Safe and timely access to medicinal products
Role of the FAMHP in the EU-regulatory framework

Patient Centricity Symposium

Brussels

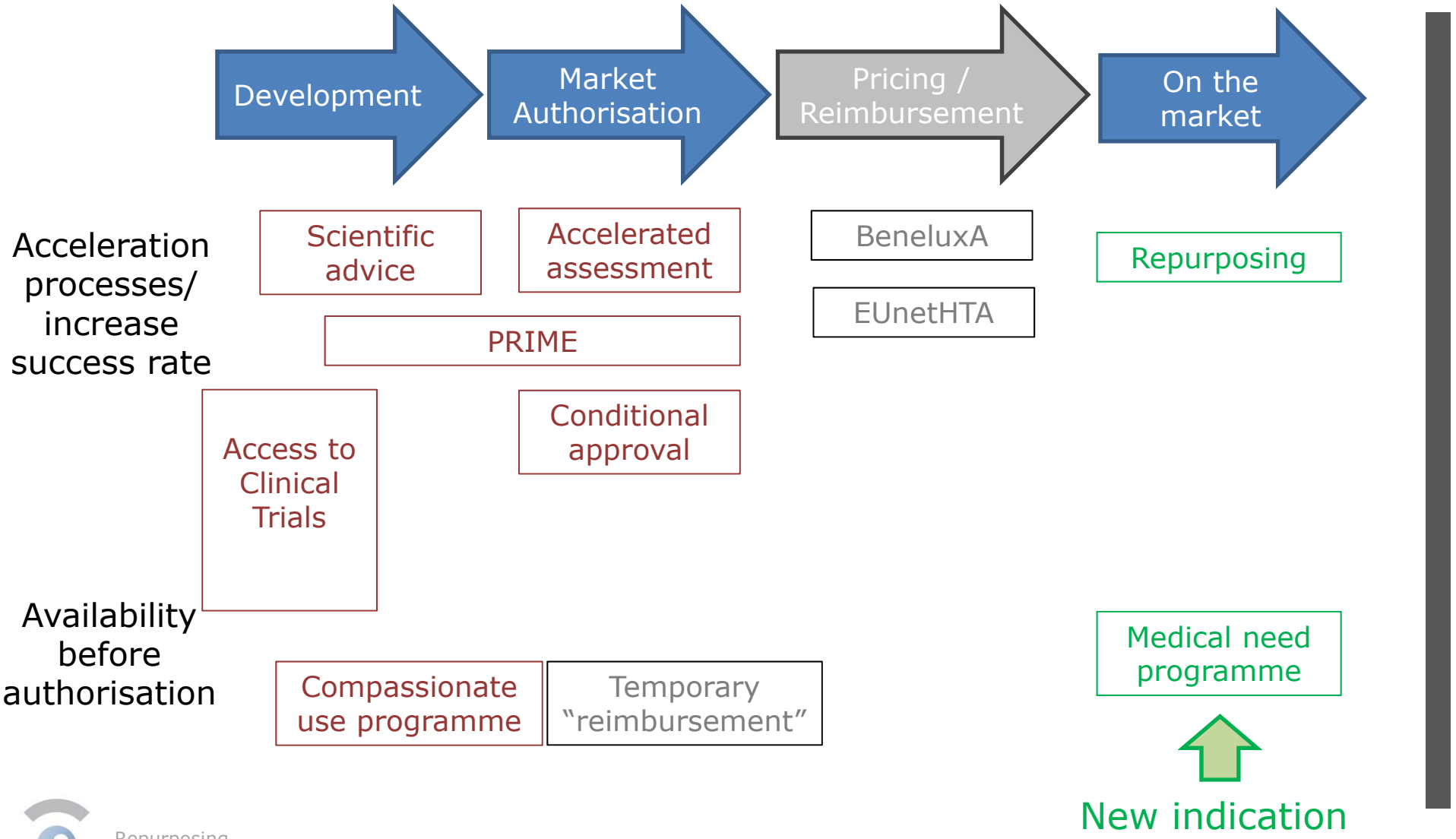
10.12.2019

Greet MUSCH

famhp
federal agency for medicines and health products

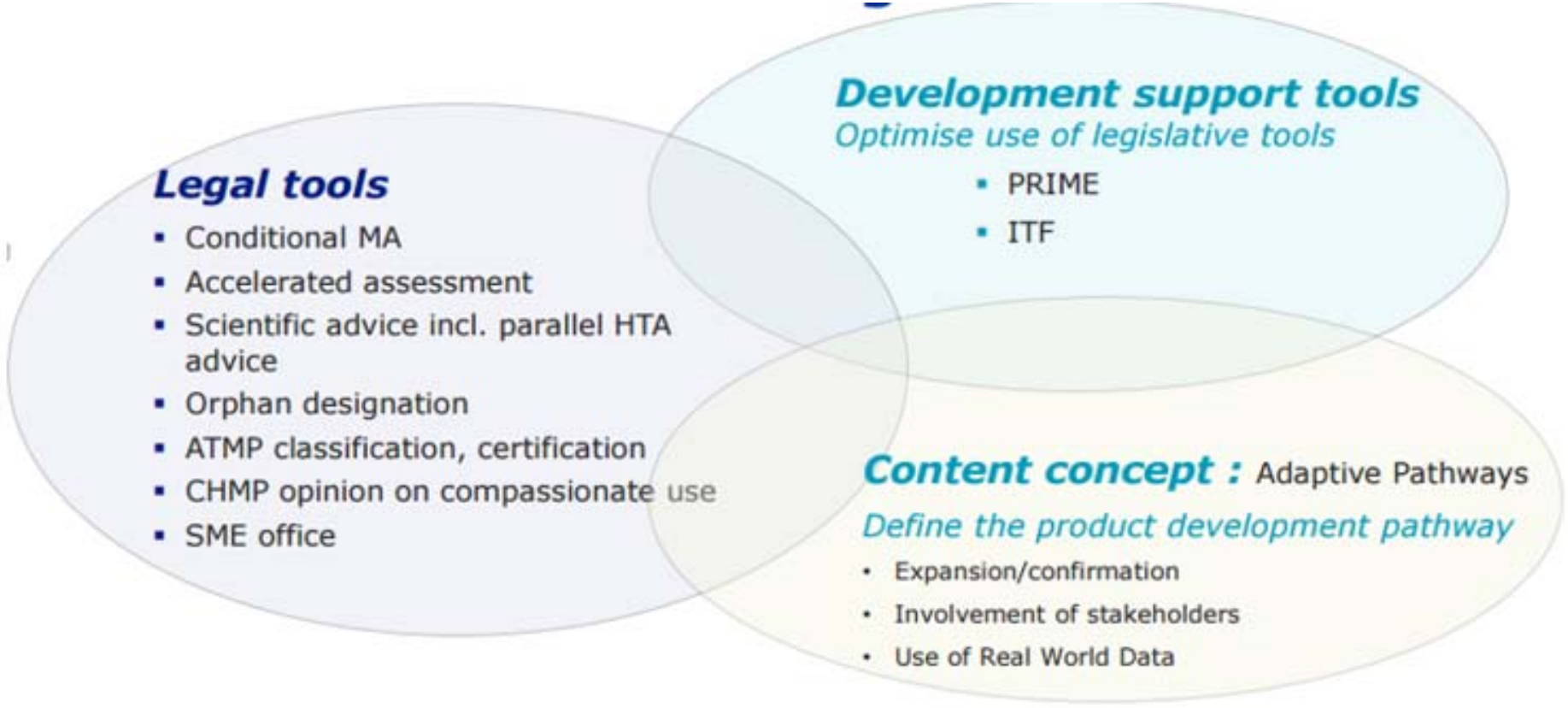
.be

Context


Development
Market Authorisation
Pricing / Reimbursement
On the market
Acceleration processes/ increase success rate
Scientific advice
Accelerated assessment
BeneluxA
Repurposing
EUnetHTA
PRIME
Access to Clinical Trials
Conditional approval
Availability before authorisation
Compassionate use programme
Temporary "reimbursement"
Medical need programme
New indication

1. Current initiatives at EU level - State of play

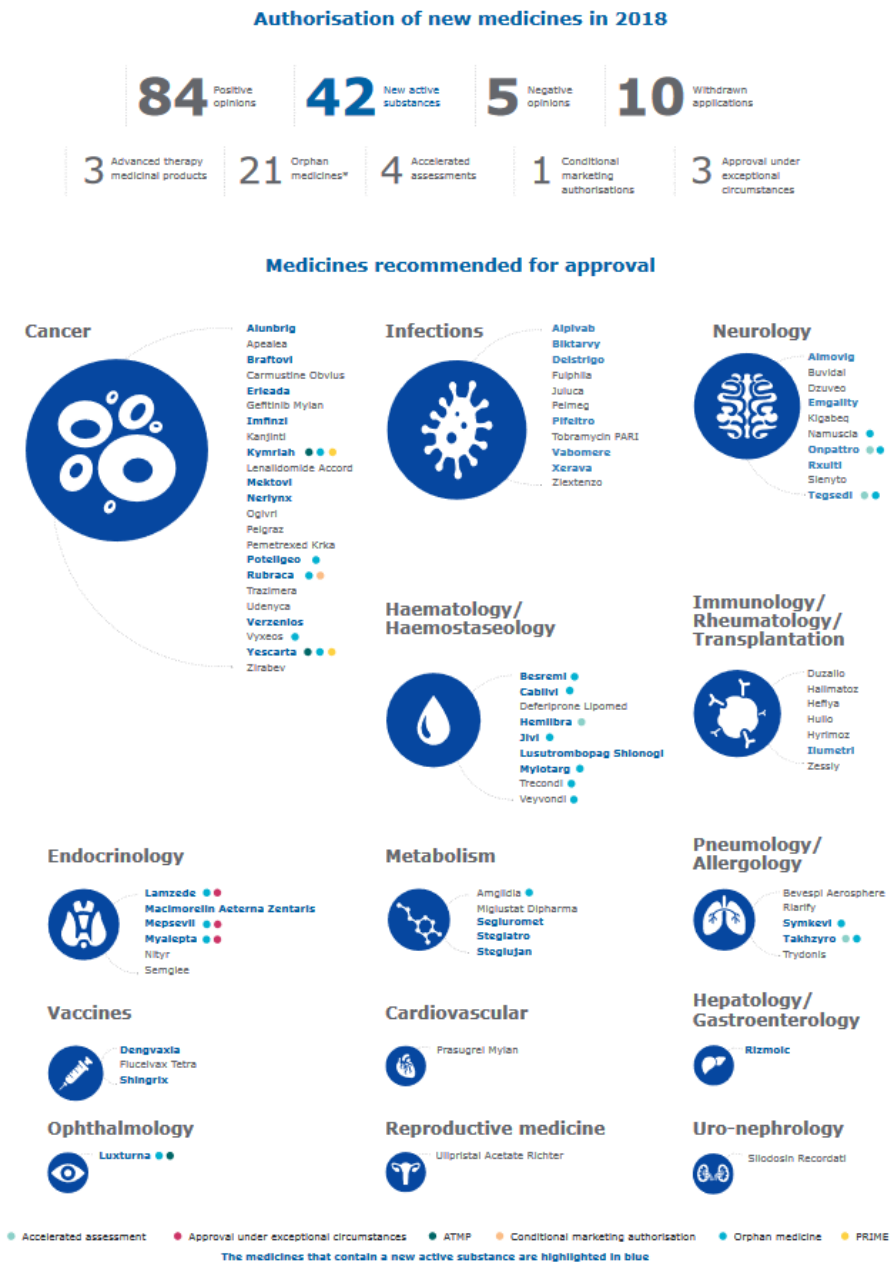
EMA development support and early access to medicines addressing unmet medical needs



1. Current initiatives at EU level - State of play at CHMP

Authorisation of new medicines in 2018

- 23/84 = 27 % oncology files
- 11/23 New Active Substance
- 2 ATMP
- 2 PRIME
- 5 orphan MP
- 1 conditional MA
- 0 accelerated procedures



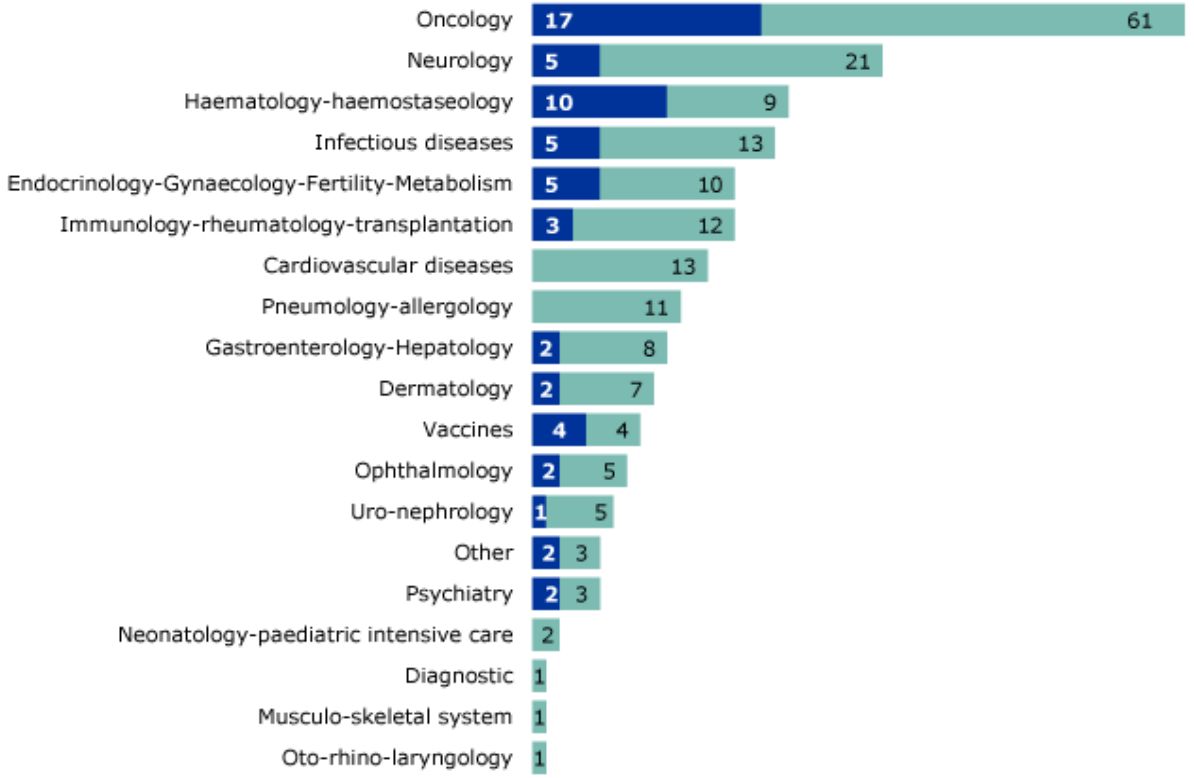
1. Current initiatives at EU level - State of play at CHMP

PRIME: PRIority MEdicines

PRIME is a scheme launched by the European Medicines Agency (EMA) to enhance support for the development of medicines that target an unmet medical need. This voluntary scheme is based on enhanced interaction and early dialogue with developers of promising medicines, to optimise development plans and speed up evaluation so these medicines can reach patients earlier.

1. Current initiatives at EU level - State of play at CHMP

PRIME: therapeutic areas



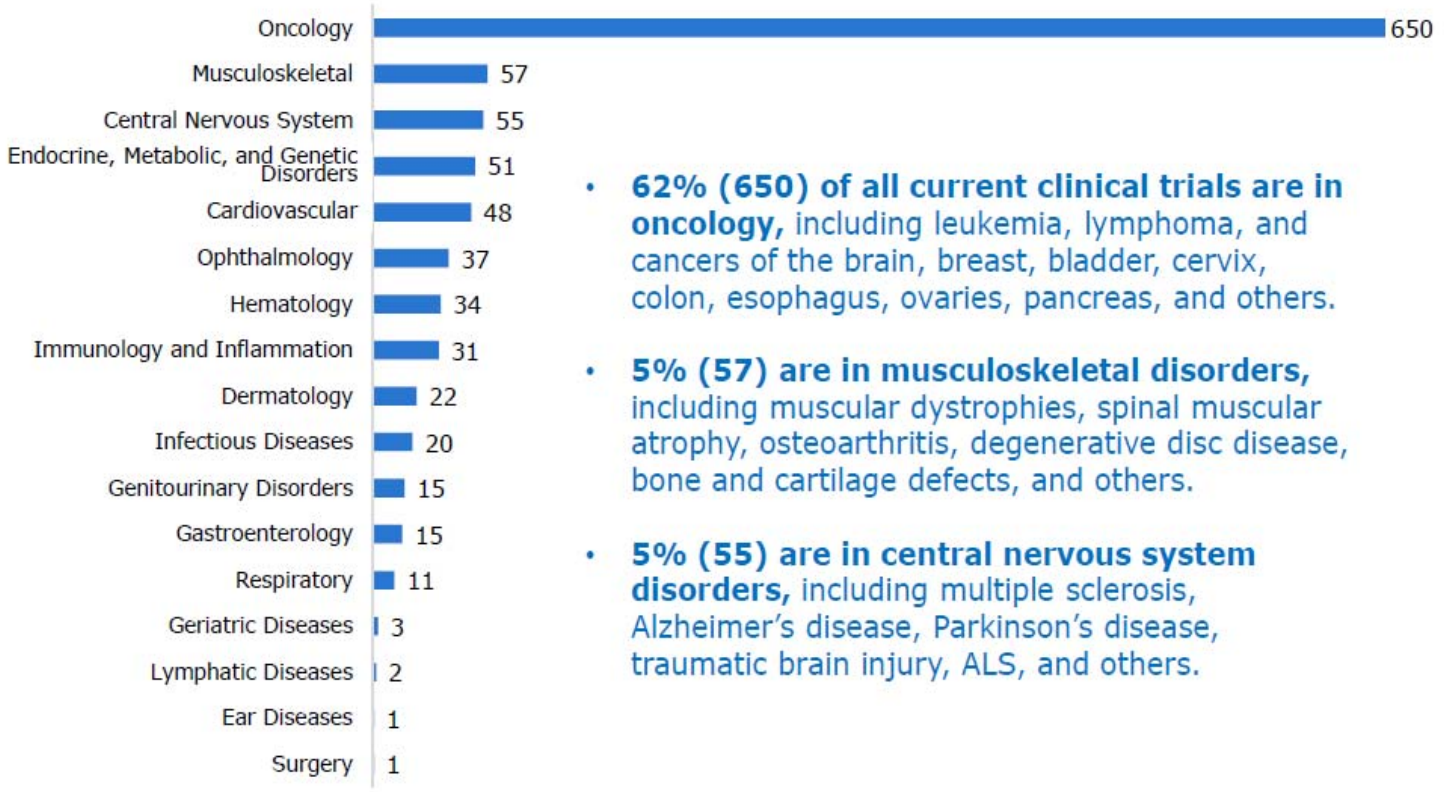
Recommendations adopted by 17 October 2019

1. Current initiatives at EU level - State of play ATMPs in oncology

- On the market:
  - Imlygic (oncolytic virus)
  - Yescarta & Kymriah (CAR-T)
- In development: oncolytic viruses, CAR-T (new generation, new construct, new target …), highly personalised immunotherapies based on neoepitopes – **clinical trials ongoing in Belgium**
- Access for patients:
  - Clinical trials (national competence)
  - Marketing authorisation (CAT, EMA)
  - Reimbursement
- All ATMPs will access market via the centralised procedure: early interactions with EMA via SAWP (SA, PRIME) is highly recommended
- Very high price of gene therapies remain a challenge for actual access to products on the market

1. Current initiatives at EU level - State of play ATMPs in oncology

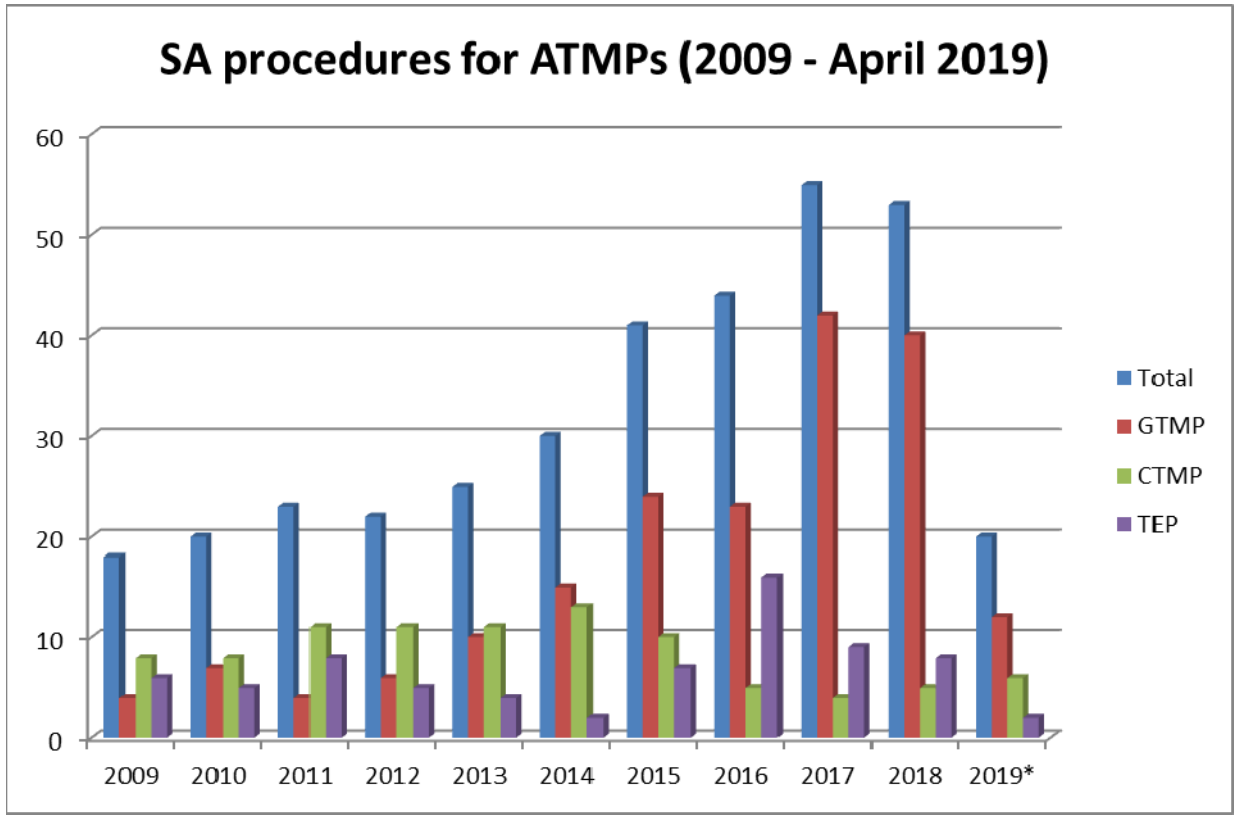
ATMP Clinical Trials by Therapeutic Area



- **62% (650) of all current clinical trials are in oncology,** including leukemia, lymphoma, and cancers of the brain, breast, bladder, cervix, colon, esophagus, ovaries, pancreas, and others.
- **5% (57) are in musculoskeletal disorders,** including muscular dystrophies, spinal muscular atrophy, osteoarthritis, degenerative disc disease, bone and cartilage defects, and others.
- **5% (55) are in central nervous system disorders,** including multiple sclerosis, Alzheimer's disease, Parkinson's disease, traumatic brain injury, ALS, and others.

1. Current initiatives at EU level - State of play Scientific Advice for ATMPs (2009-April 2019)

- 345 SA procedures started – CAT involved in all SA for ATMPs
- Increase in SAs for ATMPs over period 2012–2017



SA requests until end April 2019

1. Current initiatives at EU level - State of play COMP

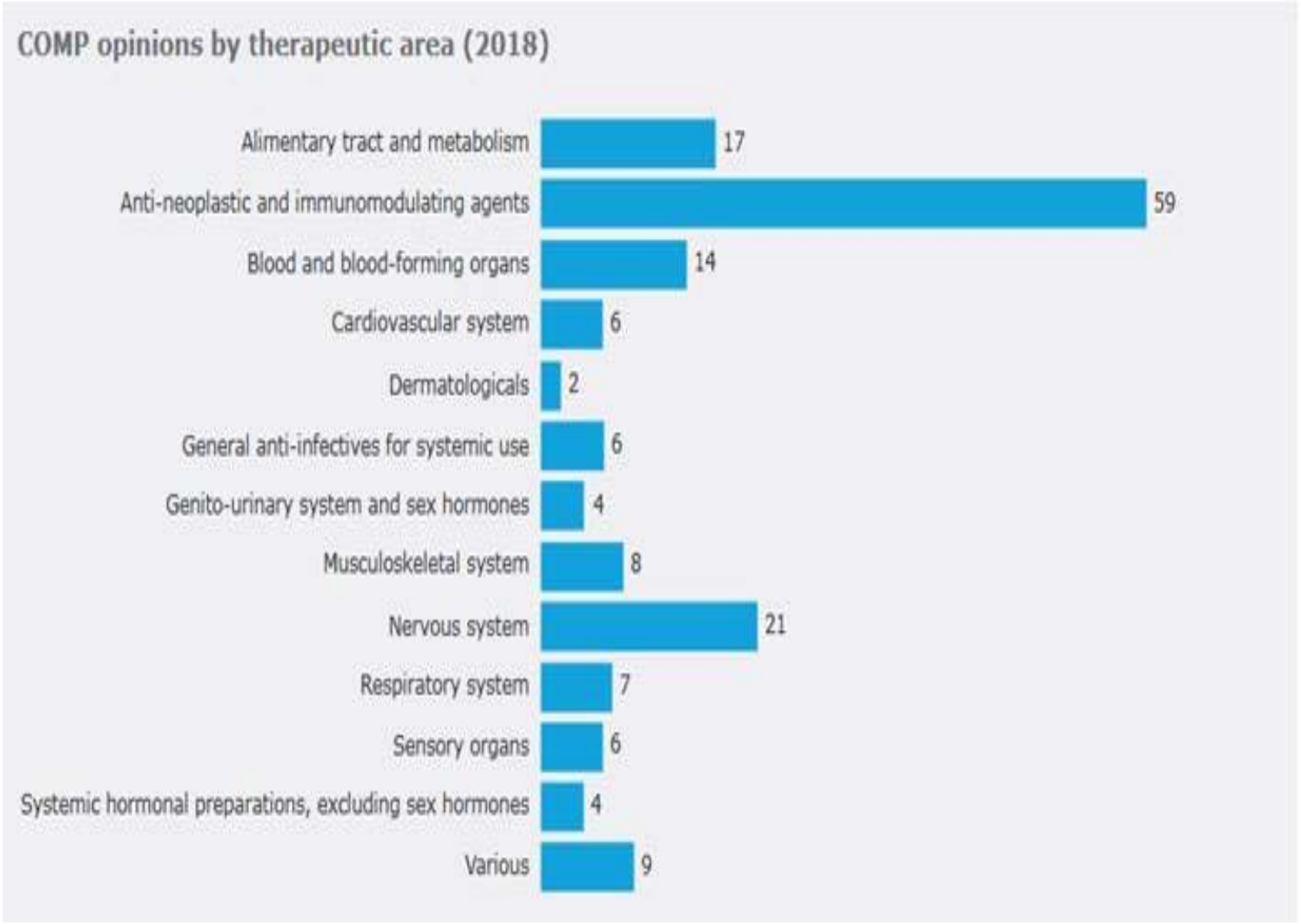
Competent EMA Committee for orphan designation = COMP

Definition of orphan status eligibility is regulated through EU Regulations (EC) 141/200, (EC) 847/2000

Basic requirements:

- Intended for diagnosis, prevention or treatment
- Condition is life-threatening or chronically debilitating
- Point prevalence in EU population ≤ 5/10,000
- Significant benefit/improvement in efficacy, safety or patient benefit versus other existing approved treatments (if any)

1. Current initiatives at EU level - State of play COMP



1. Current initiatives at EU level - State of play COMP

Rare Cancers

Since start of COMP up until the end of 2018 a total of 3,210 orphan status applications have been received.

Of these 2,134 received a positive COMP opinion

34 % of all positive COMP opinions in this timeframe were for anti-neoplastic agents.

In the period January – October 2019 **an additional 10** antineoplastic agents received a positive COMP opinion.

⚠ **Orphan Designation ≠ Marketing Authorisation** ⚠

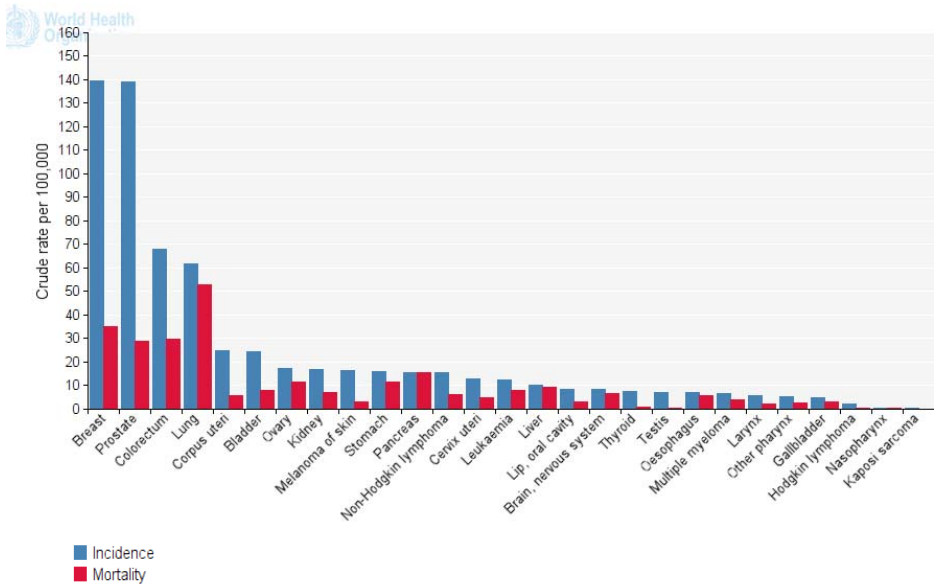
1. Current initiatives at EU level - State of play Paediatric oncology, a public health issue in the EU

Rare Cancers

- Cancer is the leading cause of death by disease past infancy among children in the EU
- **28 %** of total causes of death in the age group 5-9
- **23 %** of total causes of death in the age group 9-14
- Every year, more than 6,000 young people in Europe die of cancer.
- There are more than 300,000 European childhood cancer survivors (**in 2020, there will be nearly half a million**): two thirds of them have some late side effects of treatment, that are severe and impact the daily life of half of those affected.
- http://ec.europa.eu/eurostat/statistics-explained/index.php/Cancer_statistics, Gilles Vassal, et. al, 2016

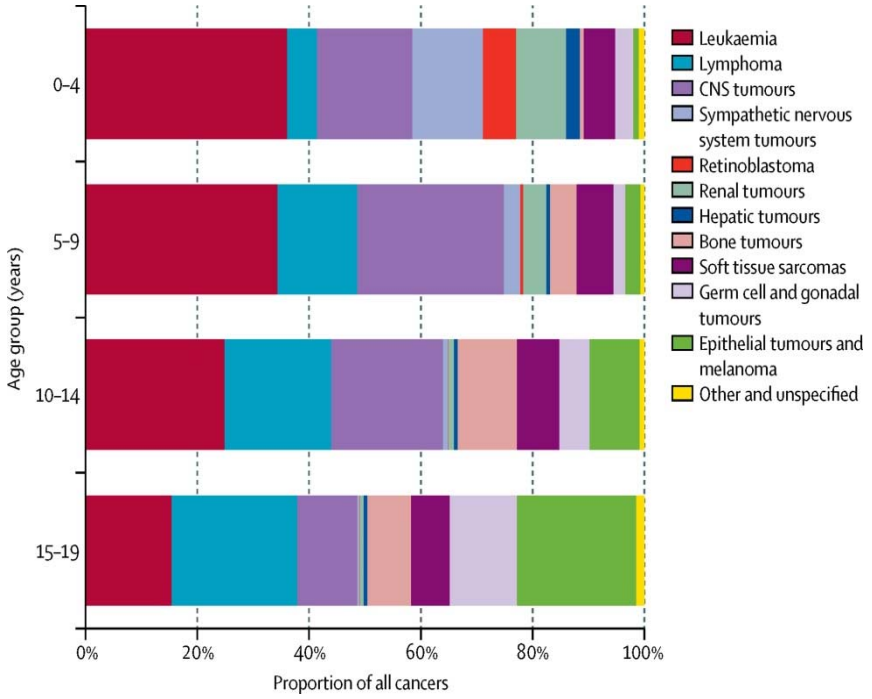
Spectrum of cancer types: adults vs children

European Union (EU 28), both sexes, all ages



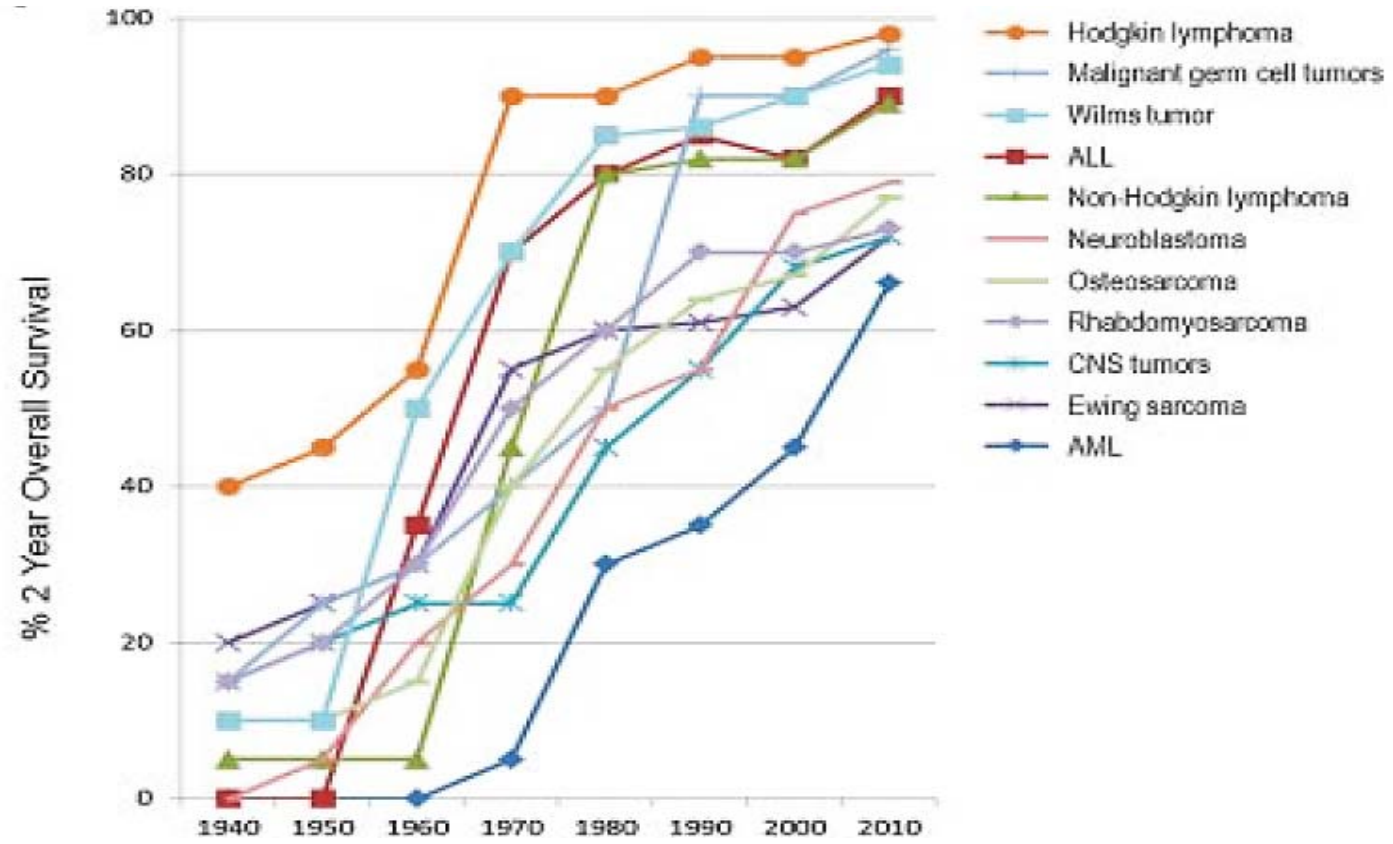
GLOBOCAN 2012 (IARC)

Proportional distribution of cancer type by age group, 2001–10



The Lancet Oncology 2017 18, 719-731DOI: (10.1016/S1470-2045(17)30186-9

Improved survival, but … not for all, and at high cost



Rössig et al.: Effective childhood cancer treatment: The impact of large scale clinical trials in Germany and Austria. Pediatric Blood & Cancer 2013 doi:10.1002/pbc.24598

1. Current initiatives at EU level - State of play Paediatric oncology strategy forum

Main aims:

- Review unmet therapeutic needs of children with certain types of cancer
- Review opportunities for targeted paediatric development of innovative anti-cancer medicines
- Bringing together all relevant stakeholders (patient organisations, academia, pharmaceutical industries and regulators)
- Convened relevant academic researchers, patients and industry
- Precompetitive platform for collaboration
- Defined clinical features, biology and unmet therapeutic needs including 'possible' prioritisation of medicines
- Shared up-to-date non-clinical and clinical data
- Discussed best approach to address lack of paediatric medicines
- Participants from Regulatory bodies: PDCO oncologists, CHMP, COMP, SAWP, Oncology Working Party members, EMA, FDA

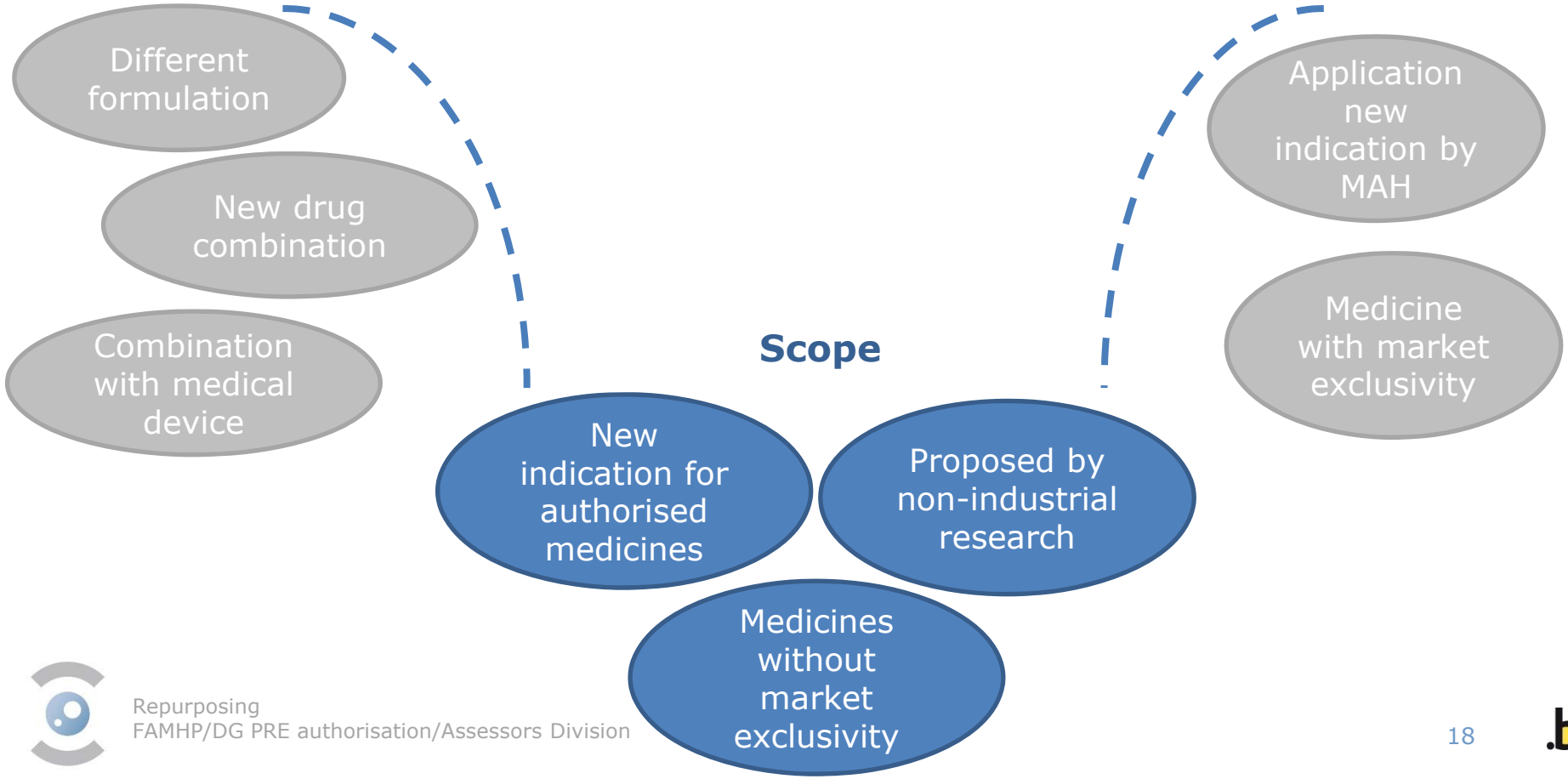
1. Current initiatives at EU level - State of play Paediatric Regulation: achievements in paediatric oncology

- **83 PIPs (about 10 % of all PIPs) concern paediatric cancers**
  - Since 2007, 14 paediatric indications for anti-cancer medicines were centrally authorised, 7 based on PIPs. **Before the Paediatric Regulation, only 3 anticancer medicines had been authorised under the centralised procedure.**
  - Until September 2017, MAAs for 68 new anti-cancer medicines for adults fell under the paediatric regulation (art. 7). For 41 medicines, pharmaceutical companies had previously obtained a waiver of paediatric studies. **Most of these 41 waived anti-cancer medicines would have a potential for addressing unmet therapeutic needs in other cancers affecting children.**

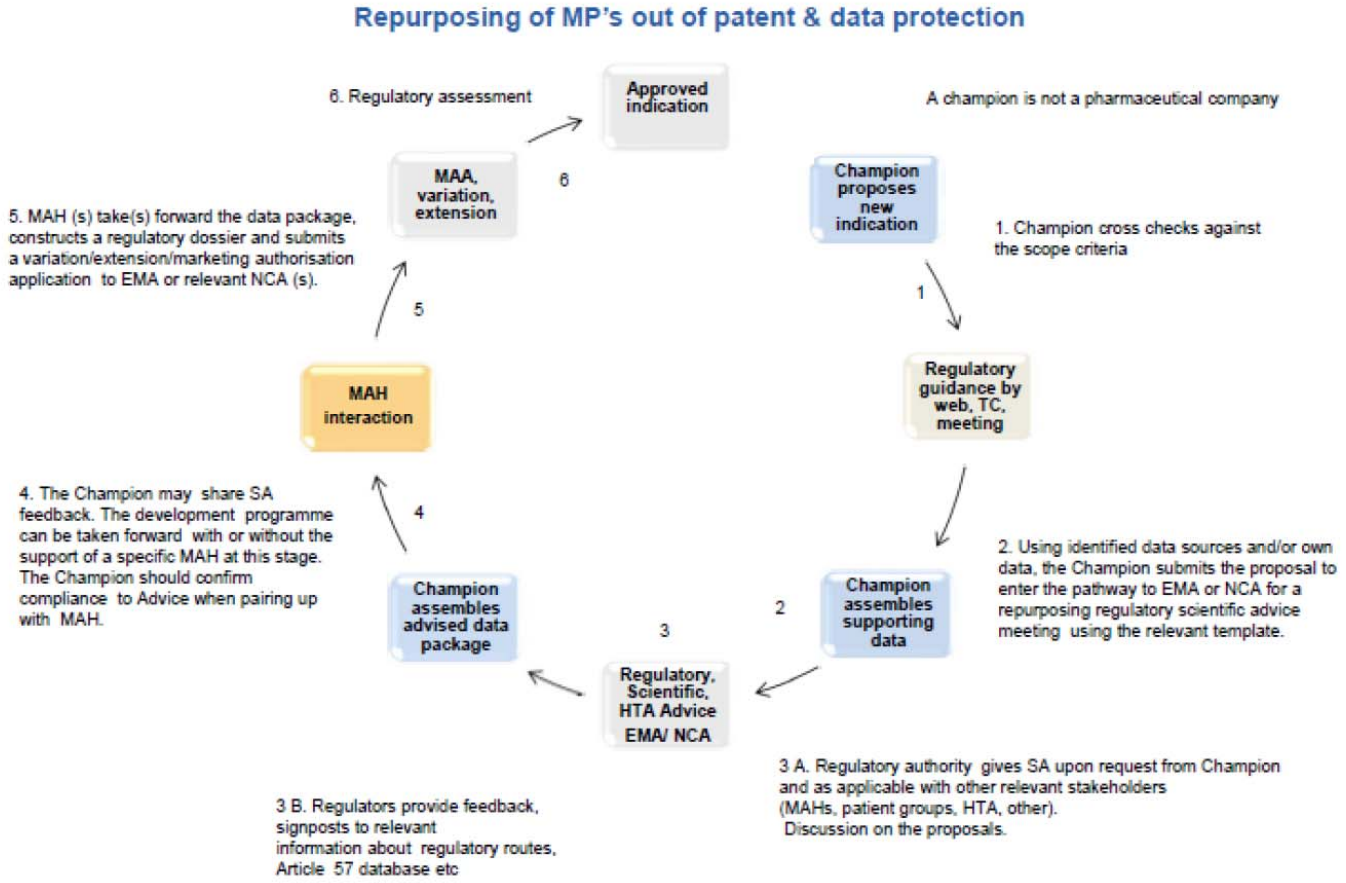
Repurposing - Definition & scope

(Provisional) definition (STAMP 08.12.2017)

" Drug repurposing is the process of identifying new uses for existing medicines in indications outside the scope of the original approved product information " (STAMP 08.12.2017)



1. Current initiatives at EU level - State of play Repurposing

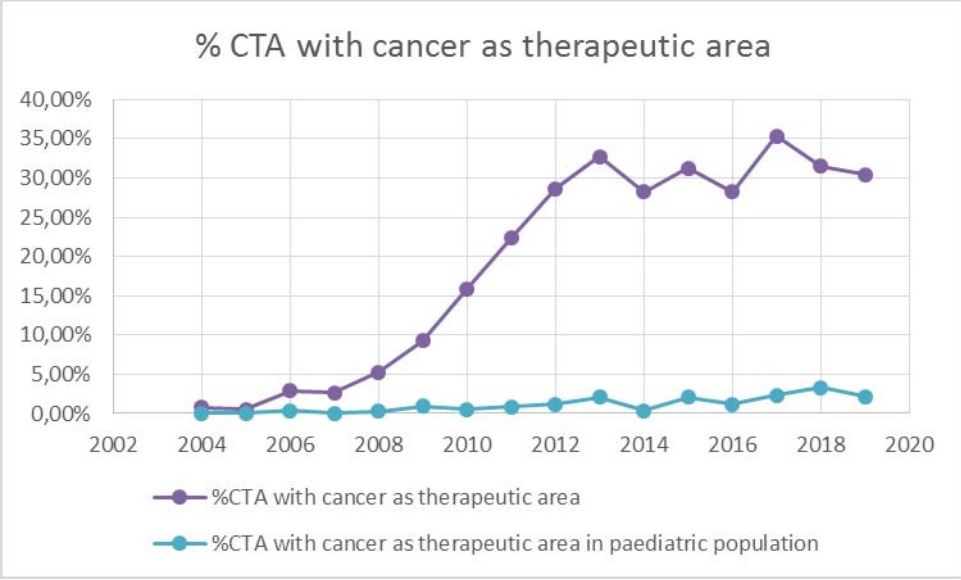


FAMHP ready to take pilots (especially in the domain of oncology)

2. Current initiatives at national level - State of play

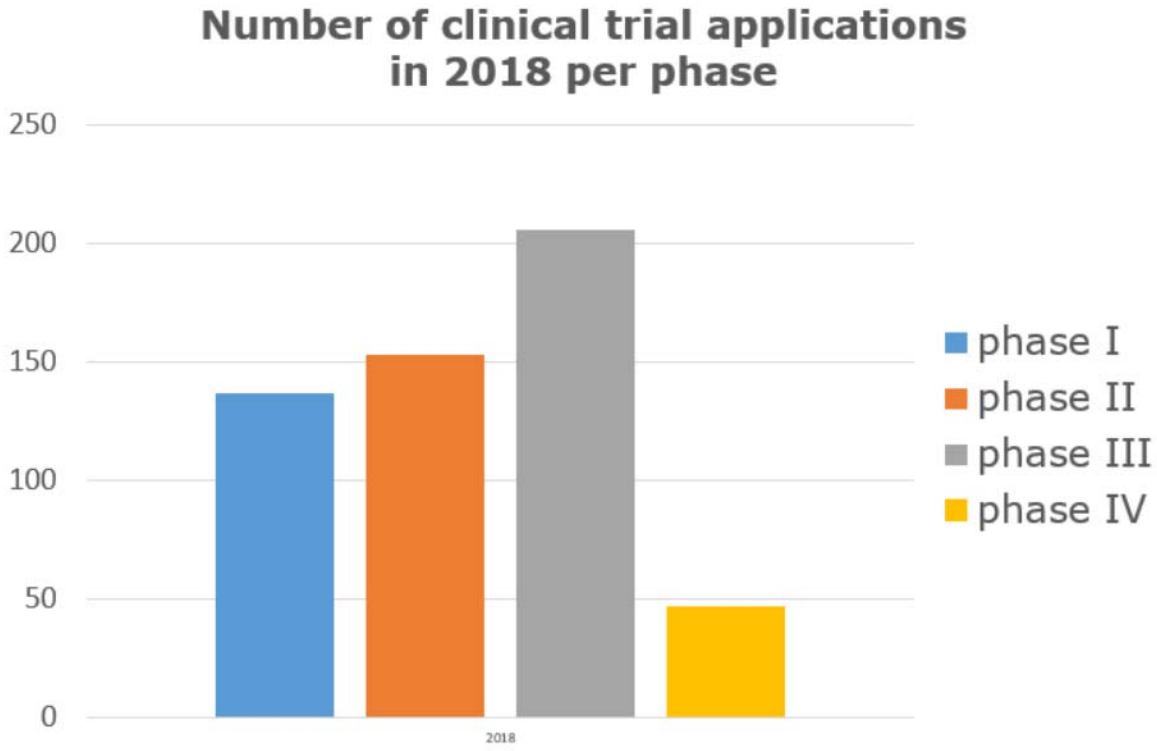
Clinical trials

Year	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
#CTA	267	529	523	559	630	530	559	488	510	569	546	615	506	524	543	506
#CTA with cancer as therapeutic area	2	3	15	15	33	49	89	109	146	186	154	192	143	185	171	154
#CTA with cancer as therapeutic area in paediatric population	0	0	2	0	2	5	3	4	6	12	2	13	6	12	18	11
%CTA with cancer as therapeutic area	0,75%	0,57%	2,87%	2,68%	5,24%	9,25%	15,92%	22,34%	28,63%	32,69%	28,21%	31,22%	28,26%	35,31%	31,49%	30,43%
%CTA with cancer as therapeutic area in paediatric population	0,00%	0,00%	0,38%	0,00%	0,32%	0,94%	0,54%	0,82%	1,18%	2,11%	0,37%	2,11%	1,19%	2,29%	3,31%	2,17%



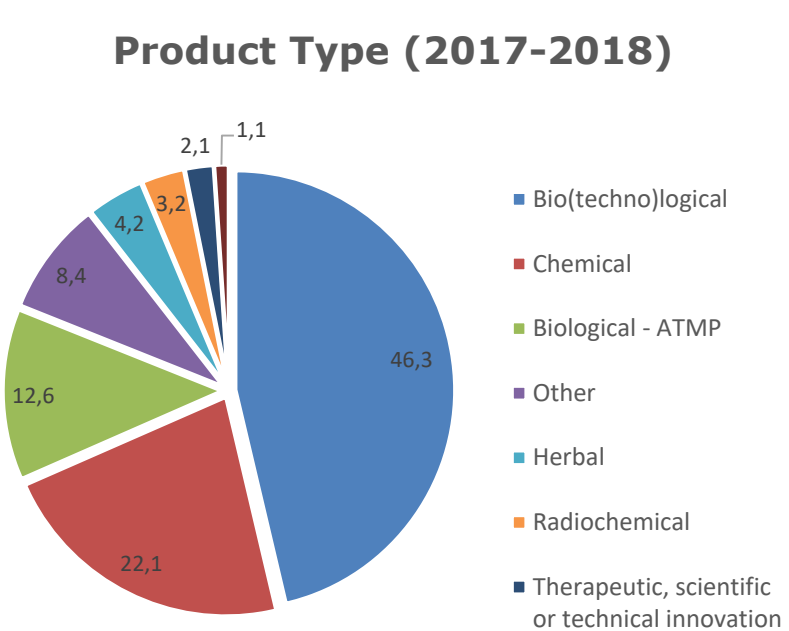
2. Current initiatives at national level - State of play

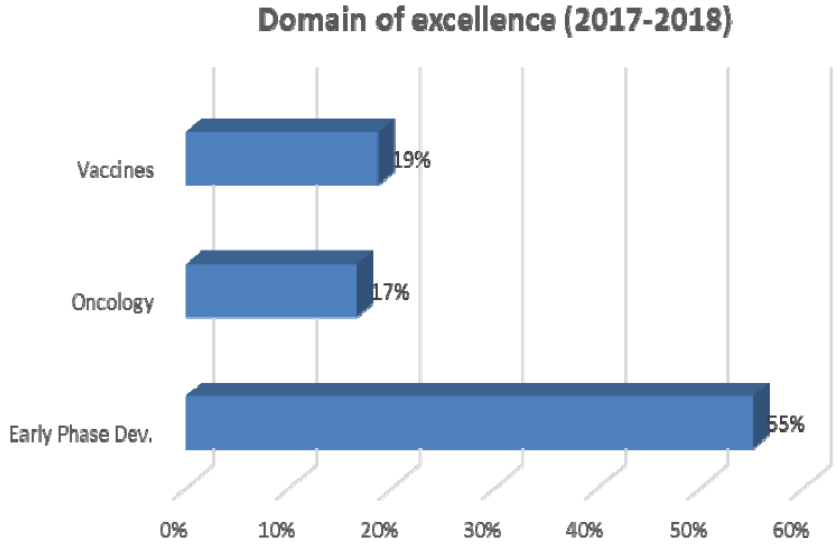
Clinical trials

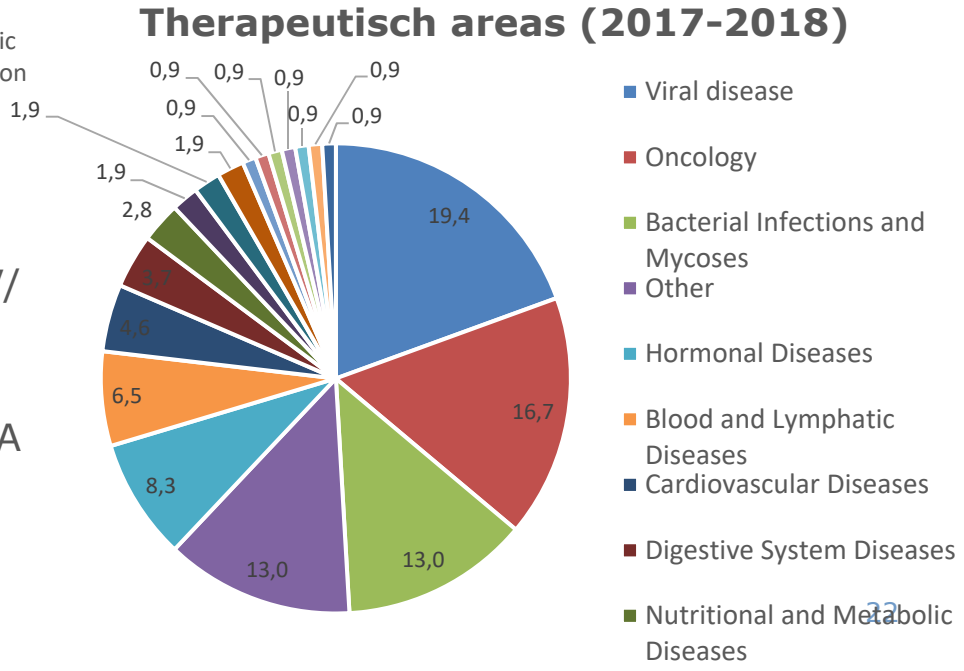


- Assessment of clinical trials in oncology in 2018: 12 pilots, 6 CTAs in paediatric population, 7 for ATMPs, 8 CTAs in VHP procedure

2. Current initiatives at national level - State of play National scientific advice







- 6 joint scientific-HTA advices with RIZIV/ 53 advices in total (2018)
- Strong link between:
  - National STA & CTAs (up to 70 % CTA related)
  - National STA & FAMHP domains of expertise

2. Current initiatives at national level - State of play

Unmet medical need

Compassionate use program and medical need program: foresee an early access to innovative medicinal products or with a major therapeutic value.

2. Current initiatives at national level - State of play

Article 83 of regulation 726/2004

National transposition
(national law of medicine 1 May 2006)

ETA = CUP/MNP

Compassionate Use Program (CUP): for medicinal product **without ANY** authorisation. Art. 106 of RD 14 December 2006

Medical Need Program (MNP): for medicinal product with **at least one** approved indication. Art. 107 of RD 14 December 2006

Urgent request of compassionate use (for medicinal product without ANY authorisation). Art. 107/1 of RD 14 December 2006

Legal Framework

Cornerstone: Regulation (EC) 726/2004

Objective of a Compassionate Use Program

In order to meet, in particular, the legitimate expectations of patients and to take into account the **increasingly rapid progress of science and therapies**, **accelerated assessment** procedures should be set up, reserved for medicinal products of major therapeutic interest, and procedures for obtaining **temporary authorisations** subject to **certain annually reviewable conditions**. In the field of medicinal products for human use, a common approach should also be followed, whenever possible, regarding the criteria and conditions for the compassionate use of new medicinal products under Member States' legislation.

Facilitating the translation of innovative scientific advances into medicinal products meeting adequate standards and accelerate patients' access to promising therapies fulfilling unmet medical needs.

Legal Framework

Regulation (EC) 726/2004

Art. 83: Compassionate Use (CU)

"Making a medicinal product available for CU reasons to a group of patients with a **chronically** or **seriously debilitating disease** or whose disease is considered to be **life threatening** and who **cannot be treated satisfactorily** by an **authorised** medicinal product."

⇨ A global **worldwide common terminology** "compassionate use".

⇨ "Authorised" means approved **in the indication**.

Legal Framework

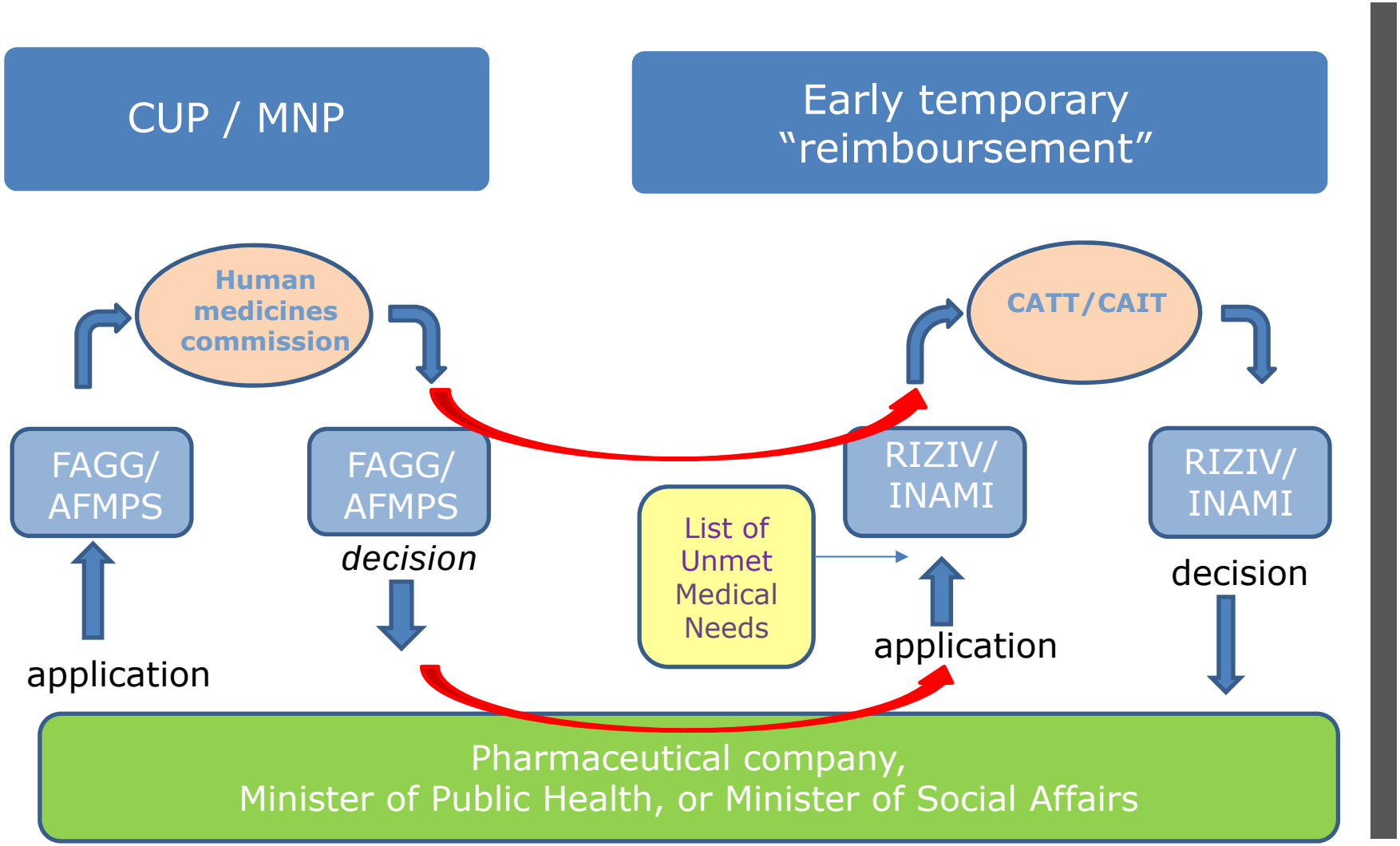
Common generalities for CUP and MNP

- ⇨ There is an unmet medical need OR clear added value of the new therapy
- ⇨ The medicinal product must be **subject of a MA** application or must be **undergoing a Clinical Trial** in the EU and/or elsewhere
- ⇨ **NOT** a substitute for properly conducted trials
- ⇨ Patients should always be considered for inclusion in clinical trials **before** being offered a CUP/MNP.

2. Current initiatives at national level - State of play

- National procedure of 55 days
- Consolidated advice from Commission on Medicinal Products and one Ethics committee
- CUP/MNP could cover a gap between the current development of medicinal product and its commercialisation
- Free access for patients
- Ensure new access/opportunity for patients with unmet medical need
- Could ensure the continuity of treatments after clinical trials up to commercialisation

CUP – MNP at national level: ETA-ETR



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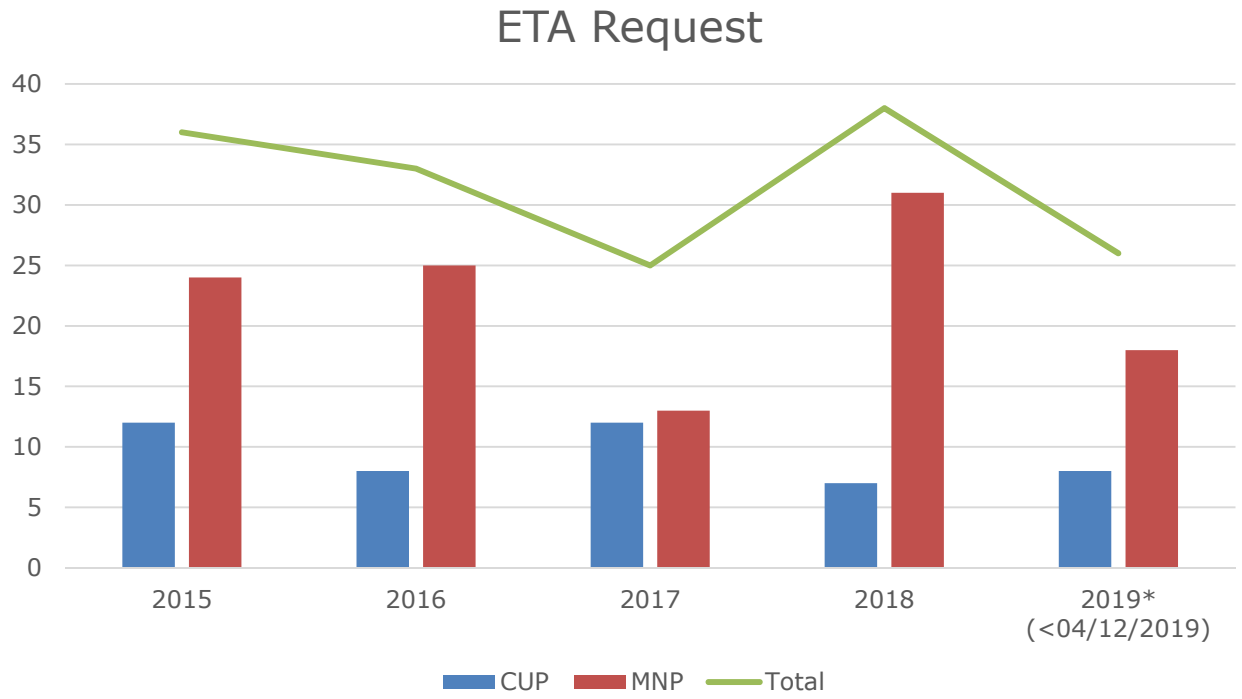

- Mean/year: 10 CUP/24 MNP
- Intention to request ETR: 10 CUP and 3 MNP
- ~30 % Orphan designation (41 % of CUP and 25 % of MNP submitted)

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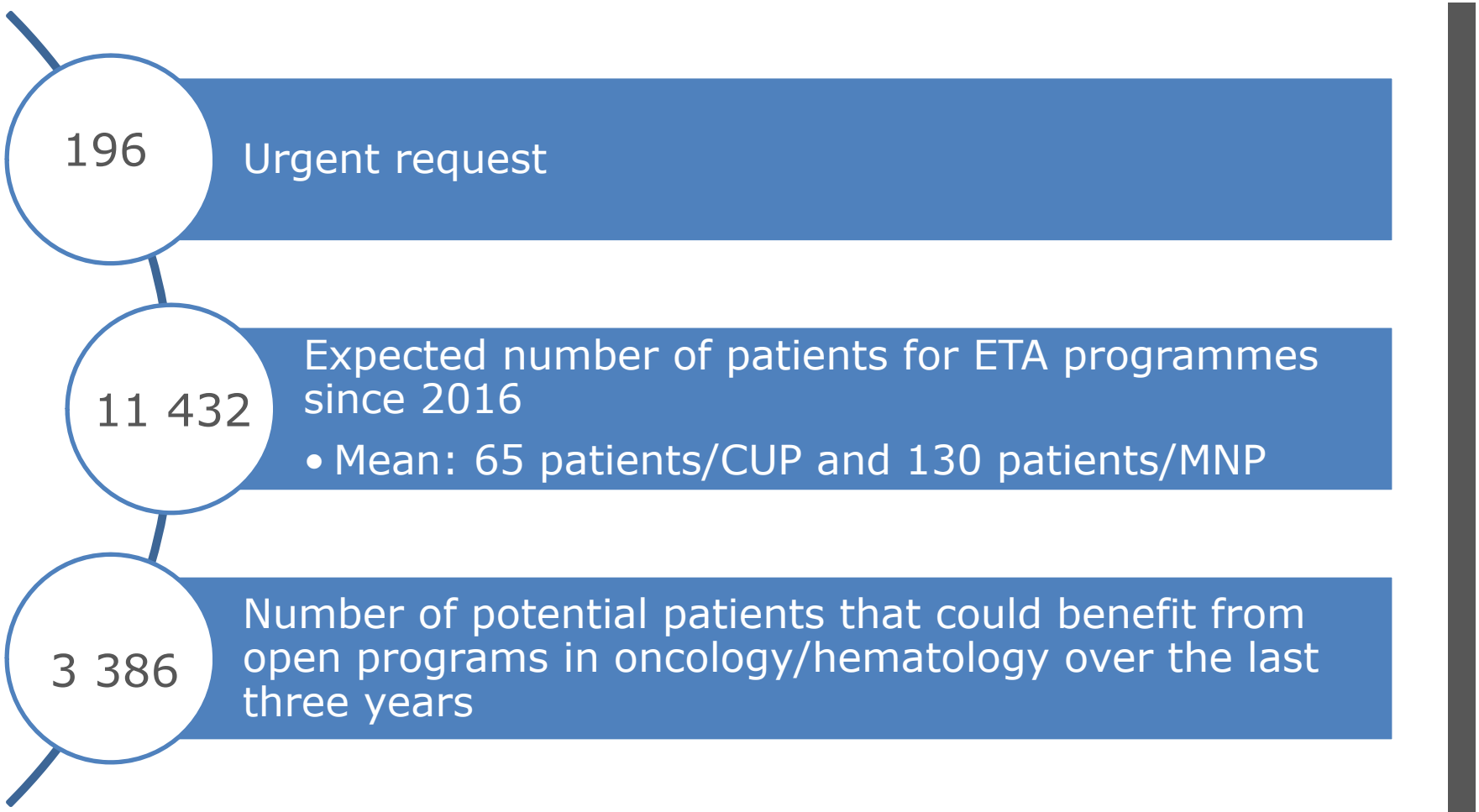
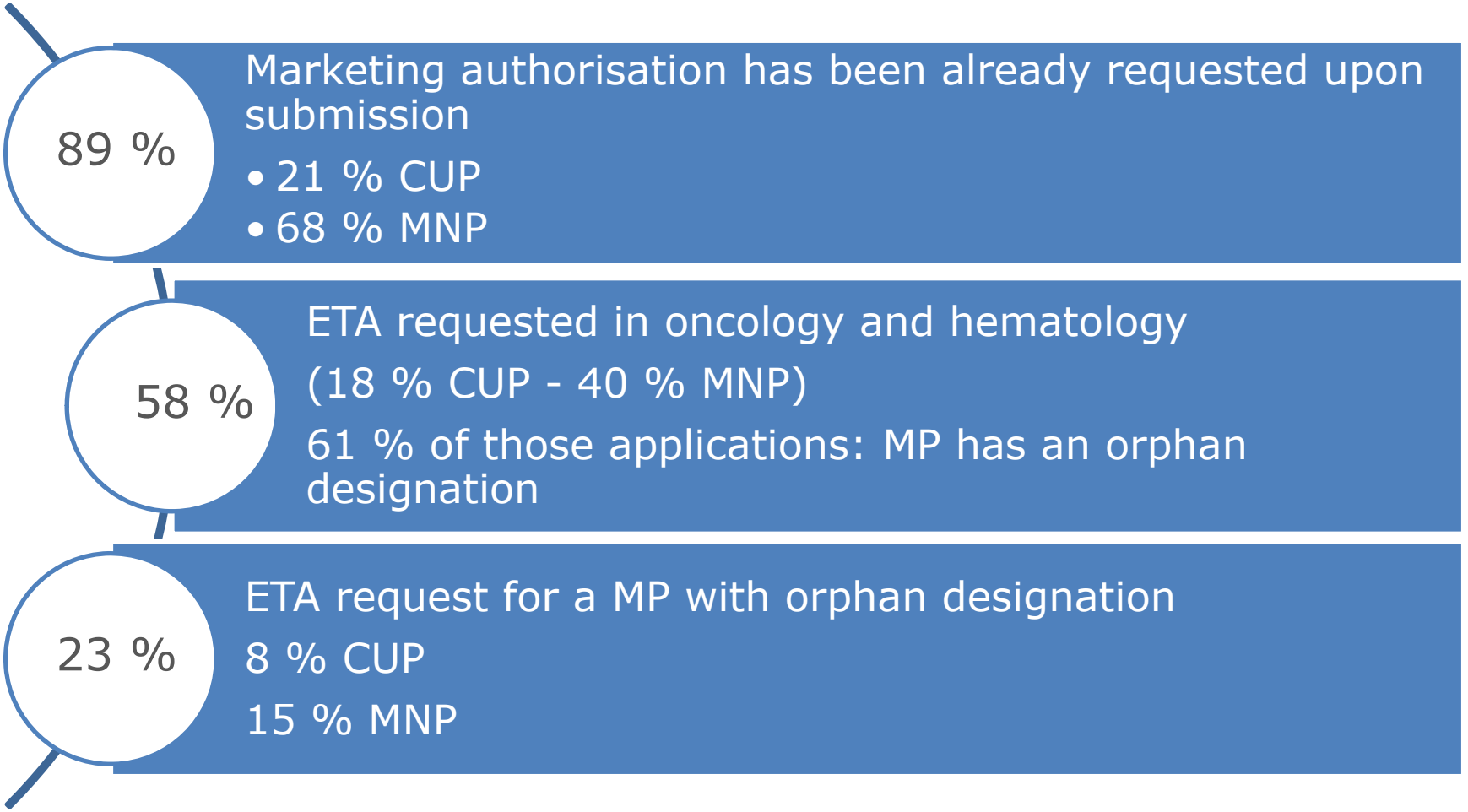
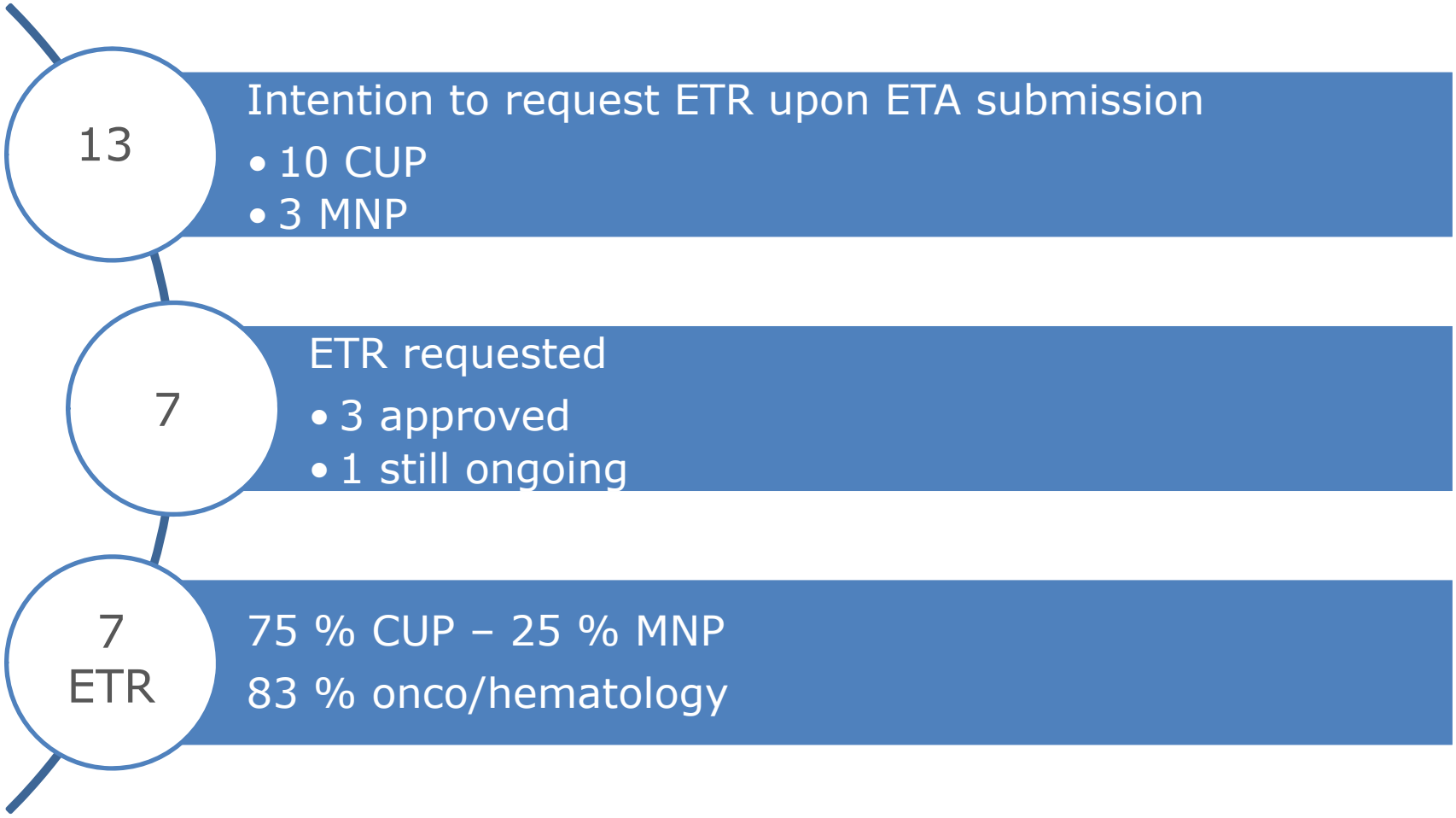

196
Urgent request
11 432
Expected number of patients for ETA programmes since 2016
• Mean: 65 patients/CUP and 130 patients/MNP
3 386
Number of potential patients that could benefit from open programs in oncology/hematology over the last three years


89 %
Marketing authorisation has been already requested upon submission
• 21 % CUP
• 68 % MNP
58 %
ETA requested in oncology and hematology
(18 % CUP - 40 % MNP)
61 % of those applications: MP has an orphan designation
23 %
ETA request for a MP with orphan designation
8 % CUP
15 % MNP


13
Intention to request ETR upon ETA submission
• 10 CUP
• 3 MNP
7
ETR requested
• 3 approved
• 1 still ongoing
7
ETR
75 % CUP – 25 % MNP
83 % onco/hematology

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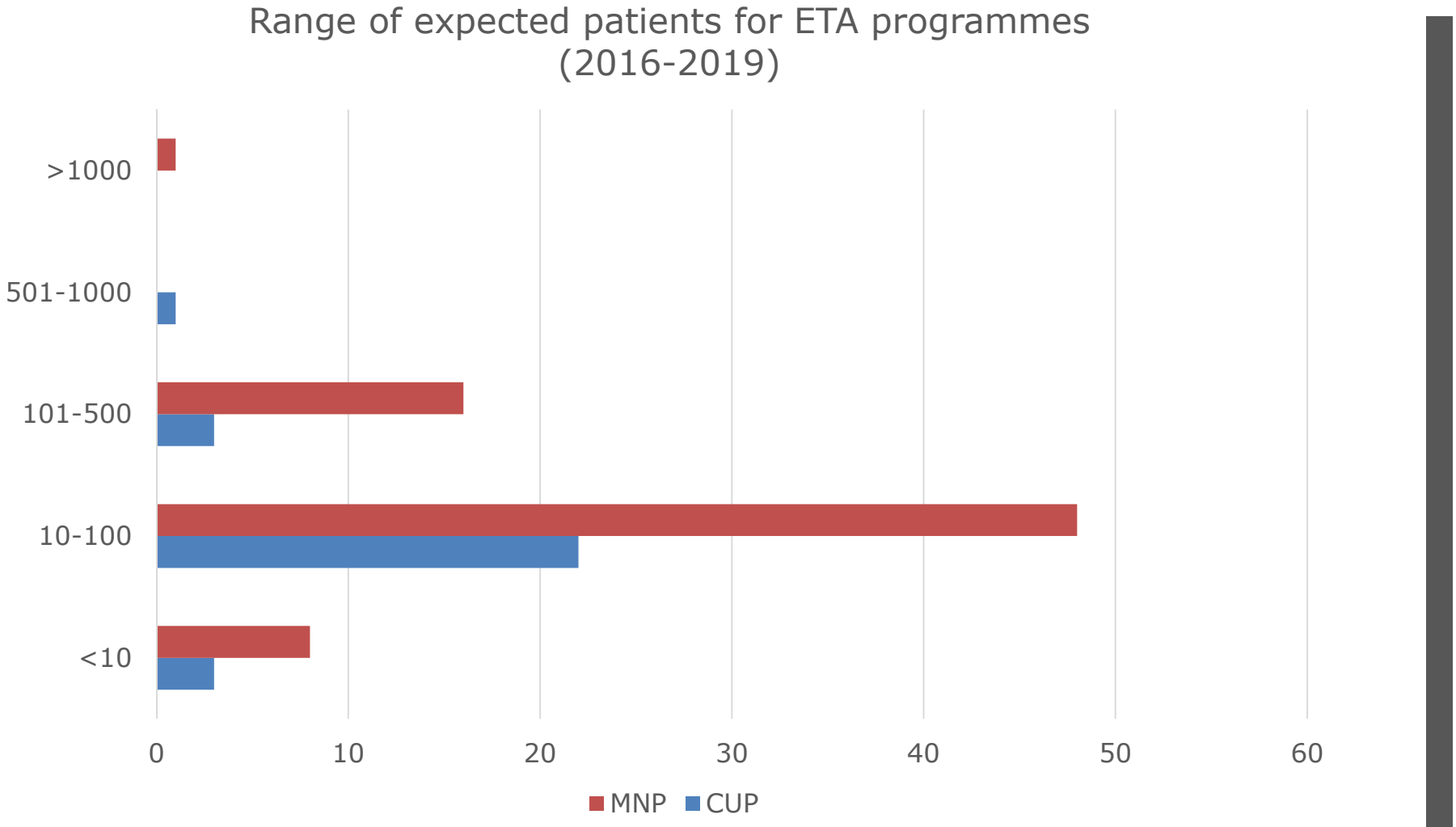
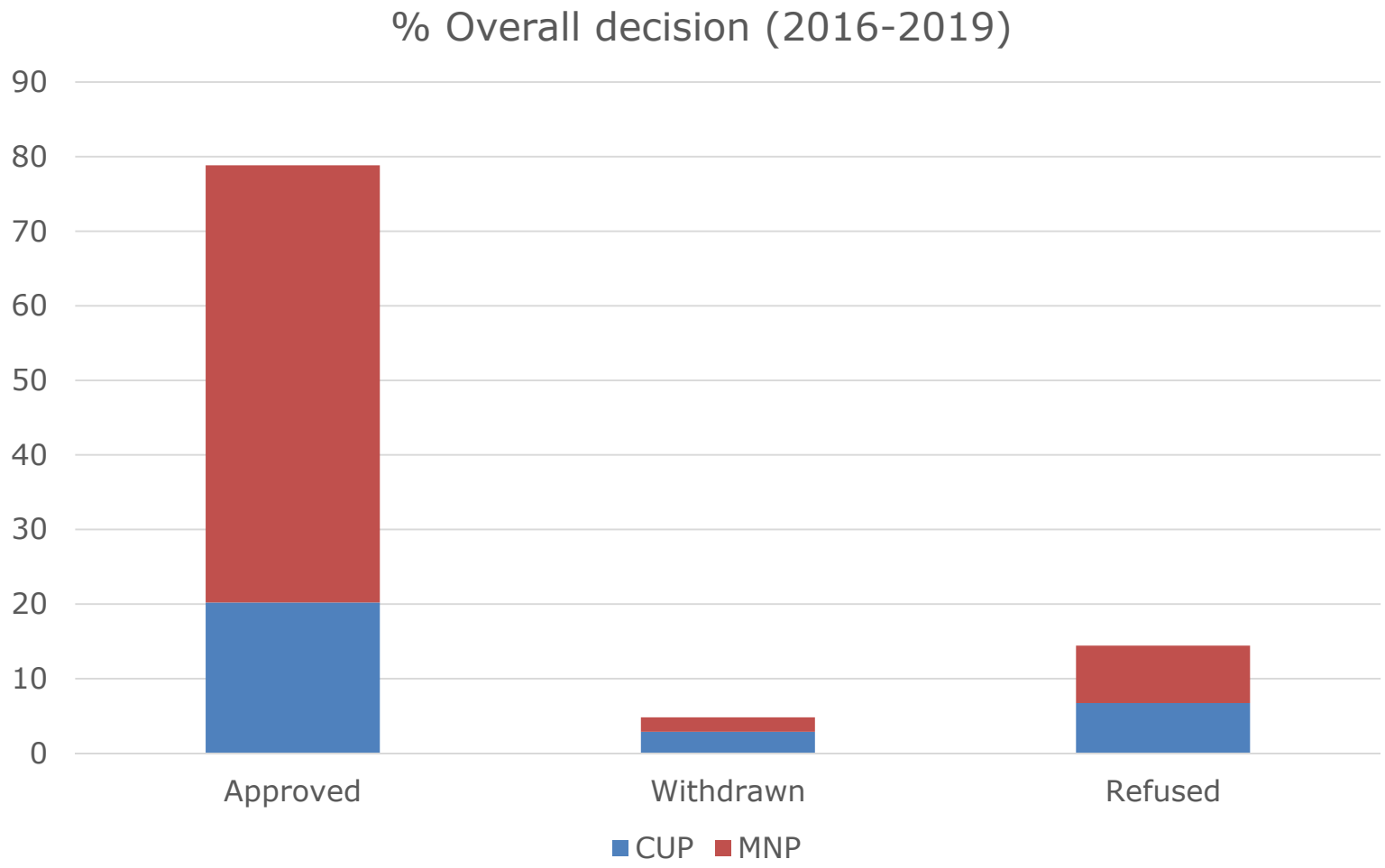

Range of expected patients for ETA programmes (2016-2019)
>1000
501-1000
101-500
10-100
<10
0
10
20
30
40
50
60
MNP
CUP

Some data


% Overall decision (2016-2019)
90
80
70
60
50
40
30
20
10
0
Approved
Withdrawn
Refused
CUP
MNP

2. Current initiatives at national level - Involvement of the patients

- Patient representatives at the Commission on medicinal products for human use
- Collaboration with patient organisations (disease oriented) for the scientific advice procedure:
  - 5 post hoc procedures
  - Pilots started in the real time (including 1 application in the domain of oncology)
  - Positive feedback and willingness to continue
- Objective to expand step wise to clinical trial applications and CU/MNP procedures

3. Opportunities for the future

- ICH patient focused development reflection paper
- Accelerate science for the benefit of patients
  - National Innovation office @ EU-INNO
  - Clinical trials: care option?
  - Digitalisation:
    - Patient recruitment
    - Patient compliance
    - Awareness raising
    - Patient support (remote clinical trials …)
- **Data**
  - Returning data to patients
  - Real World Data complementing Randomised Clinical Trials
- **Affordability**
  - Reducing R&D costs
  - Innovate regulations and regulate innovation
  - Reimbursement: Onco Budget challenges: Round table initiative organised by RIZIV-INAMI, 07.11.2019

Thank you for your attention

Contact

Federal Agency for Medicines and Health Products – FAMHP

Victor Hortaplein - Place Victor Horta 40/40
1060 BRUSSELS

tel. + 32 2 528 40 00
fax + 32 2 528 40 01
e-mail welcome@fagg-afmps.be

www.famhp.be

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