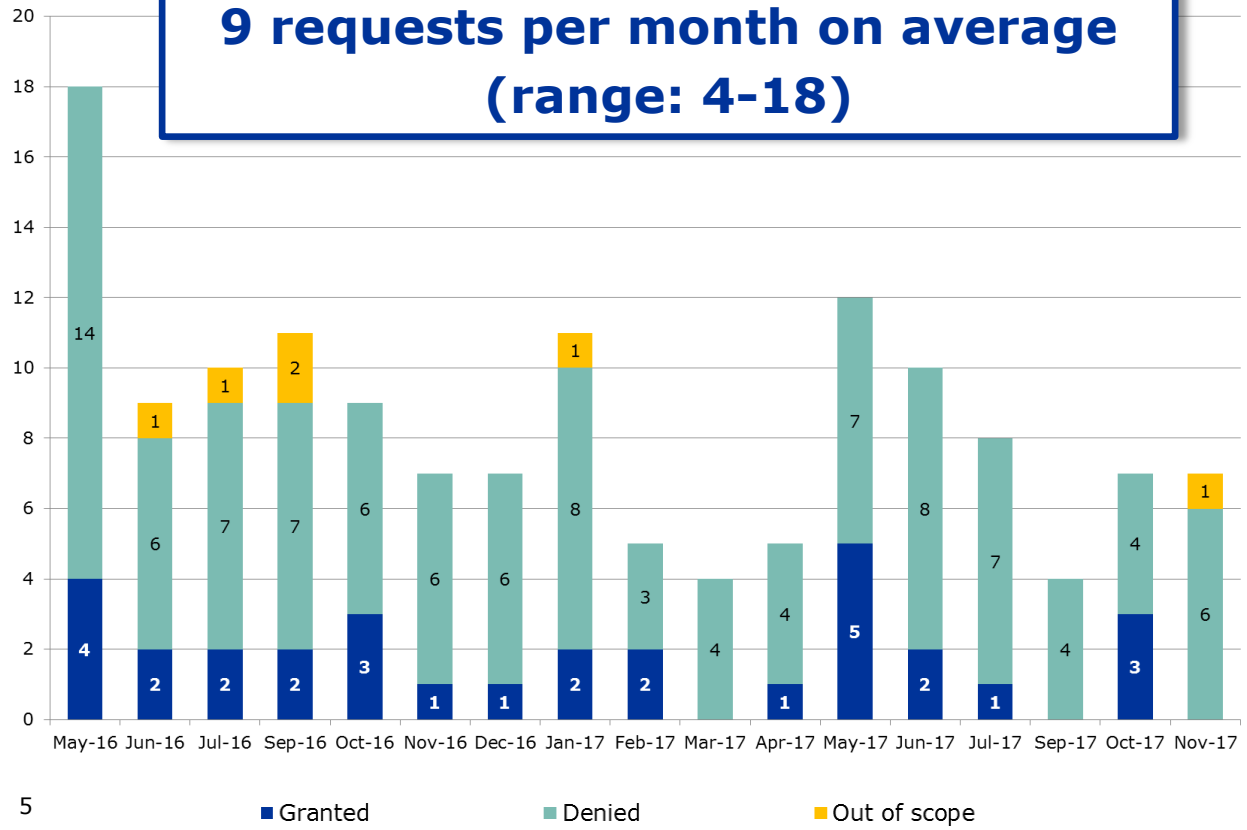
>50% requests received

44% of products granted

PRIME over time

EUROPEAN MEDICINES AGENCY

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

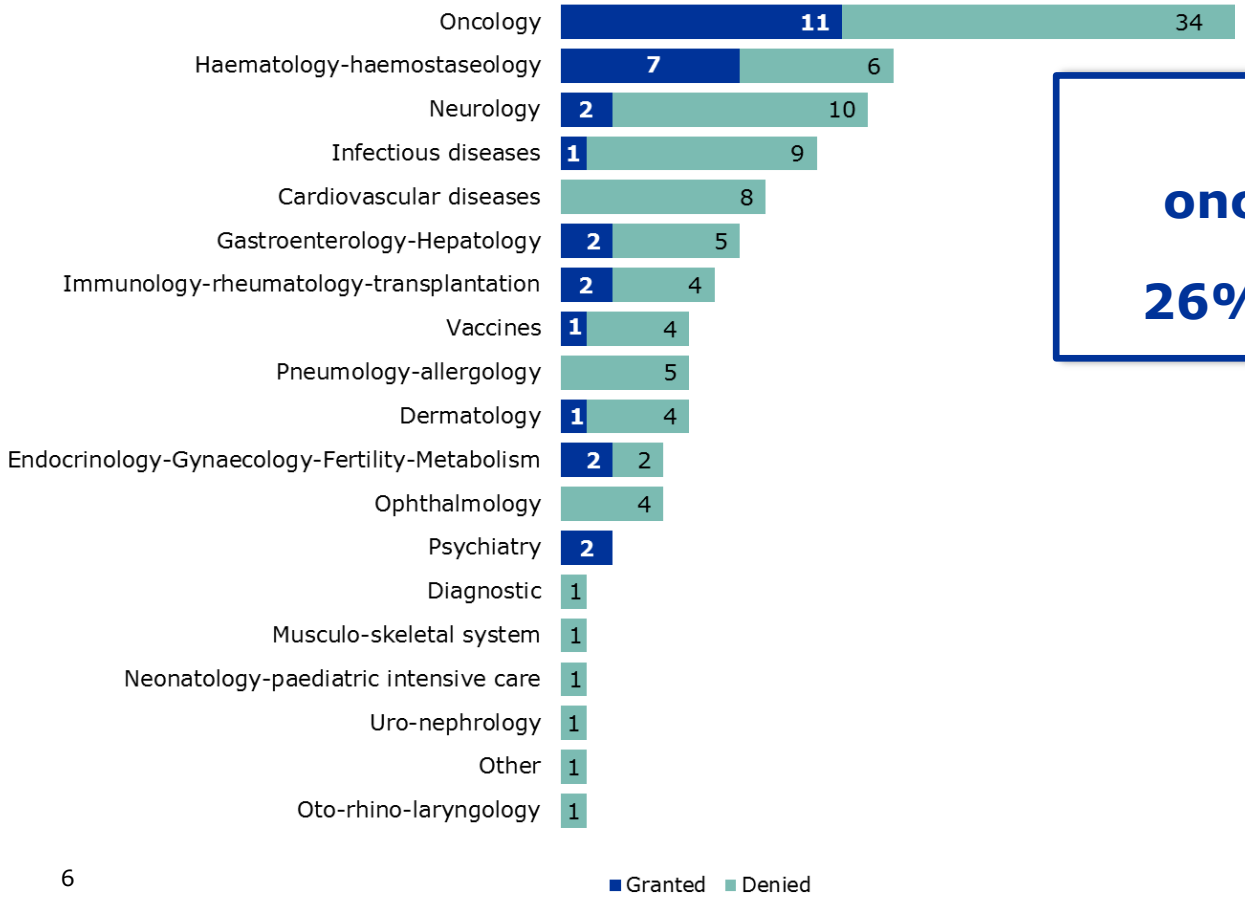


Good quality of applications

Few 'out of scope' applications

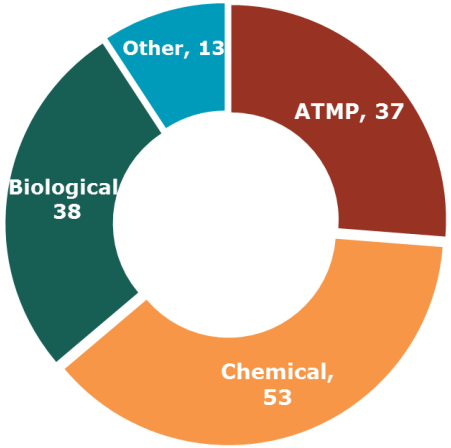
- Academic or SME with no FIM data
- Non-SME with no exploratory data
- Issue with definition as medicinal product
- Resubmission with no new data

Requests covering wide range of therapeutic areas and product type

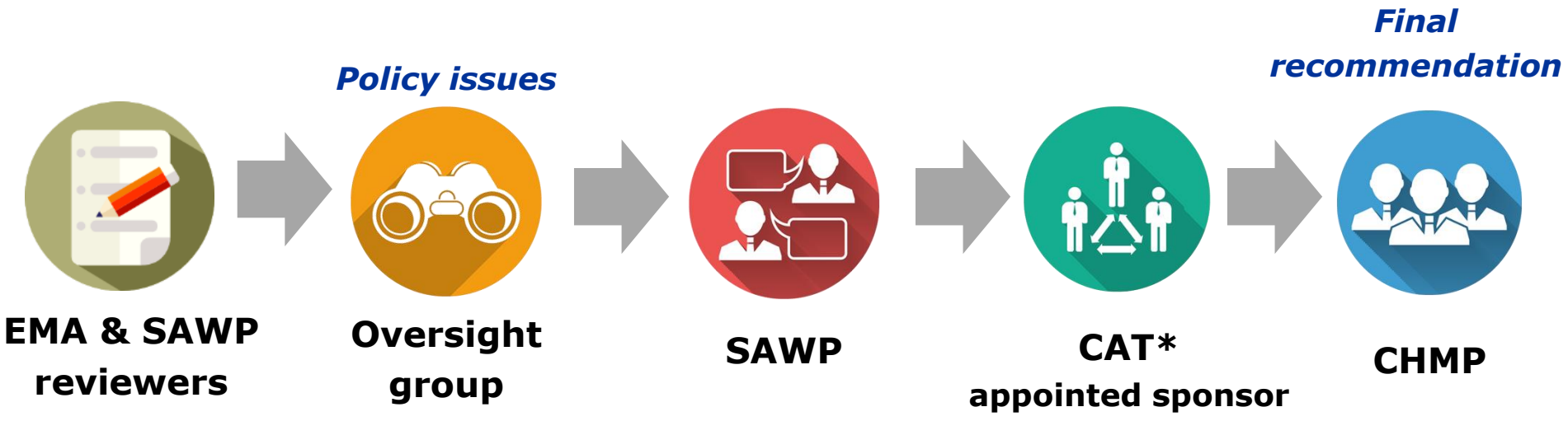


43% requests in oncology/haematology

26% requests for ATMPs



Assessment of eligibility requests: 40-day procedure



Short, lean process, involving multiple committees for robust assessment

*For advanced therapies

Justification for eligibility to PRIME

1

Why there is an unmet medical need in the proposed indication

- Epidemiological data
- Description of available treatments

→ *No treatment,*

or

→ *Existing treatment: discuss limitations and how a major therapeutic advantage could be brought*

2

Data on product showing potential to significantly address the unmet medical need

- Description of observed and predicted effects, clinical relevance, added value and impact
- If applicable, expected improvement over existing treatments

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

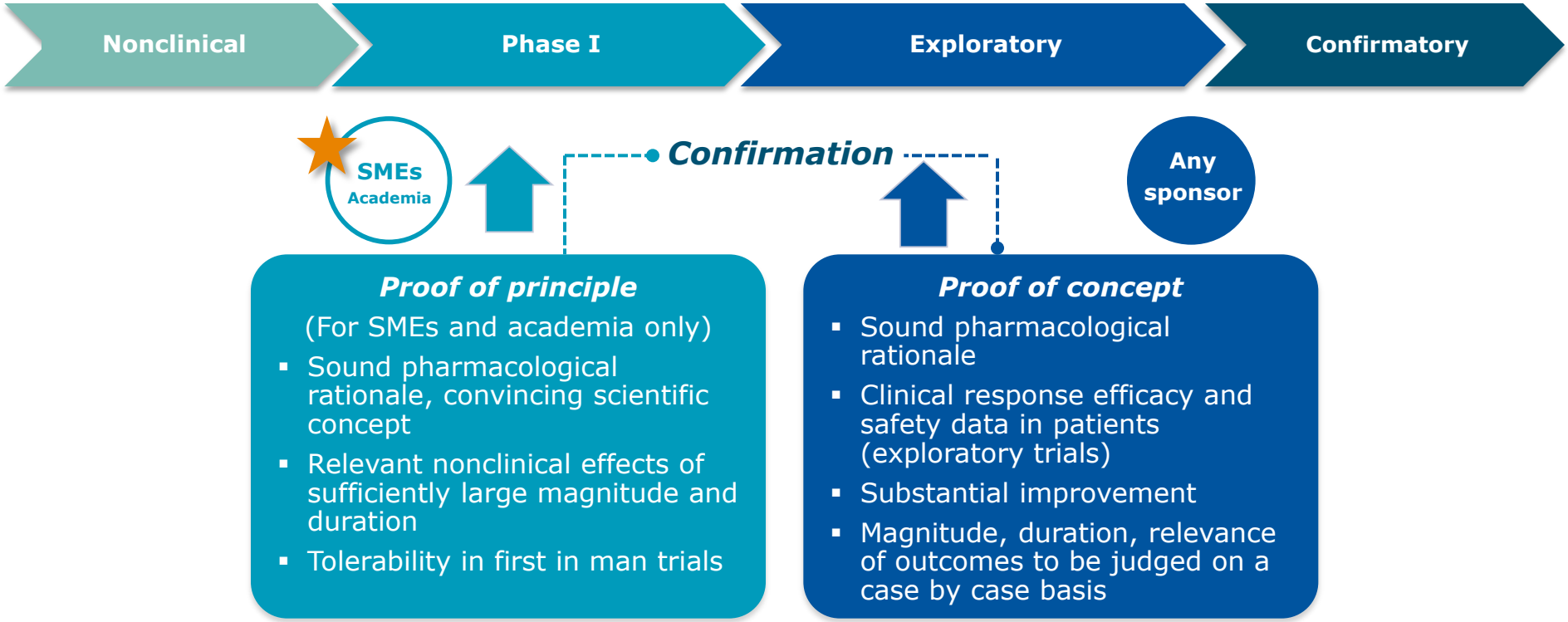
Expect data generated with the product itself

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

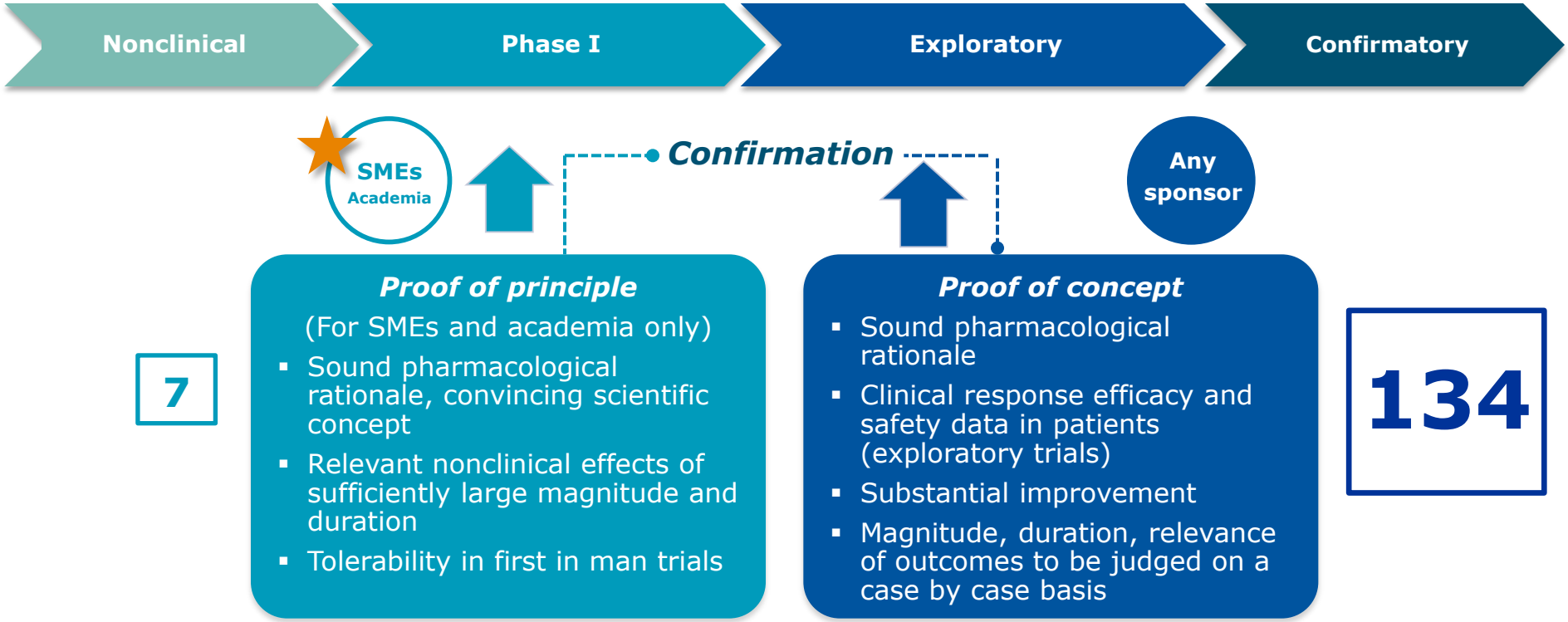
Requests based on literature

Extrapolation of data from other products

Entry points PRIME eligibility and required evidence



Entry points PRIME eligibility and required evidence



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)

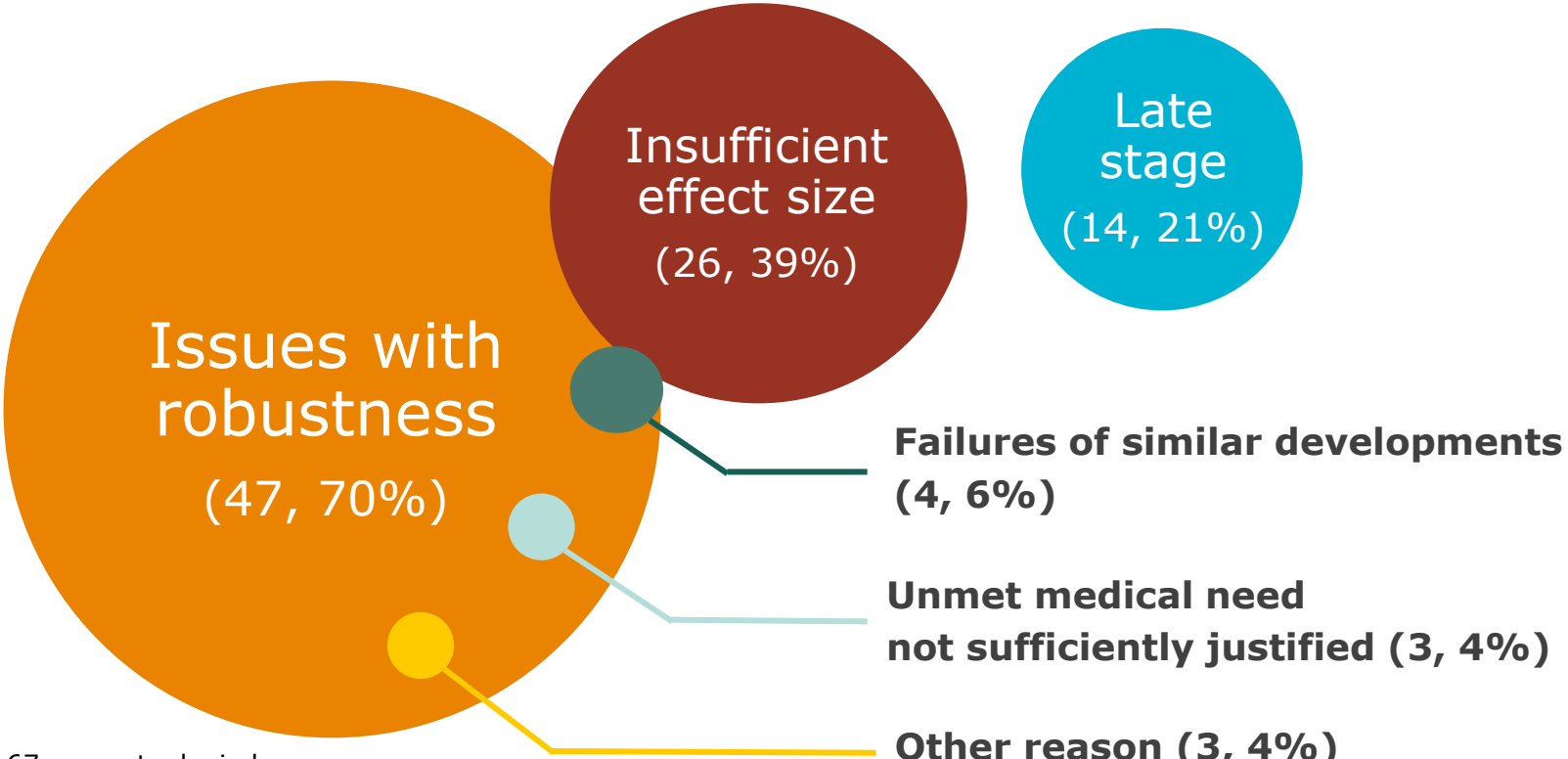
Clinical exploratory data on **relevant endpoint**

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

Magnitude of the effect size supporting major therapeutic advantage

EUROPEAN MEDICINES AGENCY

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 e.g. treatment effect not isolated from other factors, use of concomitant treatments

Failed study

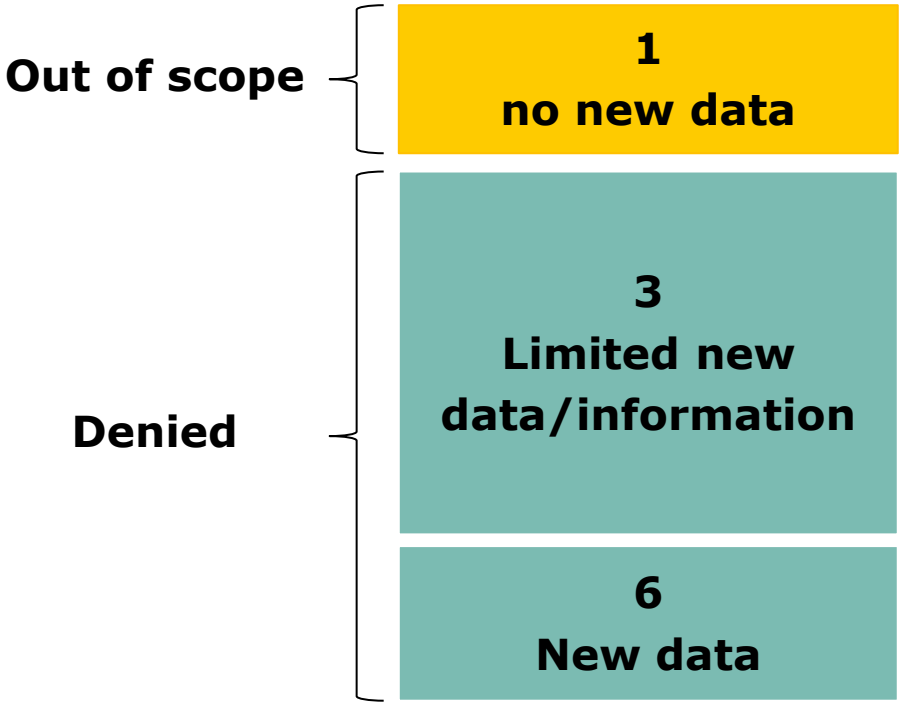
Inconsistency of results
across studies, study groups or endpoints

Claim in subgroup insufficiently justified

Sample issues
size, heterogeneity, insufficient information on baseline

Comparison to inadequate historical control data

10 re-submissions following denied eligibility



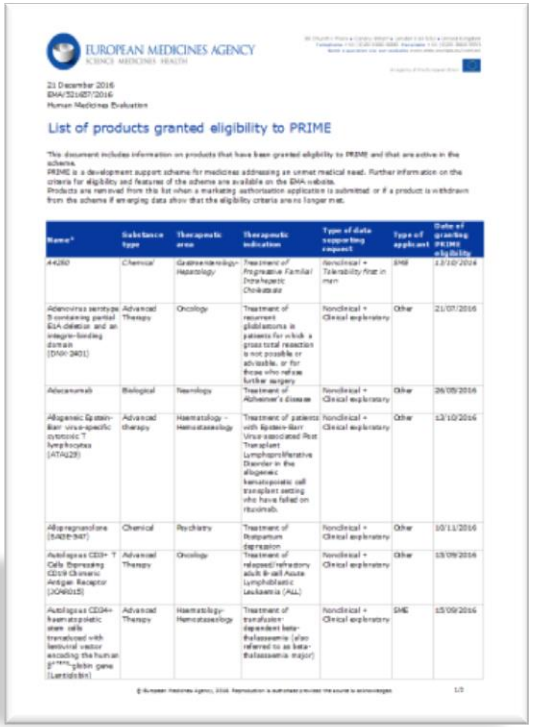
If unclear outcome, applicants can **contact EMA** for further clarification

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**

34 products granted eligibility to PRIME so far



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

21 December 2016
EMA/516407/2016
Human Medicines Evaluation

List of products granted eligibility to PRIME

This document includes information on products that have been granted eligibility to PRIME and that are active in the scheme.
PRIME is a development support scheme for medicines addressing an unmet medical need. Further information on the criteria for eligibility and features of the scheme are available on the EMA website.
Products are removed from this list when a marketing authorisation application is submitted or if a product is withdrawn from the scheme if emerging data show that the eligibility criteria are no longer met.

Name*	Substance type	Therapeutic area	Therapeutic indication	Type of data supporting request	Type of applicant	Date of granting PRIME eligibility
A4250	Chemical	Gastroenterology-Hepatology	Treatment of Progressive Familial Intrahepatic Cholestasis	Nonclinical + Tolerability first in man	SME	13/10/2014
Adenovirus serotype 5 containing partial E1A-deletion and an integrin-binding domain (DNX-2401)	Advanced Therapy	Oncology	Treatment of recurrent glioblastoma in patients for which a gross total resection is not possible or advisable, or for those who refuse further surgery	Nonclinical + Clinical exploratory	Other	21/07/2016
Alacanumab	Biological	Neurology	Treatment of Alzheimer's disease	Nonclinical + Clinical exploratory	Other	26/05/2016
Allogeneic Epstein-Barr virus-specific cytotoxic T lymphocytes (ATA129)	Advanced therapy	Haematology - Haemataseology	Treatment of patients with Epstein-Barr Virus-associated Post Transplant Lymphoproliferative Disorder in the allogeneic hematopoietic cell transplant setting who have failed on rituximab.	Nonclinical + Clinical exploratory	Other	12/10/2016
Allopregnanolone (SAGE-547)	Chemical	Psychiatry	Treatment of Postpartum depression	Nonclinical + Clinical exploratory	Other	10/11/2016
Autologous CD3+ T Cells Expressing CD19 Chimeric Antigen Receptor (JCAR015)	Advanced Therapy	Oncology	Treatment of relapsed/refractory adult B-cell Acute Lymphoblastic Leukaemia (ALL)	Nonclinical + Clinical exploratory	Other	13/09/2016
Autologous CD34+ haematopoietic stem cells transduced with lentiviral vector encoding the human β^A-T87Q-globin gene (Lentiglobin)	Advanced Therapy	Haematology-Haemataseology	Treatment of transfusion-dependent beta-thalassaemia (also referred to as beta-thalassaemia major)	Nonclinical + Clinical exploratory	SME	13/09/2016

© European Medicines Agency, 2016. Reproduction is authorised provided the source is acknowledged. 1/3

- Some very innovative products with several advanced therapy medicines
- Across therapeutic areas, including rare cancers, Alzheimer’s disease
- Majority in rare diseases

Features of the PRIME scheme

Early access tool, supporting patient access to innovative medicines.

- **Written confirmation of PRIME eligibility** and potential for accelerated assessment;
- **Early CHMP Rapporteur appointment** during development;
- **Kick off meeting** with multidisciplinary expertise from EU network;
- **Enhanced scientific advice** at key development milestones/decision points;
- **EMA dedicated contact point**;
- **Fee incentives** for SMEs and academics on Scientific Advice requests.

Early Rapporteur appointment

Opportunity for **knowledge gain** on the product
Identification of **relevant expertise** and build adequate team
Opportunity to **influence** development

Very positive views on the **kick-off meeting**
- ✓ Importance of preparation and tailored agenda
- ✓ Facilitate interactions across committees and with EMA

Timing of PRIME eligibility is critical for fruitful engagement
Involvement in follow-up **scientific advice** and workload
Need to **improve follow-up communications/updates**

Kick-off meetings: experience on 22 products

EUROPEAN MEDICINES AGENCY

Who

- Applicant
- Rapporteur and assessors
- CAT/CHMP/SAWP chairs
- EMA
- Representatives from PDCO, COMP and PRAC

When

- ~ 4 months after eligibility
- In margins of CAT/CHMP meetings
- Find optimal timing, particularly if ongoing SA

How

- Briefing document (~3-4 weeks in advance)
- Internal preparatory teleconference (~2 weeks)
- Tailored agenda

What

- Broad discussion on development and regulatory strategy
- Identification of issues for future scientific advices
- Raise awareness on post-authorisation planning & HTA interactions

Enhanced scientific advice

12 products
20 SA requests
following kick-off meetings

Multi-stakeholder
4 EMA/HTA parallel advice
Patients involved, as applicable

Rapporteur involvement
through one of SAWP coordinator

All aspects covered
Quality, nonclinical, clinical

Flexibility
Shorter pre-submission
3 adopted in 40 days

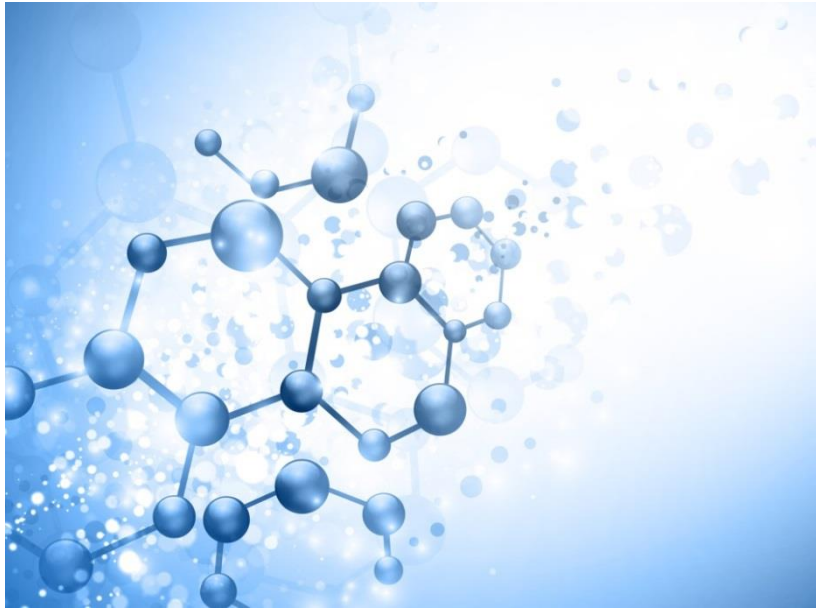
Other interactions with the applicant: EMA contact point

Address or direct queries

Ad hoc teleconference/meeting with Rapporteur and EMA

Area for improvement:
Applicant to provide regular updates on development progress and milestones

In summary,



Eligibility review: robust, short time, in writing

Rapporteur appointment enables
early identification of potential issues

Scheme triggers discussions across product type / class

Excellent collaboration across committees

Iterative scientific advices with opportunity for patients and HTA involvement

Thank you for your attention

Further information

European Medicines Agency
30 Churchill Place • Canary Wharf • London E14 5EU • United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

Follow us on **@EMA_News**