EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

OMP Working Group Meeting

3 November 2022

Competition Law Compliance Policy

EUCOPE brings together representatives innovative companies to discuss common issues, challenges and trends affecting the pharmaceutical industry. This activity can be perfectly legitimate. However, certain competition law risks may arise in relation to EUCOPE's activities.

EUCOPE's European Union ("EU") compliance policy ("Policy") explains these competition law risks and aims to ensure compliance by all members and EUCOPE staff with the rules applicable in the EU. EUCOPE itself and its members are subject to these rules when engaging in any EUCOPE related activities. Any anticompetitive behavior adopted by a member can result in serious financial, criminal and/or disciplinary penalties, as well as other harm (e.g., reputational harm) for EUCOPE, represented companies and for meeting participants personally.

Competition Law Compliance Policy

There are certain matters which **should not** be discussed with competitors before, during or after any such meetings. These include:

- Territorial restrictions, allocation of customers, restrictions on types of services, or any other kind of market division;
- Prices, price changes, conditions of sale (including payment terms and guarantees), price differentials, discounts;
- Current market conditions and issues, including industry pricing policies or patterns, price levels; capacity (including planned or anticipated changes regarding those matters), except where limited to the discussion of historical or public information;

[cont'd]

Competition Law Compliance Policy

- Individual costs, cost accounting formulas, methods of calculating costs;
- Individual company figures on market shares, sources of supply, capacity;
- Information as to future plans of individual companies concerning technology, capacity, marketing or sales; and
- Matters relating to individual suppliers or customers.

Attention: these rules equally apply to informal discussions before, after, or during each meeting. If any sensitive information is discussed or disseminated, insist that the discussion be terminated immediately and make sure that your objection is recorded in the minutes. If necessary, leave the meeting and immediately inform EUCOPE's General Counsel.

Agenda

I. Welcome & introduction

II. OMP Regulation revision

- Latest intel on OMP proposal
- Work on unmet medical needs and launch obligations
- 2022 activities roundup
- 2023 priorities and action plan

Agenda (cont)

IV. The financial ecosystem of pharmaceutical R&D: An evidence base to inform further dialogue – Study commissioned by Dutch Ministry of Health, Simon Middleton, Europe Life Sciences L.E.K. Consulting

V. Italian Political Environment post elections – outlook on rare disease policies, Francesco Macchia, Rarelab

IV. Important Projects of Common European Interest (IPCEI) – OMP and G&CT, Laura FABRE, European healthcare industry, French Ministry for the Economy, Finances and the Recovery

Agenda (cont)

VII. Swedish Political Environment post elections – outlook on rare disease policies, Kajsa Wilhelmsson, Oxford Health System Reform Group

VIII. Regulation (EU) 2021/2282 on health technology assessment

IX. AOB

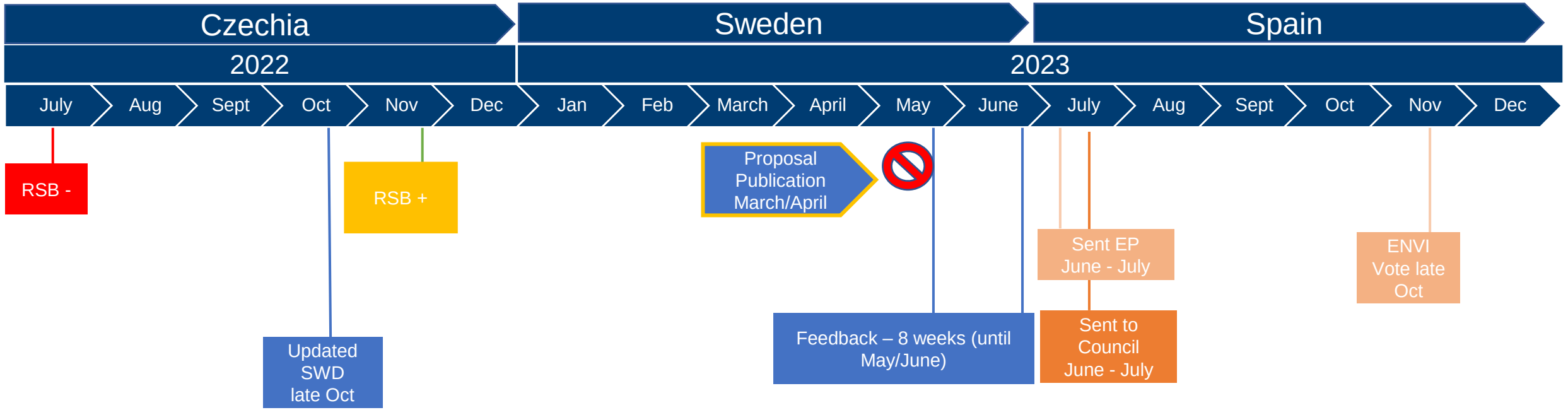
Next meetings

- 09 November: Digital Health Working Group Meeting
- 29 November: Regulatory Working Group Meeting
- 06 December: Cell & Gene Therapy Working Group Meeting
- 07 December: P&R/Market Access Working Group Meeting

I. Welcome & introduction

II. OMP Regulation revision

Legislative Overview and intelligence



Cut off point for EC proposal presentation : MAY

Council position might not be reached but discussions will start

EP Plenary vote on proposals in 2024?

These timings are indicative and rough estimates, not official – it assumes a ‘fast’ process

MEP Overview - ENVI

Possible rapporteurs and Shadows

Below are possible MEPs that might be interested in key EUCOPE files or are already engaged on different topics.

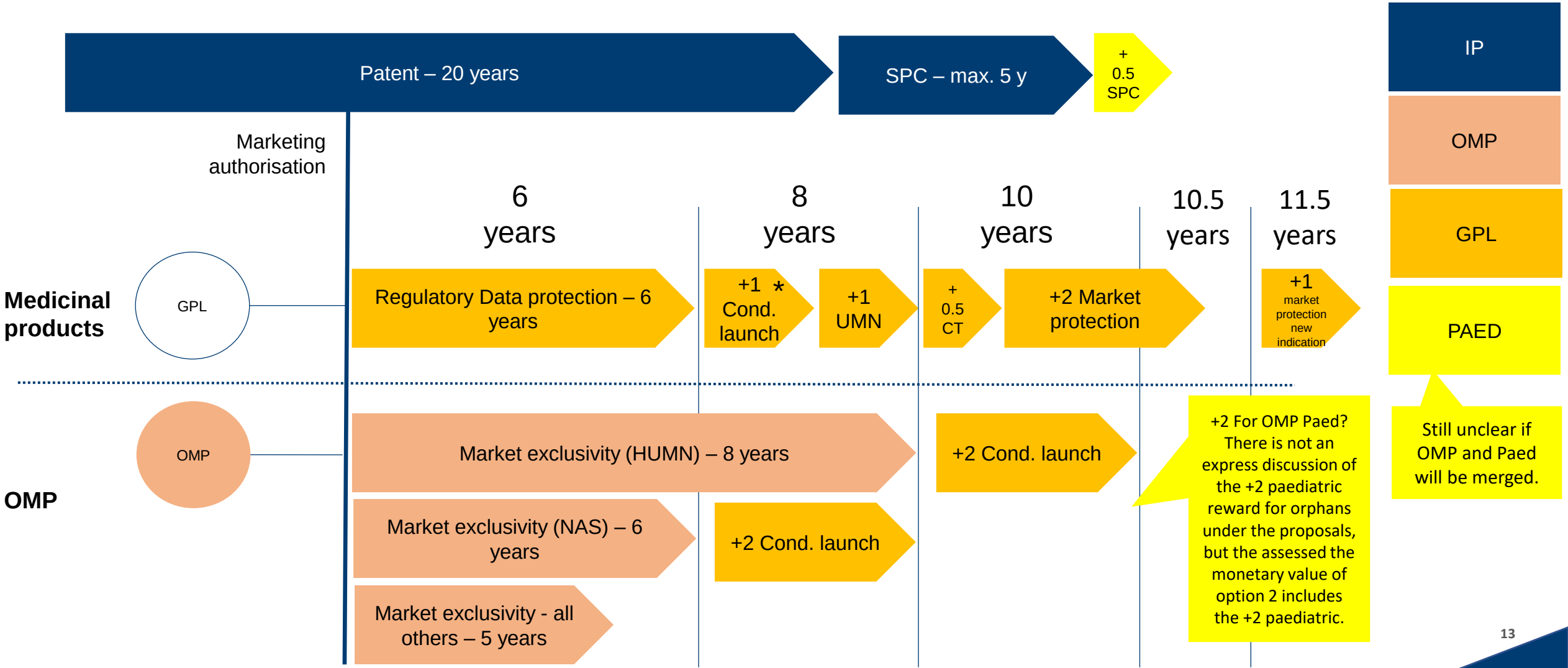
These are predictions and subject to significant changes and updates

GPL

OMP

Paediatrics?
Rumors of combining not confirmed

OMP, PAED and GPL: how they interact



*Assumes +1 RDP for launch – possible RDP is extended to 6, 8, 9, 9.5 +2 MP

Informal intel

Czech presidency meeting on rare diseases and beyond

- Our alternative on modulation widely disseminated +Eurordis opening challenged the baseline of 5 years
- Commission mentioned some of our concerns will be addressed
- Commission informally spoke of safeguards to address our concerns on launch conditionalities/obligations
- Swedish presidency very topline on their focus on rare disease rather spoke of health in general: EHDS, Genomics and ERNs
- Next step: additional meeting with DG grow at DG level, follow up with SANTE in Q1

EURORDIS Call for a rare disease action plan

Rare disease conference, Prague

- **The call to Action** focuses on the following EURORDIS longstanding asks:
- To support the early diagnosis of people living with a rare disease, specifically newborn screening programmes.
- To evolve the incentives framework to maintain predictability for sponsors while enhancing Europe's competitiveness through the upcoming revision of the Orphan Medicinal Products and Paediatric Regulation.
- To improve access to treatments, including further exploring European cooperation in pricing and negotiations.
- To foster holistic care and integrate the European Reference Networks into national health systems.
- **NEXT STEPS**: bringing the call to action up for discussion at the December EPSCO for the endorsement of the other member states.

EUCOPE's messages

EUCOPE's position

Where are we focusing now?

Proactive points

- Alternative approach to modulation, not based on UMN but business case along with our proposal to carry over SB in HTA
- Maintain as broad as possible the designation (including avowing narrow HUMN definition and cumulative prevalence)

Reactive points/result of Sept workshop

- Develop an approach to HUMN governance
- Develop criteria for products to be exempted from launch obligations:
  i. Size and distribution of the target patient population
  ii. Whether a company has a footprint (or the ability to be present) in all Member States
  iii. Technological or technical limitations that prevent launch in all Member States

Joint advocacy with other trade associations (TBC)

- UMN: a broad cross trade call against a restrictive definition
- Paediatric: if proposal stands the most controversial aspect is that Studying a medicine in children may only be delayed by maximum 5 years after their adult equivalent is authorised, possible joint positions of the associations on this

UMN and conditionality/obligations

UMN intel update

- Commission's intension is to establish a **criteria-based approach**, potentially consisting of **disease level and product level** criteria.
- Mixed perception in the broader community

EPF supports a criteria-based approach while maintaining a broad understanding

EURORDIS sees UMN as a process:

- Recognize the need to avoid criteria
- Establish process to allow very early stage dialogue with multi-stakeholder format
- Establish patient focused drug development group to support early dialogue (e.g. FDA Patients' Focus Group)

EUCOPE UMN White Paper

Structure

1. What is at Stake
   - Summary of key messages
2. Lack of a consensus
   - Challenge in finding a single definition and the consistency of UMN after treatment (MM & MPN)
3. Possible implications of the legislative review
   - Inability to direct research and the consequence on pricing
   - Cure as an inappropriate criterion
4. UMN in the Orphan context
   - An appropriate proxy already exists, and the HUMN approach creates an inappropriate ranking without addressing the underlying challenge
   - Modulation should look a the probability of success e.g. the investment case
5. EUCOPE Recommendations

EUCOPE UMN White Paper

Recommendations

1. Establish a multi-stakeholder dialogue along the drug development path, that includes patient representatives, developers, clinicians, regulators, HTA experts and payers, that can continuously refine and update existing assumptions on unmet needs;

2. Maintain a broad understanding of UMN at EU level by not formally codifying the concept in the General Pharmaceutical, OMP and Pediatric legislation, to encourage continued research for all patient populations who can benefit from therapeutic innovation. The necessary guidance is already provided in various legislative and non-legislative documents;

3. Avoid including the concept of ‘cure’ in any criteria for (H)UMN as this cannot be fully assessed at the time of marketing authorization and consider disease modifying criteria instead;

4. Launch an EU-wide rare disease strategy to support access to and development of novel therapies, especially in the 95% of rare diseases where no therapeutic options exist;

5. Modulate Orphan incentives through the lens of the probability of success i.e. the investment case, rather than through a ranking of unmet needs. This, along with policy initiatives that go beyond the OMP regulation, such as public private partnerships, can help addressing in particular the 95% of rare diseases without an approved treatment.

Outstanding discussion points

"EUCOPE understands that the **European Commission is considering adopting a restrictive and criteria-based definition of UMN and highest unmet medical need (HUMN)**. This **would have long-term and significant implications** … It should be acknowledged that the absence of a common understanding of UMNs can lead to misalignment and inconsistent decisions (e.g. between Regulatory and HTA bodies) and ultimately lead to access delays"

Next Steps

- EUCOPE to share pre-final version next week for final review (focus on language and validation – not revising positioning)
  - EUCOPE will include an executive summary that can serve as a stand-alone document
  - To be shared 7 November
  - **Deadline feedback**: 14 November

- Dissemination – discussion of activities
  - Q&A document
  - Animated position paper
  - Simplified speaking points
  - Other suggestions?

Conditionality Paper

- Content & key messages
  - Various obligations already exist to place a product on the market
  - Barriers to a launch obligation
    - Unique characteristics of therapies and diseases
    - Resource constraints of small and mid-sized companies
    - Non-proportional response in line with MAH powers
  - Legal assessment

- Next steps
  - Volunteers to develop carve out criteria
  - Need for additional dissemination activities?

2022 Activities

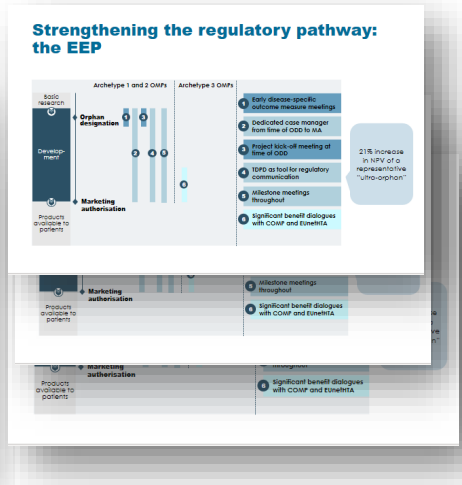
Material/Evidence developed so far

Tools

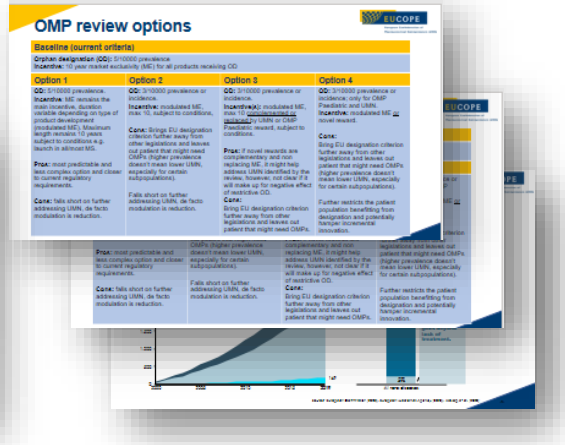
Position Paper

Position paper in brief

OMP Regulation info sheet



Archetypes approach



Messages deck

- **Partnerships:** European Expert Group on OD Incentives
- **With pharma TF:** Conditionality Paper and UMN paper (discussed today)

Overview of advocacy to date

Activities

Strong partnership, especially with EURORIDS on the lifecycle approach and how incentives are needed all across it, discussed with different policymakers for about 18 months with the backing of a multistakeholder community.

Go beyond SANTE in delivering the messages on the ‘holistic’ approach to incentives.

Identification and building of alliances in the Parliament through other relevant files and partnerships and ad hoc engagement.

Ad hoc in country advocacy, driven by coalition of the willing spreading messages and EUCOPE’s roundtables on the OMP review (x6). Covered countries: France, Italy, Netherlands, Spain, Germany, Sweden, Denmark, Czech republic, Ireland

Engagement with Member States

Activities

- Secretariat and members engaged with MS through events and follow ups
- EUCOPE: CZ, DE, ES roundtable + join FEDER roundtable, and outreach to SE, NL
- Members: Italy, Ireland, Nordics

Rationale

- As Member states are the ones to actually vote on European legislative reviews and the positions are developed in capitals, we organised a set of activities to
  - Raise awareness of the impact of the OMP legislation review
  - Share our position
  - Mobilise local stakeholders on the topic

Insights

- Except for top line messages on access and sustainability, the core of the issues remain largely technical
- Attaches and EPSCO remain focused on files on the table
- Payers becoming more ‘political’. Groups of payers also engage separately with the EC
- Many MS don’t have a final position but preliminary overview shows little alignment with industry

Communication & Dissemination

To be continued in 2023

- Podcasts & website
- Thought leadership
- Partnerships narrative

POLITICO

PHARMA BOARDROOM

REQUEST FOR BLOG POSTS – OMP; rare disease lifecycle; OMP UMN; RWE etc…

Information exchange and stakeholder network

OMP working group

OMP legislation review

- Cooperate, contribute and validate the work of the ISG

EU rare disease policies (R&D and HCPs)

- RD partnerships and EJPRD
- ERNs (evolution and assessment, ERICA project)

Global level policies

- IRDiRC-RDI Global Access Working Group to initiate research into barriers to accessing rare disease medicines
- UN Resolution on Persons Living with a Rare Disease

Work with Patients

- Connection with EURORIDS on their work e.g. ECRD

National updates

- CZ, Ireland, Germany, France, Sweden, Italy, UK

2023 Plans

Rationale of 2023 activities proposal

The legislation might be further delayed, small chance it is postponed all together.

We propose to scale up engagement, comms and visibility and be very nimble with evidence generation that should be support ad hoc proof points and amendments.

If the legislation is not published, further engagement with payers (drivers behind the review) and preparation to 2024 elections engagement could be considered (scenario 2/back up proposal in annex). We will remain flexible if something needs to be lifted from the ‘back up proposal’ into our 2023 (previously agreeing it with the ISG).

As for the engagement with the in-country colleagues, we don’t propose further roundtables but to maintain the informal network we created so that there can be coordination and exchange of intel.

Coordination of Member States Activities

Activities

- Maintain network of national affiliates, coordinate and share intel
- Make sure that national colleagues are alerted if meeting in Brussels with national stakeholders happens
- Create a platform for volunteer ad hoc activities

Rationale

- As Member states are the ones to actually vote on European legislative reviews and the positions are developed in capitals, we organised a set of activities to Raise awareness of the impact of the OMP legislation review
- At this point, it is in the hand of local contact to carry on the messages and input where they deem appropriate, not all MS have a fully formed position on the legislation, hence there's room for action

Evidence Generation

Legal support

1. Flashing out the **criteria for exemption from launch obligation**

Max 2 page, criteria need to be written in a way they could be included in legislation, we already have the explanation in current paper, some examples could be useful.

2. Support in **amendments drafting**

COVINGTON

Economic consultancy

Develop counter points based on the IA and PPMI report to challenge e.g.:

- on the cost effectiveness of restrictive HUMN
- on the cost effectiveness of punitive modulation
- on the cost effectiveness of restricting ODD

To be brainstormed with the ISG and come in the form of pointers to be used with legislators (not paper to be published)

Copenhagen Economics CE

Communication & Dissemination

To be continued and increased in 2023

- Podcasts & website
- Thought leadership
- Partnerships narrative

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PHARMA BOARDROOM

REQUEST FOR BLOG POSTS – OMP; rare disease lifecycle; OMP UMN; RWE etc…

Rare Disease Week 2023

Media Buy options

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MORNING HEALTH CARE

Sponsor Morning Health Care newsletter the week before to promote our efforts to a targeted and influential audience directly into the inbox.

Investment: 10,000€/week

- 10 newsletter messages,
- logo on top,
- MPU banner mid-section
- banner adjacency to health care section
- **Financed by Eucope**

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Post-Rare Disease Week Takeover

Publish an article/op-ed after the event that will be promoted in the following 3-4 weeks on POLITICO.eu and social media.

Investment: 13,500€

- 1 day on our homepage to capture traffic on our most visited page (earning all available impressions)
- 100K in-story impressions across POLITICO.eu
- 100k social media impressions on Facebook and Twitter

2023 Engagement plan

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

Close doors Engagement and 1:1

Pre-legislative phase

Legislative phase

Swedish Presidency Starts 1 Jan 2023

COM proposal for OMP review to be published (Q1 2023 or early Q2)

Spanish Presidency Starts, 1 July

Belgian Presidency Starts, 1 Jan 2024

Jan - Feb | Mar- Apr | May – June | July - August | Sept- Oct | Nov | Dec

1:1 Engagement with MEPs and Attaches

Briefing sessions with political groups and groups of attachés

1:1 engagement with MOHs? before and shortly after the proposal

Leveraging engagement, contacts and briefing sessions of

European Expert Group on OD Incentives

European Alliance for Transformative Therapies

2023 Engagement plan

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

Public engagement and milestones

Close doors Engagement and 1:1

Pre-legislative phase

Legislative phase

Swedish Presidency Starts 1 Jan 2023

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Jan - Feb | Mar- Apr | May – June | July - August | Sept- Oct | Nov | Dec

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Take over of rare disease week

European Expert Group on OD Incentives

Final recommendations

1:1 Engagement with MEPs and Attaches

Briefing sessions with political groups and groups of attachés

1:1 engagement with MOHs? before and shortly after the proposal

Leveraging engagement, contacts and briefing sessions of

European Expert Group on OD Incentives

European Alliance for Transformative Therapies

Public engagement opportunities/ milestones

RAREDISEASEDAY.ORG

DIA EUROPE 2023 ADVANCING HEALTH PRIORITIES 22-24 March 2023 | Basel

NORDIC RARE DISEASE SUMMIT

EUROPEAN HEALTH FORUM GASTEIN

RareConversations

World OrpharDrug Congress Europe

EUROPEAN HEALTH SUMMIT

What can this group do?

- Propose additional activities to strengthen engagement and amplify message
- Bring national colleagues into the informal national colleagues network (coordination, sharing messages, EUCOPE support national activities where at least 1 national member leads)
- Input on 2023 focus of the OMP

IV. The financial ecosystem of pharmaceutical R&D: An evidence base to inform further dialogue –, Simon Middleton, Europe Life Sciences L.E.K. Consulting

The financial ecosystem of pharmaceutical R&D

Presentation to EUCOPE OMP Working Group

Simon Middleton, L.E.K. Consulting – November 2022

SiRM. Strategies in Regulated Markets

L.E.K.

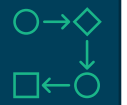
RAND

VWS commissioned a descriptive study into the financial ecosystem of pharmaceutical R&D to stimulate a well-informed societal debate

Goal of the study

- It is crucial for governments and other stakeholders to understand how the financial ecosystem of pharmaceutical R&D operates in order to conduct well-informed debates and make well-informed decisions.
- In addition, insights on how it has developed over recent decades and how it may further evolve provide crucial input for societal debate.

Process



- A consortium of Strategies in Regulated Markets (SiRM), L.E.K. Consulting LLP (L.E.K.) and RAND Europe was selected to execute the study.
- VWS established a Scientific Advisory Committee (SAC) to provide methodological guidance. The SAC provided feedback on the methodology used and the robustness and credibility of the study results.

SiRM. Strategies in Regulated Markets L.E.K. RAND EUROPE

We used a mixed-methods approach, combining desk research and quantitative data with in-depth interviews and workshop

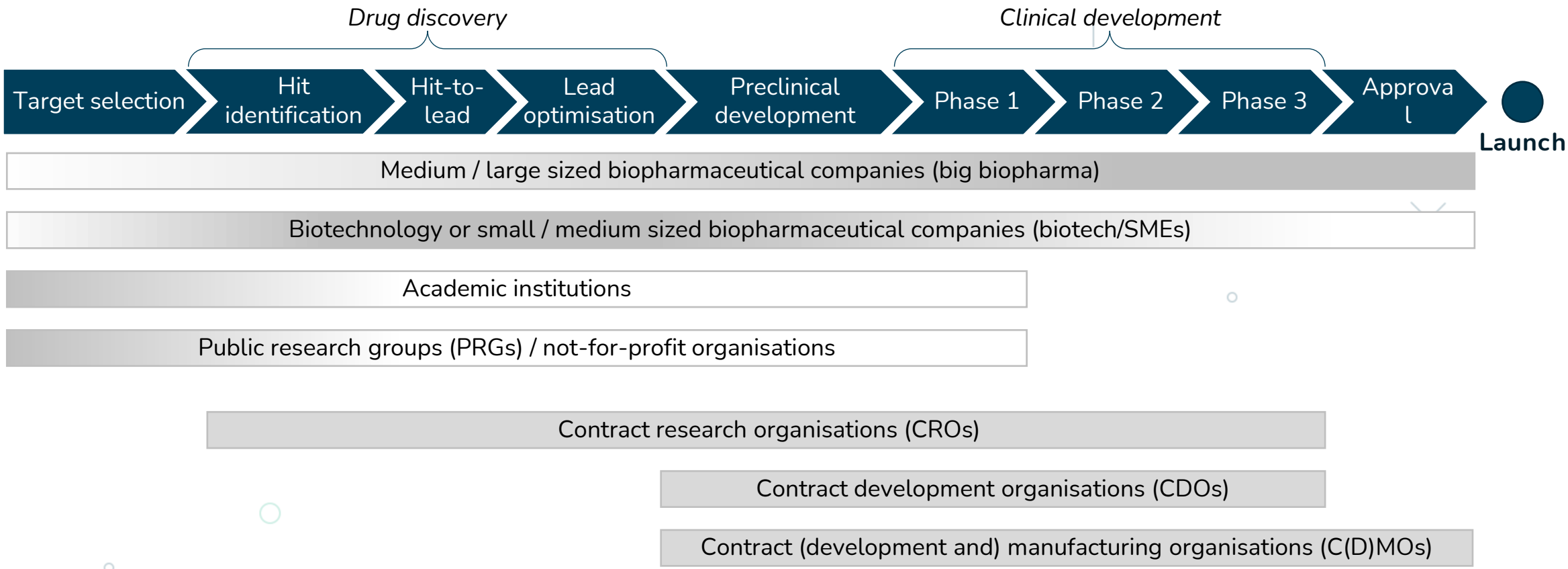
Desk research and quantitative data

- We examined, analysed and classified existing knowledge and information on the financial ecosystem by reviewing academic and 'grey' literature, including industry publications.
- We supplemented existing knowledge with new research based on analysis of (proprietary) databases (>10) and financial statements adding concrete quantitative data.

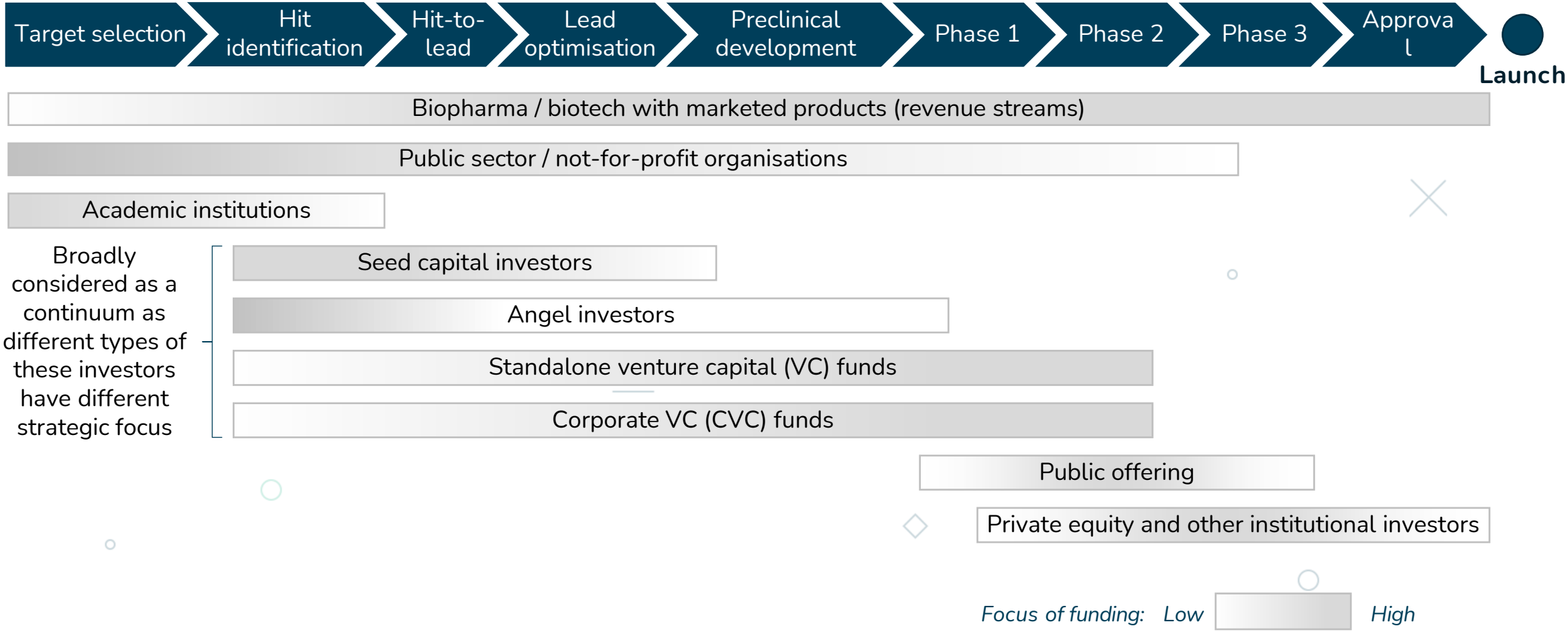
In-depth interviews and workshop

- We conducted 56 interviews to enrich the knowledge base with experts from both industry as other stakeholder groups, such as the financial investment community, academia and experts from the wider public and not-for-profit sector.
- We explored relevant aspects and considerations for future directions of the financial ecosystem on pharmaceutical R&D during a workshop with multiple stakeholders. We used multiple scenarios for the goal of this workshop.

Various executors perform pharmaceutical R&D. Their activity depends primarily on the development phase.

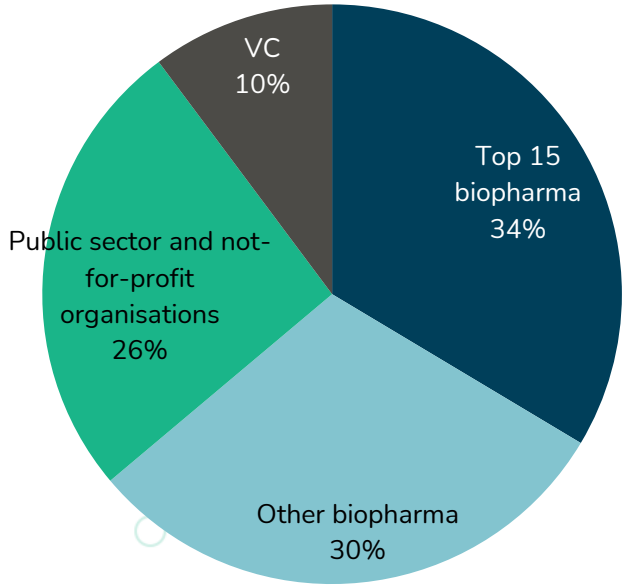


Multiple investors play a role in financing pharmaceutical R&D. Their activity primarily depends on the development phase.



Total global investments in R&D were circa $300bn in 2020, of which almost two-thirds attributable to private investment by biopharma

Estimated R&D spend by investor type in 2020 [percentage, total = $303bn]

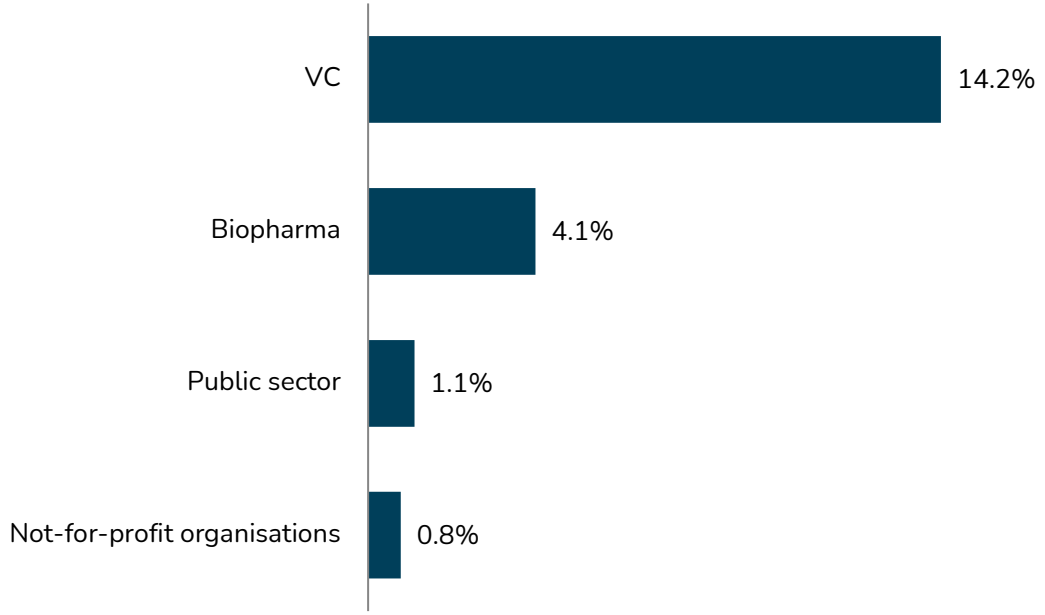


- Although the investments from public sector and not-for-profit organisations and VCs are much smaller, in terms of the number of deals it is estimated to represent a much higher percentage.
- Public and not for profit investment may be smaller in absolute terms but is essential for feeding the pipeline for the private sector to invest in downstream.
- The amount excludes the cost of capital and anything not directly related to R&D, such as sales and marketing.
- The private investment by biopharma is based on the EvaluatePharma database. R&D spend from this database should reflect actual R&D spend, including basic licenses, and is not affected by M&A, equity transactions and asset purchases.

Sources: L.E.K. analysis based on proprietary databases.

Global VC investment has seen strong and accelerating growth in recent years, starting from a low base

CAGR by investor type, 2011-2019 [percentage]



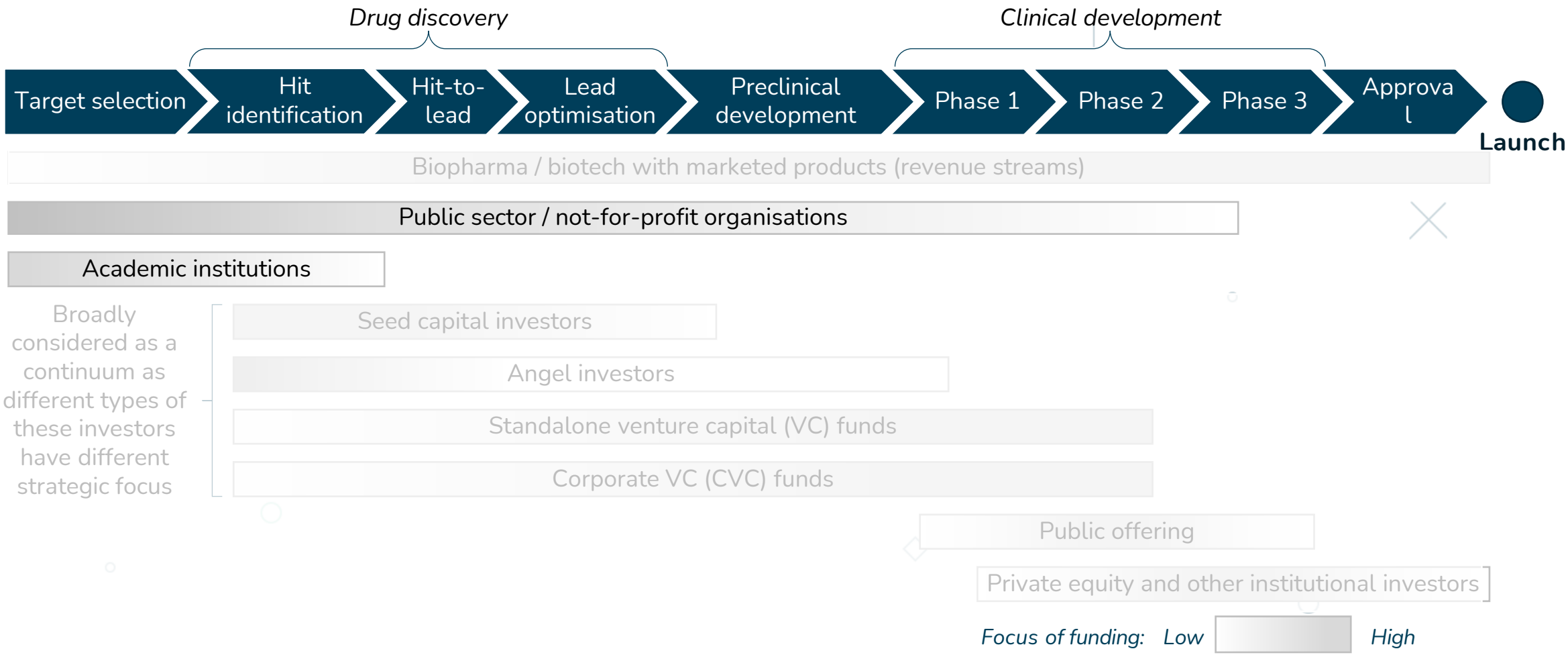
	North America	*Europe*	*APAC*
VC	11.3%	12.3%	27.4%
Biopharma	7.3%	1.6%	0.8%
Public sector	1.3%	-0.1%	2.8%
Not-for-profit organisations	1.2%	-0.4%	2.8%

- VC investment growth is likely driven by scientific and technological advances in drug research, unmet need, a wider group of investors and better exit opportunities fueling investor confidence.
- It is primarily driven by deal value rather than deal count. Increasing deal values are driven by increased valuations, increased competition among VC's and increased VC fund sizes.

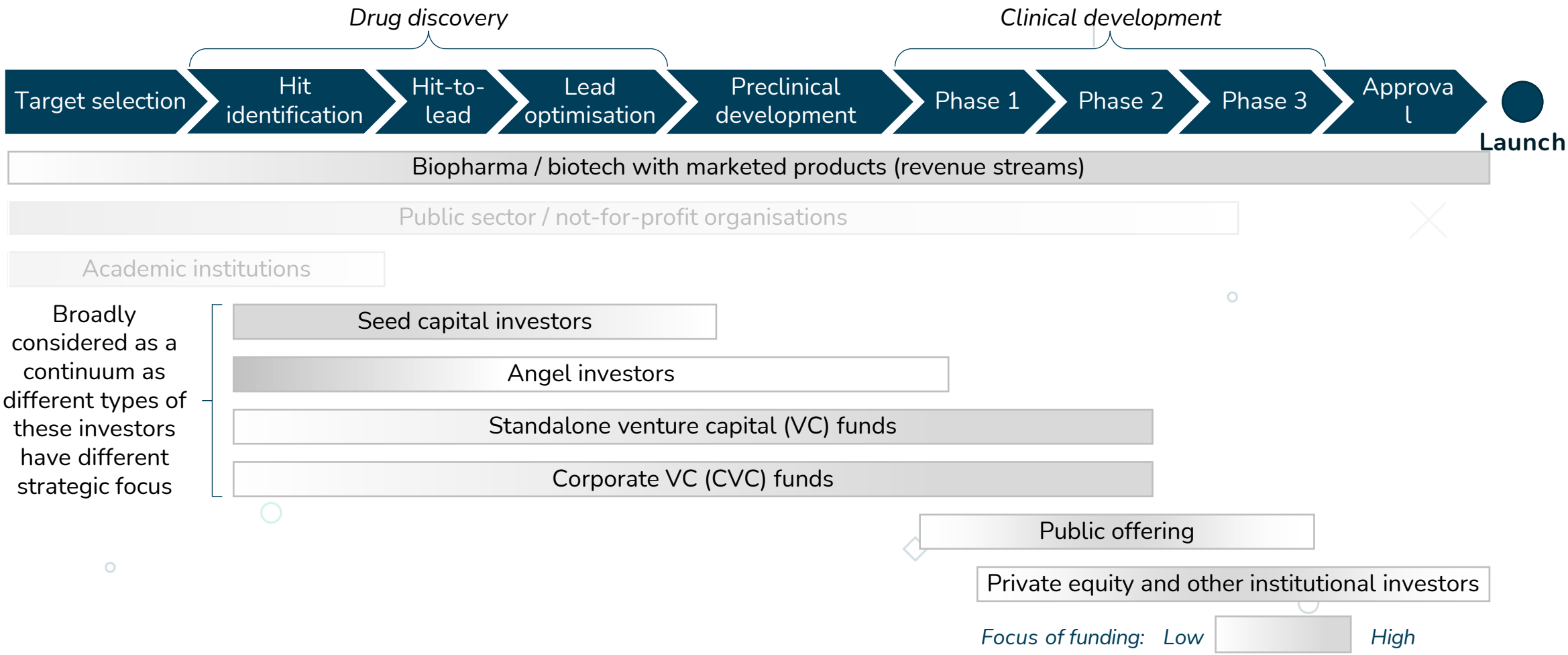
Sources: L.E.K. analysis based on proprietary databases.

Ultimately, financial return determines a drug's development

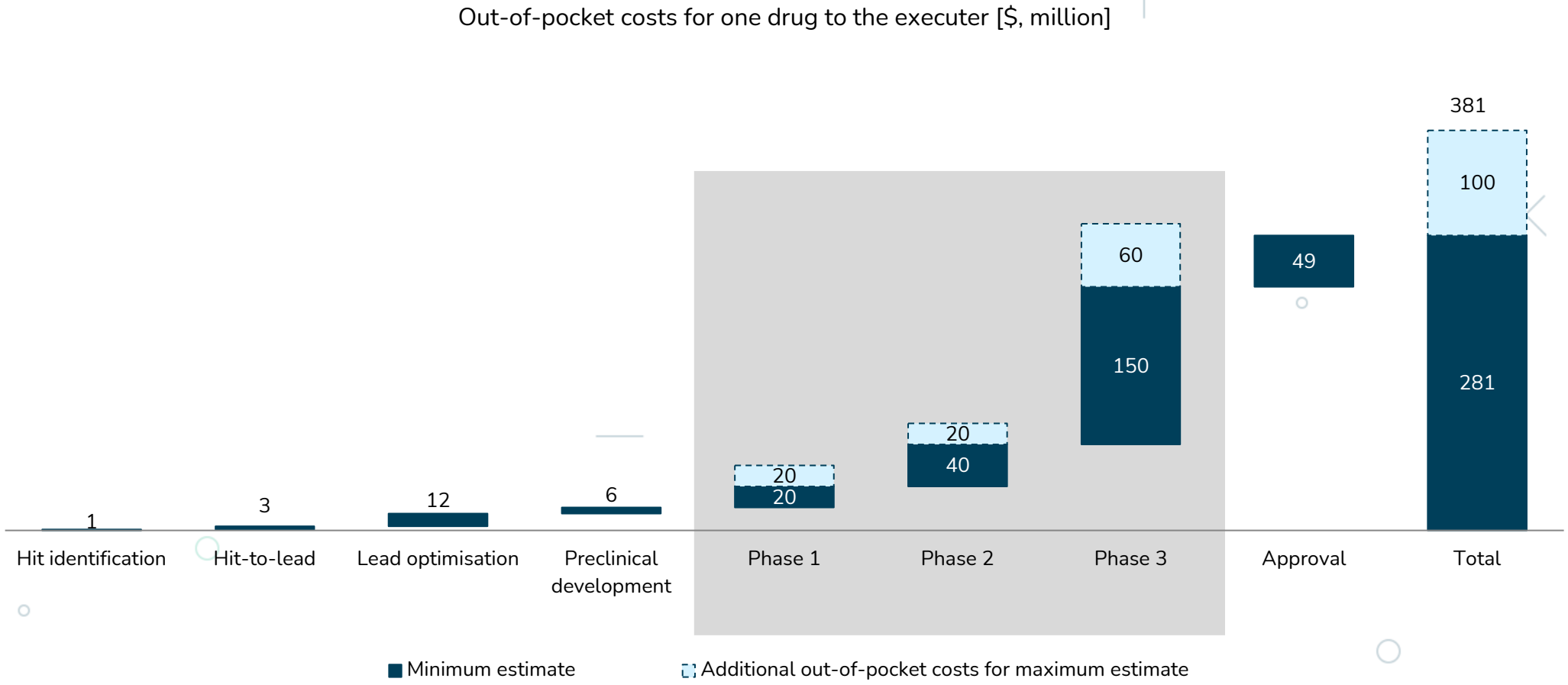
Early research is often funded by public sector and not-for-profits primarily motivated to create societal impact



Bringing a drug to launch however requires private investors primarily motivated by expected financial returns



Private investment is crucial to finance high-cost clinical-development phases, especially Phase 3



Source: DiMasi & Grabowski, 2007; DiMasi, Grabowski, & Hansen, 2016; Paul et al., 2010.

Expected financial return is a key determining factor in private investors' investment decision-making

VCs seek sufficiently high returns for their investors

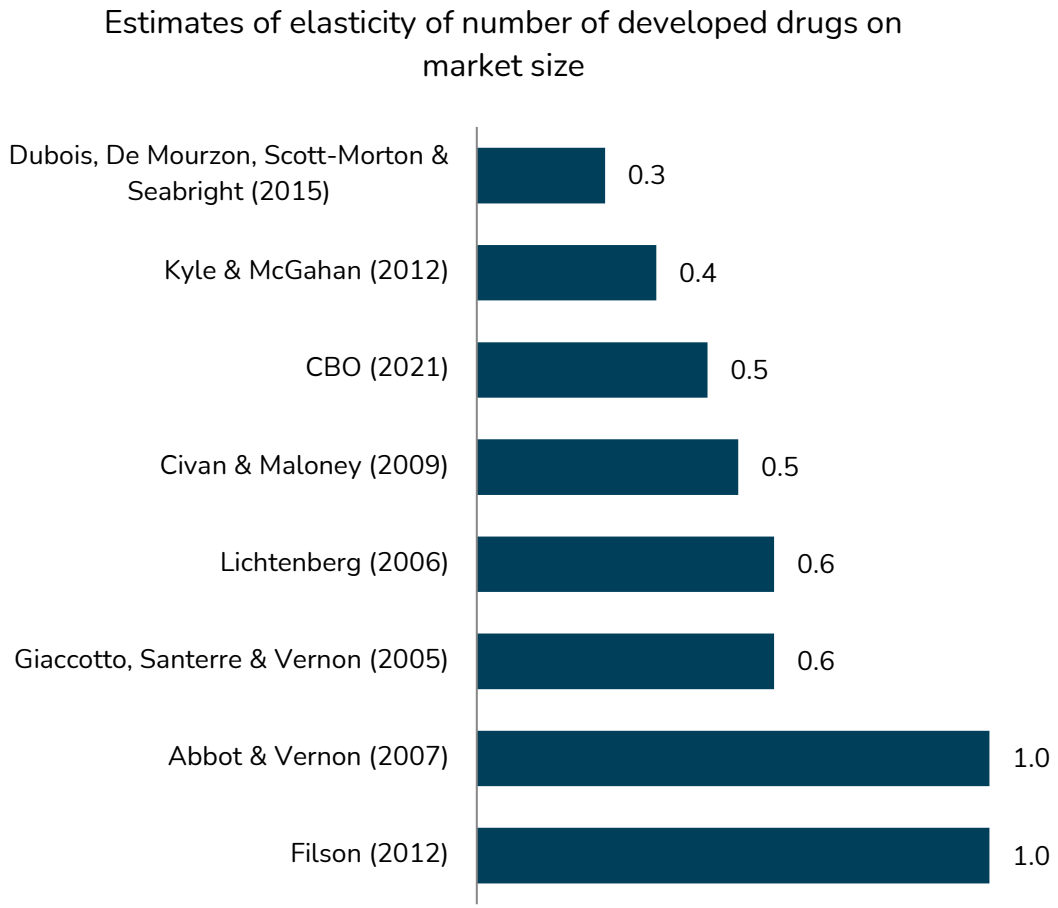
- VC investors typically expect a 2.5–3x net ROI and/or a 20–25% internal rate of return (IRR).
- For VCs to achieve these expectations, they generally need a circa 4–5x ROI multiple averaged across investments in their portfolio with a 3–8 year holding period depending on the stage.
- VCs will typically invest in a mixture of low-risk (circa 2–3x ROI) and high-risk investments (circa 10x ROI), accepting that a proportion may generate no returns.

Big biopharma is driven by consistent value creation for their shareholders

- Big biopharma use consistent dividend policies to attract stable investors. Large companies typically offer annual or quarterly dividends. They aim to have stable growth in annual dividends per share pay-outs. Smaller companies often do not distribute dividends.
- Big biopharma may use share buy-backs as a flexible, tax efficient alternative to dividends to return capital to shareholders.

Willingness to pay considerably influences supply and distribution across areas

Lower expected willingness to pay for pharmaceutical drugs could result in fewer novel drugs being launched in the coming decades



- Affordability issues in key global markets such as the US or Europe could translate into a lower willingness to pay.
- A shift in pricing policies in some key global markets could significantly change the landscape as payers balance rewarding innovation with pharmaceutical affordability and accessibility.
- Such changes could translate into fewer compounds meeting the expected financial threshold and therefore fewer novel drugs being launched, as illustrated by the positive elasticity of drug development on market size.

A few other studies find estimates above 2, for example Acemoglu and Linn (2004), Finkelstein (2004) and Blume-Kohout & Sood (2013).

In addition to expected willingness to pay, various other factors influence the supply of novel drugs (1/2)

Pace and nature of scientific advances

- The pace and nature of scientific advances influence the supply of innovation and the private sector's willingness to invest in higher-risk therapeutic areas.
- Without breakthroughs, pharmaceutical R&D would most likely focus on lower-risk clinical innovation areas.

Ability to leverage data and digital-technology advances

- The ability of R&D systems to leverage data and digital-technology can impact the nature, pace and cost of R&D.
- Examples of applications include designing smarter and potentially less costly trials or using machine learning to more efficiently identifying drug targets and candidate compounds.

In addition to expected willingness to pay, various other factors influence the supply of novel drugs (2/2)

Regulatory developments

- Regulatory development can impact R&D costs and investor appetites for investments in specific geographies.
- Regulatory innovation can support smarter trials and tackle disincentives presented by fragmented regulation.

Collaboration landscape

- Pharmaceutical R&D has become increasingly collaborative and the dynamics of collaboration and competition is changing.
- Incentives that enable effective collaboration and that manage competition landscape matter for executers and investors.

Drugs with the highest expected willingness to pay are the most likely to be developed, leaving several areas currently underserved

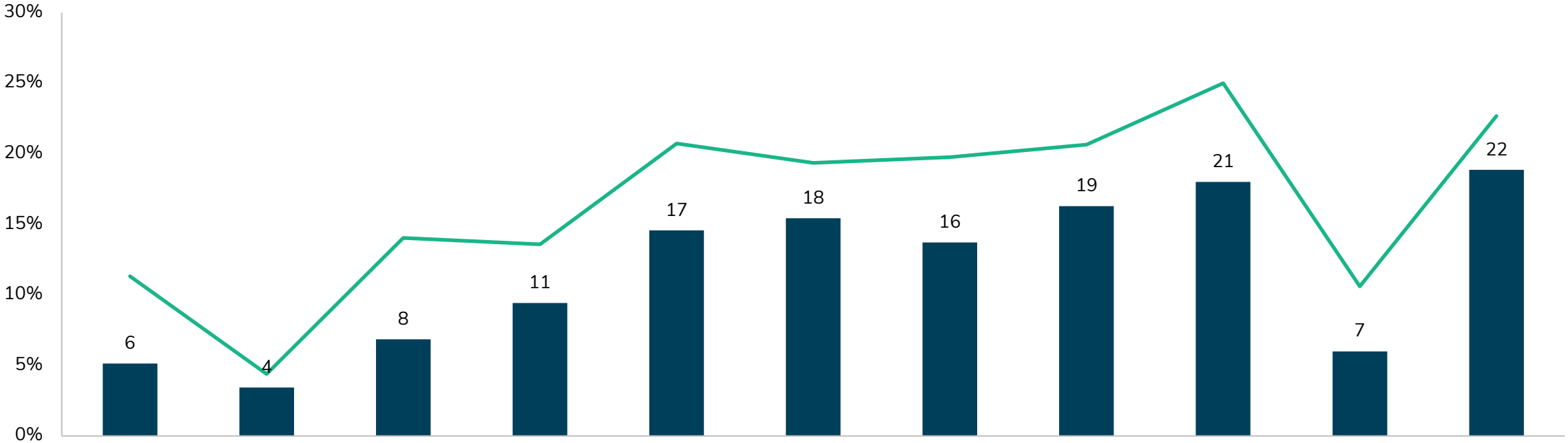
Therapeutic areas where suboptimal alternative treatments exist struggle to secure private investment

Societies could better prioritise which drugs are needed and create viable markets for them

- Pricing is primarily high in disease areas where no effective alternative treatments exist, especially regarding life-threatening diseases.
- In areas where alternative treatments do exist, payers often use reference-pricing models. Even though R&D investment in these areas could still create societal value, therapeutic and clinical areas where suboptimal alternative treatments exist may struggle to secure private investment for pharmaceutical R&D.
- Compounds with most favourable business cases are most likely to be developed.
- This may lead to suboptimal allocation of available funds in tackling diverse areas of unmet need. For optimal allocation of available funds, societies could better prioritise which drugs are needed and create viable markets for them.
- European efforts on orphan drugs are an example of prioritisation and incentivisation.

European policies have resulted in an increase in the number of orphan medicinal products granted market authorisation by the EMA

Authorised orphan medicinal products [% of total authorised medicinal products, number of authorised orphan medicinal products, 2010-2020]



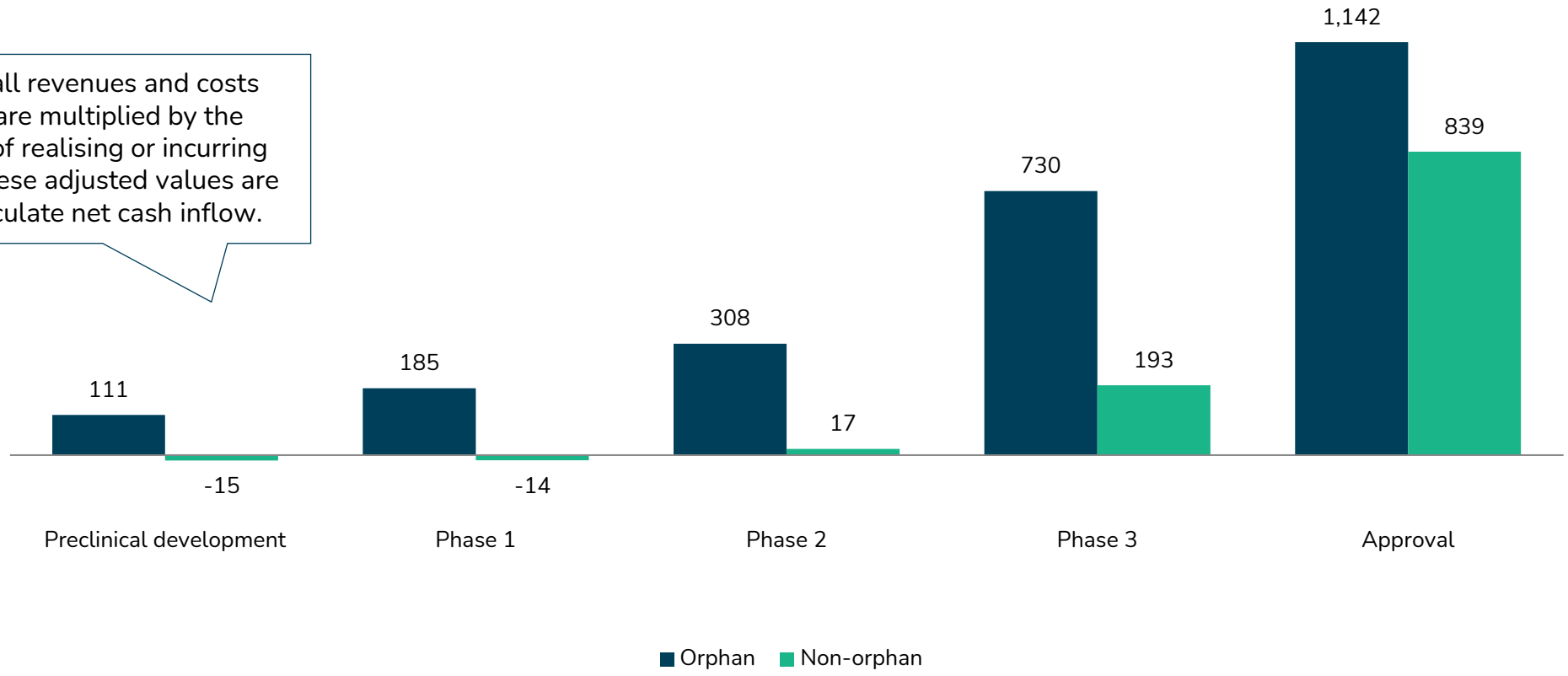
	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Total number of authorised products	53	91	57	81	82	93	81	92	84	66	97

Source: EMA annual reports, press releases and human drugs highlights

The eNPV model developed for this study demonstrates the current attractive business case for orphan drugs

Risk adjusted eNPV by drug type for assets per start phase [$, million]

Per phase all revenues and costs assumed are multiplied by the probability of realising or incurring them, and these adjusted values are used to calculate net cash inflow.



Source: L.E.K. analysis

Thank you for your attention

- L.E.K. Consulting Simon Middleton - s.middleton@lek.com

V. Italian Political Environment post elections – outlook on rare disease policies, Francesco Macchia, Rarelab

Italian Political Environment post elections outlook on rare diseases policies

3 November 2023, OMP Working Group; Eucope

RARELAB

RARELAB

RARELAB Srl is a communication and advocacy provider that works, in collaboration with institutions and companies, in the service of patients with Rare Diseases.

RARELAB Srl is a communication, patient advocacy, market access and public affairs provider based in Rome. The company was founded in 2013 by the meeting between:

- Francesco Macchia (current CEO), professional from the pharmaceutical world, expert in public relations and specialized in pharmaceutical marketing;
- Ilaria Ciancaleoni Bartoli (Current President) journalist, founder and director, in 2010, of Observatory of Rare Diseases - OMAR (www.osservatoriomalattierare.it).

RARELAB

20+
people with different profiles, highly specialized in rare diseases and orphan drugs.
10+
years of experience
400+

Our distinctive factors

Our DNA and our genes

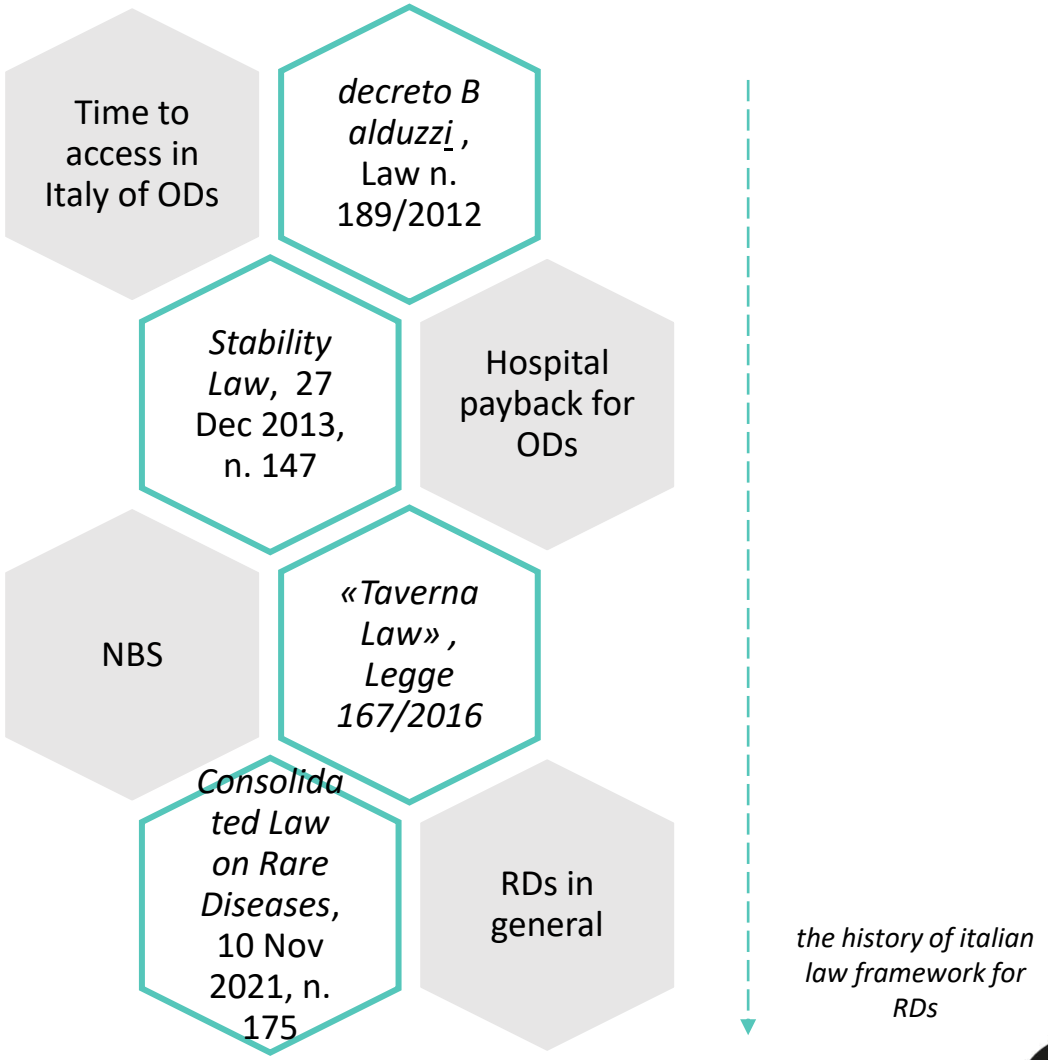
The Orphan Drugs Observatory is the first think-tank devoted entirely to the development of policies for governance and sustainability in the field of rare diseases. Born in 2016 as a joint initiative of the research centre C.R.E.A. Sanità (Consorzio per la Ricerca Economica Applicata in Sanità - Consortium for Research in Economics Applied to Health) and the Osservatorio Malattie Rare (Observatory for Rare Diseases) OMAR, with the aim to systematize the existing information, fill the gap of knowledge and information about the field, encourage an open and direct confrontation between institutions and key stakeholders.

Observatory for Advanced Therapies was founded at **the beginning of 2019 with the aim of disseminating correct, accurate and up-to-date information on advanced therapies with a clear and simple language** both through the website and the events dedicated to the general public.

RARELAB srl is editor of **Observatory of Rare Diseases** (OMaR) is an Italian newspaper/journal registered at the Roman Press Court since 2010. **O.Ma.R. is the first and only online newspaper and news agency, in Italy and Europe, entirely dedicated to rare diseases and rare cancers. The newspaper is available for free online and is aimed at all stakeholders in the sector.** The Observatory's mission is to produce and circulate information that is easily understood, but scientifically correct, on topics that are still little known, making its expertise available to other media, patients and all stakeholders.

State of the art of rare diseases of the XIX Italian Legislature

In the past, the Italian Legislator has, on several occasions, analyzed the issue of rare diseases and orphan drugs, without however elaborating, until **November 2021, an organic and sectoral law relating to these issues.**



Spotlight on RDs law in Italy

An important legislation on RDs and ODs with exceptional therapeutic relevance is "*authorization fast track*" (*law n. 189/2012 named «Legge Balduzzi»)* : a procedure according to which the regulatory agency – AIFA has a maximum evaluation time of 100 days.

Despite the presence of a clear regulatory reference to the timing, the deadline indicated above is poorly respected. According to the findings of OSSFOR - Orphan Drugs Observatory, the time for defining the evaluation and negotiation of the price by CTS and CPR is 174 in the two-year period 2019/2020 (V Rapporto Annuale OSSFOR* - *Rare diseases and orphan drugs tested for PNRR*).

Spotlight on RDs law in Italy

Another example of legislation that has generated a positive impact in the context of rare diseases and which has begun to bring the issue of rare diseases into the institutional debate, before the advent of a real legislation in the sector, was the amendment to **Stability Law 2014 (Law 27 December 2013, n. 147**) which established that drugs with the qualification of orphan drugs Reg. (EC) no. 141/2000, are not called to write off the surplus of pharmaceutical expenditure, when the limit established by law is exceeded.

*This objective has been achieved by the **GLFO – Orphan Drugs Working Group**, an informal working group between pharmaceutical companies coordinated by Rarelab, through a profound awareness-raising activity on the issue of rare diseases and on the need to encourage research and production of orphan drugs.*

Spotlight on RDs law in Italy

The first organic law aimed at reorganising legislation on rare diseases was published in November 2021 (*Consolidated Law on Rare Diseases,* no. 175/2021). This law has as its primary objective, to standardize the care of people with rare diseases throughout the territory, ensuring uniformity in the provision of health services, assistance and access to therapies.

Despite the presence of a law on rare diseases, this to date is not yet fully applicable because many of the implementing decrees provided for by the text itself and referred to the competence of other institutions, including the Ministry of Health, the Ministry of Research and the Ministry of Labor, have not yet been issued**. Only one of the Decrees provided for by law has recently been produced,** the one relating to the establishment of a **National Committee for Rare Diseases**, which represents an advisory body of the Ministry of Health, called to identify the areas of interest in the field of rare diseases on which the Institutions must focus their attention. **Among the members appointed to be part of this Committee, there is also Ilaria Ciancaleoni Bartoli – Director of the Observatory of Rare Diseases, a newspaper published by Parelab.**

Spotlight on RDs law in Italy

The matter of health is part of what in our system are defined as "matters of concurrent competence", in which the **State identifies the fundamental conditions to which the individual regions** are required to comply, while allowing them to use their own organizational methods to achieve of the objectives identified at national level. This generates, in the context of Italian healthcare, profound differences between the different regions in terms of taking care of people with rare diseases, differences that vary according to the degree of organization adopted by the individual regions. **For this reason the panorama appears to be rather fragmented**.

In order to try to reduce these differences, in terms of access, the term for the inclusion of orphan drugs in the Regional Therapeutic Handbooks (list of drugs that can be prescribed by the Regional Health Service) **has been reduced from 6 months to 2 months, through an amendment proposed and supported by 'On. Fabiola Bologna, on the proposal of O.Ma.R.** ***(for more info: link)***

Spotlight on RDs law in Italy

Further critical issues in the Italian Health System are found in the subject of **Extended Neonatal Screening**, where, despite the existence in this case too of a law and a subsequent amendment to the law, both aimed at constantly updating the list of pathologies to be screened neonatal, the updating process is still blocked today due to the lack of agreement by the legions on a Decree (tariff decree - which determines the tariff that each region is required to apply in terms of services, prostheses and aids) which is be preliminary from a technical and bureaucratic point of view with respect to updating the list and those that in Italy are defined as Essential Levels of Assistance.

Spotlight on RDs law in Italy

In all these areas and in all the awareness actions carried out, Rarelab, through O.Ma.R., has operated and collaborated with the **340 Patient Associations belonging to the Rare Diseases Alliance (AMR**), a permanent technical table born on 4 July 2017 with the signing in the Chamber of Deputies of a Memorandum of Understanding wanted by Senator Paola Binetti, then President of the Parliamentary Intergroup for Rare Diseases.

For to see all the PAGs of AMR: **link**

A new beginning

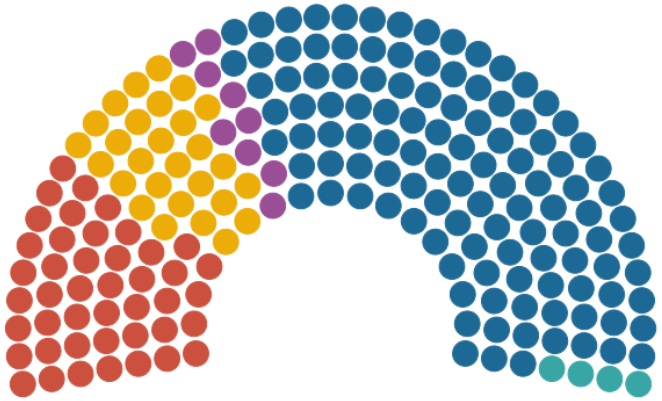
We are at the beginning of a new legislature, and it is a legislature that begins with many laws approved that must be grounded through implementing decrees and regulations.

There are so many things already started that there would be for at least half of the legislature, and given the precedents if we arrived in 5 years having canceled the delays, and without having created new ones, it would already be a success.

Stakeholder scenario

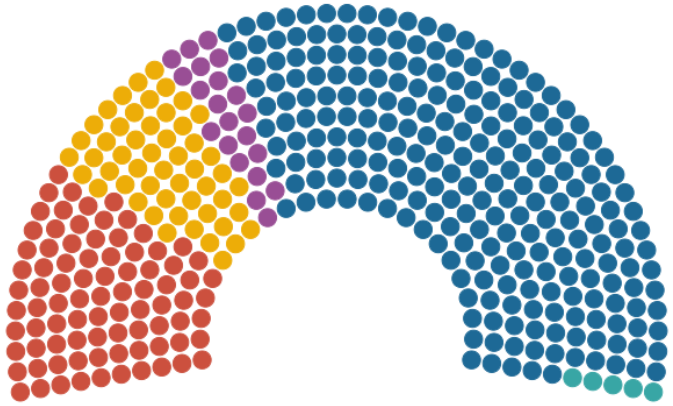
Following the elections of 25 September, the political scenario has changed profoundly. In addition to the result achieved by Fratelli di Italia, the new structure of the Parliament was also affected by the constitutional reform which reduced the number of parliamentarians and which found its first application in this legislature.

La composizione del Senato delle Repubblica



coalizione	senatori
centrosinistra	44
m5s	28
Terzo polo	9
Centrodestra	115
Altri	4

La composizione della Camera dei deputati



coalizione	deputati
centrosinistra	85
m5s	52
Terzo polo	21
Centrodestra	237
Altri	5

Giorgia Meloni
Presidente del Consiglio

Stakeholder scenario

Ministries to highlight

Stakeholder scenario

Yesterday, 2° November, there was the oath of Deputy Ministers and Undersecretaries: now the Ministry of Health is also complete and there are all the conditions for resuming the interrupted legislative activities that affect the world of rare patients.

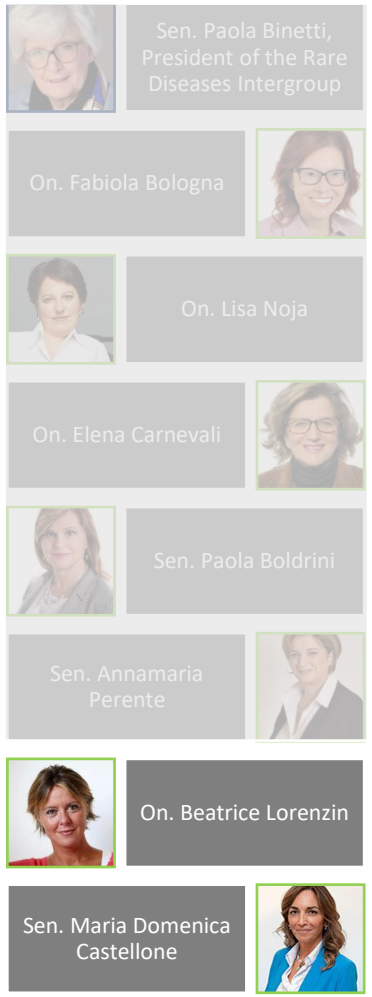
There are many activities that this Ministry will be called upon to deal with on rare diseases and for this reason the appointment of the on. **Marcello Gemmato** as **Undersecretary of Health** is very positive news.

On. Marcello Gemmato is an pharmacist and a politician capable of carrying out, with competence and tenacity, any battle he takes to heart.

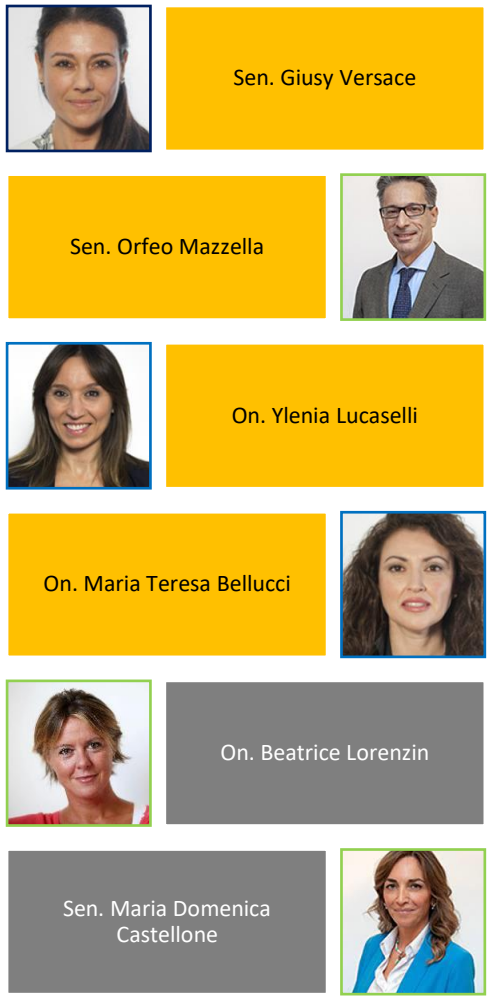
In the last two legislatures usually one of the two undersecretaries for health obtained the specific mandate for rare diseases and became an interlocutor for companies and patients; **the hope is therefore that, among the various mandates, Minister Schillaci will assigned to on. Gemmato the one on Rare Diseases**

Stakeholder scenario

From this advocates



To this new probably advocates of new government



FdI, Lega, FI

PD, M5S, ItaliaViva

Mixed group

Stakeholder scenario

Not all the institutional interlocutors mentioned above have been re-elected.

As **Rarelab we have already started a study and consequently an accreditation and contact activity with the newly elected**, identified on the basis of the academic path and previous positions gained in the health sector, similar to the field of rare diseases.

The new challenges

We are at the beginning of a new legislature, and it is a legislature that begins with many laws approved that must be grounded through implementing decrees and regulations. There are so many things already started that **there would be for at least half of the legislature**, and given the precedents if we arrived in 5 years having canceled the delays, and without having created new ones, it would already be a success. So let's see what's at stake.

- *Consolidated Law*
- publication of the new National Plan for Rare Diseases
- Solidarity fund provided for by law
- Regional Access

- LEA
- NBS panel extention

The new challenges and our next steps

Undoubtedly, efforts will be made to urge the publication of the new National Rare Diseases Plan (the previous one has now expired in 2016) which, despite the work of the specially set up table, did not find results in the XVII Legislature. The publication of the new Plan is provided for by the same law on rare diseases, which refers to one of the decrees implemented, envisaged and not yet implemented, although the terms for its enactment have now expired.

Rarelab's objective will be to ask for a funding from the same plan in order to be able to concretely implement what is foreseen.

The new challenges and our next steps

Another important issue, in our opinion, is the increase in the resources provided for by the law relating to the Solidarity Fund provided for by the law, the implementation criteria of which are not yet envisaged since, also in this case referred to one of the implementing decrees not yet issued despite the expiry of the deadline for their issuance.

It is also our intention to continue the activities already started during the last legislature to solicit the intervention of the competent institutions on what has not yet been carried out also in terms of Extended Neonatal Screening (updating of the list of diseases and reform of the methods for assigning SNE funds. Regions) and access to therapies in a uniform manner throughout the national territory.

A difficult themes in this institutional framework

Considering the ideology of the new government, some issues could face considerable difficulties, like

mitochondrial replacement technique,	Prenatal screening	End of life

But thanks to Prime Minister Giorgia Meloni's inauguration speech, **greater openness to the industrial world is expected.**

THANK YOU FOR YOUR THE ATTENTION

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VI. Important Projects of Common European Interest (IPCEI) – OMP and G&CT, Laura FABRE, European healthcare industry, French Ministry for the Economy, Finances and the Recovery

HEALTH IPCEI

Important Project of Common European Interest

Intervention during Orphan Medicinal Products WG meeting

03.11.2022

- Health IPCEI overview
- Current status
- Focus on rare diseases and CGT

- Health IPCEI overview
- Current status
- Focus on rare diseases and CGT

HEALTH IPCEI
Important Project of Common European Interest

Health IPCEI overview

Criteria

Consortia

Group of projects inserted in a common work program, under the aegis of a lead project

From R&D&I to first industrial deployment

For the development of highly innovative products or production processes that offer significant added value compared to the state of the art

Contribution to EU common objectives

Respond to common European interests (competitiveness, sustainable growth, employment, positive externalities, etc.)

Proportionnality

Assistance is justified when projects respond to market failures and cannot achieve the same results without CEIP assistance

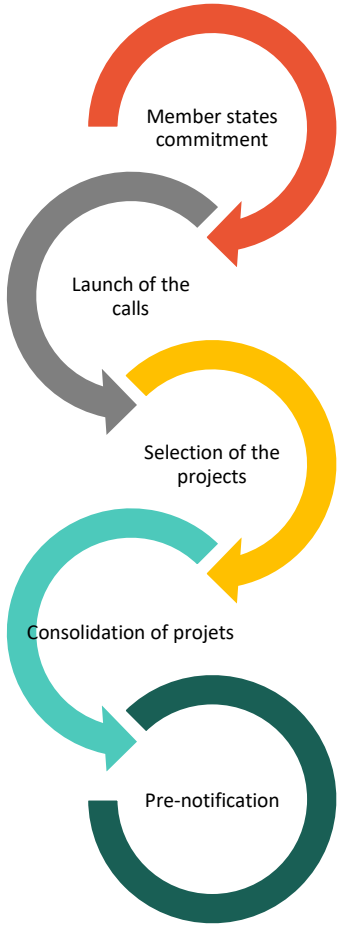
Collaboration

Projects must involve several EU Member States, involve collaboration with different types of actors and be co-financed by the beneficiaries of the aid

HEALTH IPCEI
Important Project of Common European Interest

Health IPCEI overview

5 steps initiative



Interested Member States decide to join the IPCEI by signing a joint declaration of intent with the other committed States

Committed Member States launch their own call of interest to collect projects from their national ecosystem

Chaque État sélectionne les projets qu'il souhaite financer dans le cadre du PIIEC

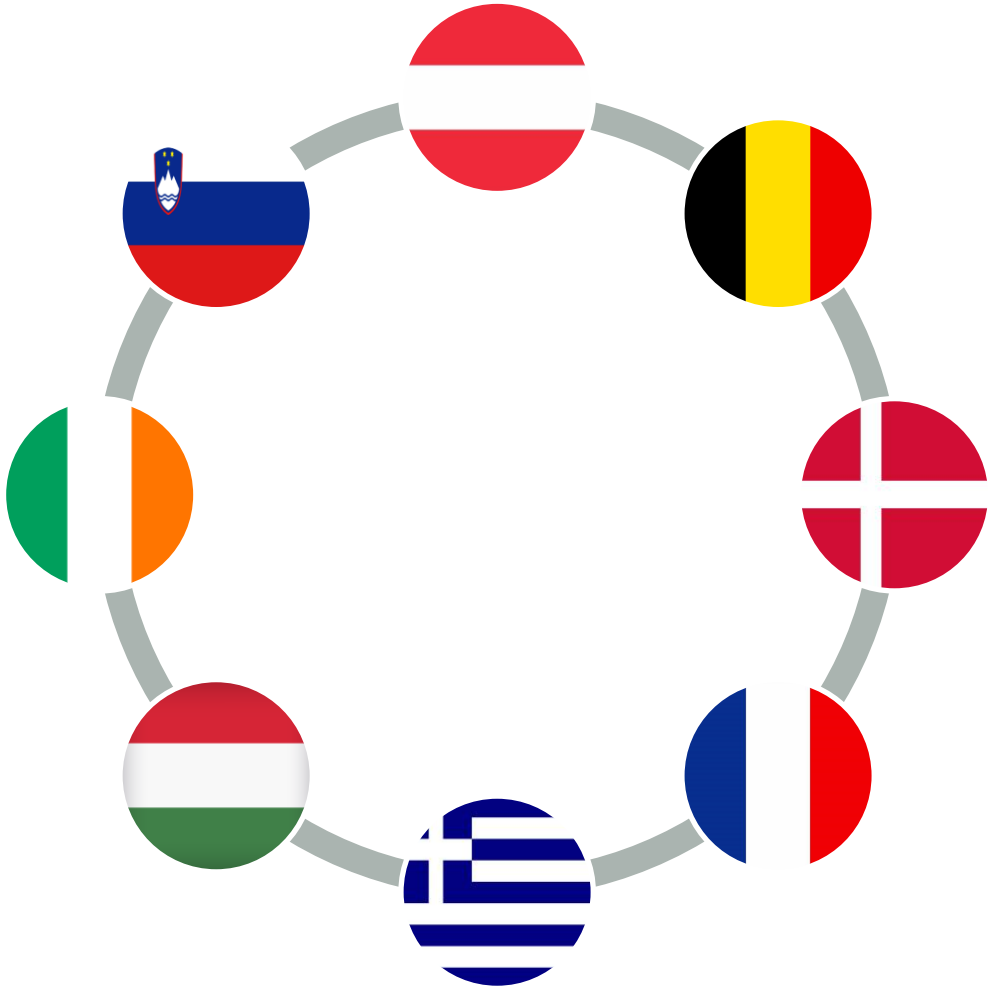
Selected projects must be consolidated at European level and must draw up the official documents (Project portfolio; Funding gap questionnaire)

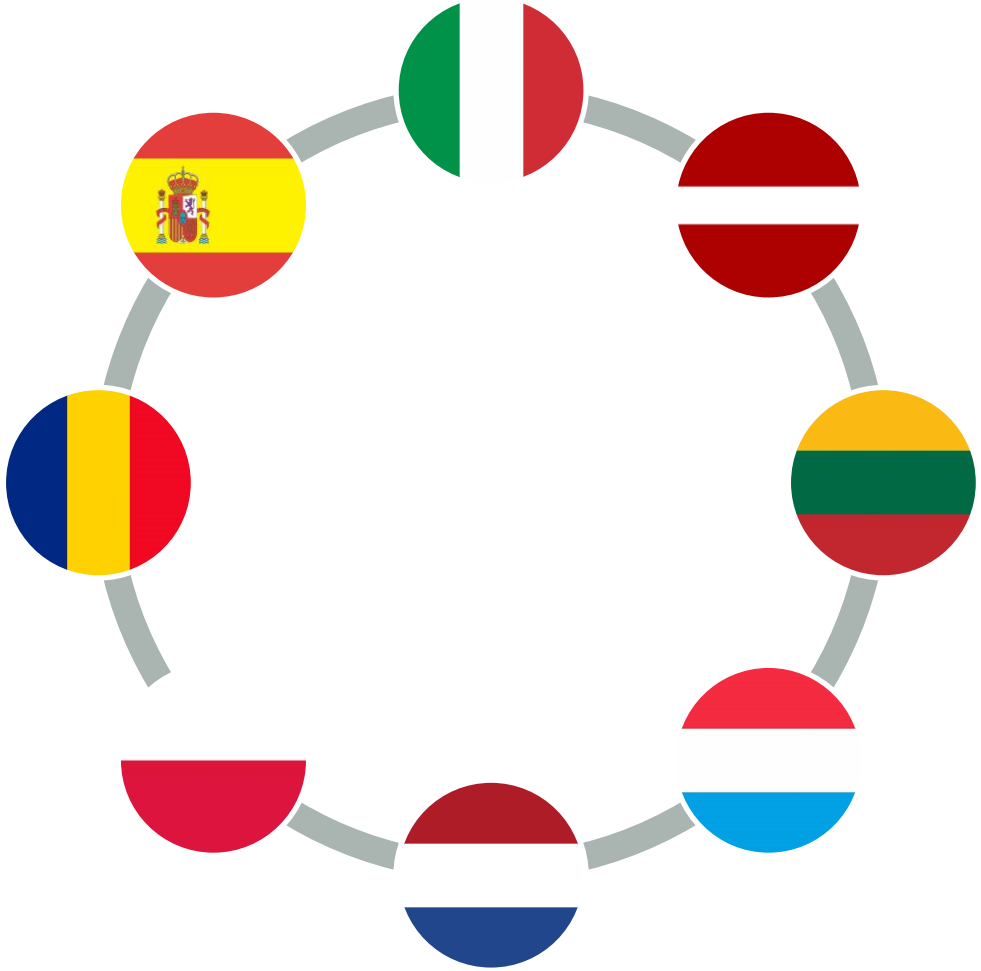
The official documents are submitted to the European Commission, which must then validate them in order to release the national PIIEC funds

HEALTH IPCEI
Important Project of Common European Interest

Health IPCEI overview

Participating MS





- Health IPCEI overview
- Current status
- Focus on rare diseases and CGT

HEALTH IPCEI
Important Project of Common European Interest

Current status

Two waves of projects

Wave 1

Innovating and greening production technologies and processes for medicines/drug products

Developing cell and gene therapies, including production processes and technologies

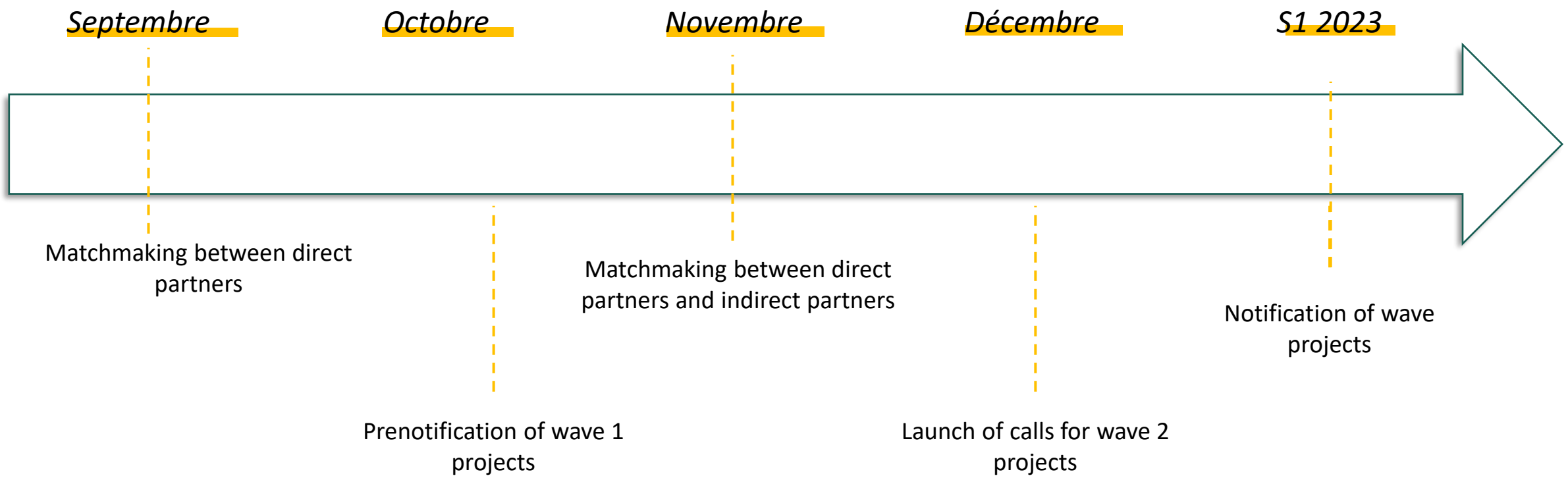
Innovation in antimicrobial resistance and rare diseases, as well as in emerging health threats where complementary to HERA

52 companies

10 Member states

Current status

Timeline



- Health IPCEI overview
- Current status
- Focus on rare diseases and CGT

HEALTH IPCEI
Important Project of Common European Interest

Focus on rare diseases and CGT

Timeline

Market Failures : these market segments are subject to **strong market failures** that hinder innovation

Collaborations and Spillovers : **spillovers** will benefit the whole sector and all types of actors involved, including small and medium enterprises

Examples of workpackages : the creation of **European bio-banks** or collaborations regarding **clinical trials**

VII. Swedish Political Environment post elections – outlook on rare disease policies, Kajsa Wilhelmsson, Oxford Health System Reform Group

Oxford Health System Reform Group

Advising on health system change through the lens of social sciences

Swedish Election and upcoming presidency
EUCOPE 2022-11-03

Current focus: Tidöavtalet

- From regional to national HC organisation to be explored, for example:
  - National principle for reimbursement and co-pay (still solidarity and needbased), Regional specialist centra, Centralisation and nationalisation of digital infrastructure, Efficiency and quality measurements
- But also, right for city councils to hire healthcare professionals in their elderly care
- Investments in areas such as: Cancer, Primary care, Womens health ie Migraine, Dental care, Mental Health,
- Patients rights: right to home abortion, named patient contact person, staff language skills, personal assistance system

Oxford Health System Reform Group Ltd

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Who matters, and what makes them tick?

Minister of Social Affairs Jakob Forssmed, Secretary of state Petra Noreback
Minister of Health Acko Ankarberg Johansson, Secretary of state Per-Anders Sunesson.
Elderly and social security minister Anna Tenje, Secretary of state Anna Pettersson Westerberg.
Minister of Social security Camilla Waltersson Grönvall, Secretary of state Minna Ljunggren

EU Minister Jessika Roswall with secretary of state Christian Danielsson and the Parliament EU ctte chair Hans Wallmark

S: Mathilda Ernkrans
SD: Linda Lindberg
SKR: Marie Morell and all the other regional lead

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Time is a critical issue don't get it wrong

Revised policy agenda by December

5th of May information Health Minister meeting
25-26 May Mutual Information System on Social Protection,
19-22 June EARC meeting

Maybe a Lifescience meeting in June?

- So not the time for Brussels, Local foot print, Emotions

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Hooks to leverage

- United Action/Co-operation request from the National Audit Office

- Social security comparative

- Tidöavtalet:
  - Make healthcare more flexible through for example a gradual transfer of patients from pedatric care to adult
  - Migraine, or rather the changes they need to put in place to address this priority

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Using these door openers

- LIF
- The Investor Network
- Don’t forget about SD
- The Commission for Innovative and Rare Pharmaceuticals
  - Upcoming workshop on framework for pricing of ATMP precision medicine
  - Been working with Ankarberg Johansson and Waltersson Grönvall
  - Solid relations with in particular Noreback
  - So give Gunnar a call: +46 70 440 10 00

Oxford Health System Reform Group Ltd

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Who we are…

The Oxford Health System Reform Group was set up in 2019 to help clients navigate the complex debate surrounding the value of and access to, healthcare.

In general, evidence building the case for health system change is based on biomedical research methodology. While this evidence is persuading to a scientific audience, it often falls short in discussions with politicians and civil servants, who usually have a background in social science methodology and practices.

We believe therefore, that in order to engage policy stakeholders in meaningful way we must bridge clients' biomedical knowledge, objectives and strategies with a social science rationale. Through tailored, evidence-based strategies, we are committed to helping clients understand the motivations of policy stakeholders, engage more effectively with them and help drive the evolution of sustainable healthcare advancement.

We use analysis and research to build compelling narratives and content which offer realistic solutions, achievable within current healthcare systems, while maintaining sight of our clients' commercial objectives.

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VIII.Regulation (EU) 2021/2282 on health technology assessment

EU HTA Regulation at a glance

- The EU HTA Regulation will make it obligatory for companies to submit a dossier for health technology assessment at EU level **(joint clinical assessment)**
- Whereas the original European Commission proposal would prevent duplication of clinical assessments**, the Regulation has softened the obligation for Member States to use the joint clinical reports**
- It creates the **risk of continued and even increased burden on companies** due to the continued possibility of additional data requests at Member State level
- **The date of application is 12 January 2025**. In the interim period joint work will be supported by EUnetHTA21 and the European Commission will prepare procedural rules and the methodology for EU HTA

Timeline for preparing the EU HTA procedure

Setting up the governance structure (link to rolling plan of implementation)

- *Setting up the Coordination Group (June 2022)*
  - Sub-group on Methodology (Q4 2022/Q1 2023)
- Setting up the Stakeholder Network (December 2022 - January 2023)

Detailed procedures and methodology

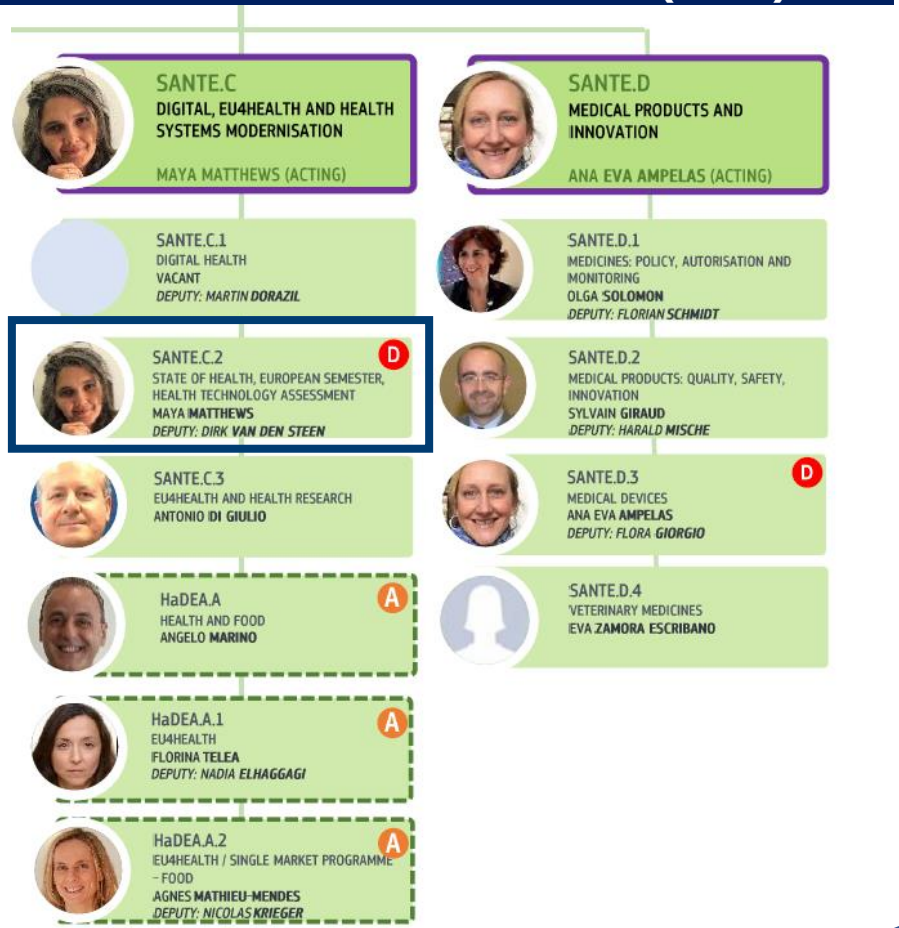
- Drafting implementing and delegated acts (2021-2024), covering inter alia:
  - Interaction and timing thereof between developers the Assessors and experts
  - General rules for the selection and inclusion of stakeholders
- Drafting guidance documents (2021-2023), to be adopted by the Coordination Group

The Commission has awarded the tender to develop advanced HTA methodology to the **EUnetHTA21** consortium

DG Sante reorganisation from 1 October

EU HTA under SANTE B.6 (old)

EU HTA under SANTE C.2 (New)



EUCOPE's five priorities for EU HTA

- The complexity of HTA processes across Member States require significant administrative and financial resources and time from developers and can cause access delays.

- **The EU HTA procedure must lead to sufficient harmonisation of existing methodologies and wide uptake of joint EU HTA reports**, to avoid the risk of additional clinical assessments being demanded at Member State level, with increasing burdens for developers and delays in patients' access to innovative treatments.

- In order to prevent duplication of work and increase the predictability for all stakeholders, **EUCOPE has the following five priorities for EU HTA:**

1. **JOINT SCIENTIFIC CONSULTATION MUST BE OFFERED TO ALL DEVELOPERS**
2. **A FLEXIBLE METHODOLOGY IS NEEDED THAT REFLECTS THE SPECIFICITIES OF OMPs AND ATMPs**
3. **PROCEDURES FOR RESOLVING THE ISSUE OF MULTIPLE AND COMPETING COMPARATOR REQUESTS**
4. **THE PROCEDURE MUST ENSURE A BROAD INVOLVEMENT OF RELEVANT STAKEHOLDERS**
5. **A TRANSPARENT AND BALANCED SELECTION OF EXPERTS IS NECESSARY**

EUnetHTA 21 methodological and procedural guidance

Key points from EUCOPE's feedback

EUCOPE has identified some key issues with the proposed updated methodology and procedural guidance from EUnetHTA 21:

- **The developer must be included in the scoping meeting** at the start of the assessment to avoid misunderstandings and ensure a robust assessment.

- **The consolidated PICO(s) should be discussed between the developer and the Assessors.** Not allowing for a discussion at the start of the assessment will inevitably result in methodological, practical and execution issues that will create issues in the dossier completion, evaluation and would result in a JCA that is flawed and not practical for adoption by Member States.

- **Additional guidance on selection of appropriate comparators for the assessment is needed.** This is currently not planned as part of the EUnetHTA21 deliverables, despite relevant EUnetHTA guidance from 2015 being referenced in several project plans.

- The choice of comparator must be evidence-based, and **the comparator must have a marketing authorisation for that indication and line of treatment.**

Key points from EUCOPE's feedback

- **There needs to be greater methodological flexibility that reflects the specificities of OMPs and ATMPs.** There is not sufficient recognition of the exceptional circumstances under which these products are routinely approved, and the practical and ethical issues of organising trials for certain types of products.

- **Evidence generated outside of the randomised controlled trial (RCT) design must be accepted**, such as single-arm trials, pragmatic trials and observational studies and more detailed guidance on the use of Real-World Evidence (RWE) is needed.

- **The proposed timelines are too short** to allow the developer to respond to clarifications or updating the dossier. Label changes frequently occur at the time of CHMP opinion, and the proposed 10 calendar days to update the dossier is inadequate, **the "grace period" should be at least 45 calendar days.**

- The deadline for responding to clarifications should be extended on request from the developer, depending on the type and complexity of the requested information.

Methodological deliverables

ID	Deliverable	Public consultation	Finalisation	Description and key concerns
D4.2	Scoping process	2 – 31 May 2022	~~29 July 2022~~ 12 September 2022	Practical guideline for the development of PICO questions • No scoping meeting/discussion of draft PICO(s) with HTDs *(informational meeting under EUnetHTA21)* • No clear methodology for selection of appropriate comparators • Comparators can be authorised or off-label
D4.3	Comparators and comparisons (D4.3.1) Methodological Guideline on Direct and Indirect comparisons (D4.3.2)	1 – 30 August 2022 2 – 31 May 2022	4 November 2022 29 July 2022	Methodological and practical guidelines on how to deal with direct/indirect comparisons in reports (and which data/documents should be requested from developers) • No clear thresholds included in the methodology, it is left to Member States to decide • Methods for non-RCT data are described but not endorsed
D4.4	Endpoints	3 October - 1 November 2022	13 January 2023	• Practical guideline on how to deal with assessment of endpoints in JCAs • Surrogate endpoints for JCA should be accepted by MS

Methodological deliverables

ID	Deliverable	Public consultation	Finalisation	Description and key concerns
D4.5	Applicability of evidence	4 July – 2 August 2022	4 November 2022	Methodological guideline for critical assessment of evidence regarding complementary analysis (e.g. subgroup analysis, post-hoc analysis, sensitivity analysis) and how to handle multiplicity issues, e.g. due to multiple subgroup analyses and analyses of multiple outcomes
D4.6	Validity of Clinical Studies	4 July – 2 August 2022	4 November 2022	Methodological guideline on how to consider, classify and label various types of evidence in the assessment reports (including RWE) for critically appraising evidence and addressing principles which determine the certainty of results (e.g. internal validity, and statistical precision). • Evidence with uncertainty could not be considered, despite the medical context (e.g. rarity of impossibility of blinding). • Assessment of applicability and clinical relevance of effect size is left to be judged at Member State level, without further methodological recommendations. • Lack of guidance on use of RWE

Excerpts from draft guideline D4.6 "Validity of Clinical Studies":

"Nevertheless, **there might be justification to not assess the evidence that ranges below a minimum level of** internal validity, applicability, or statistical precision in detail, if the PICO question can be sufficiently answered on the basis of higher-certainty results."

"Furthermore, **the certainty of results is independent of the medical context of the PICO question**. It is methodologically inappropriate, for example, to take the rareness of a disease or the impossibility of blinding as an excuse to ignore or to euphemise the resulting uncertainties in the clinical evidence."

Joint Clinical Assessments

ID	Deliverable	Public consultation	Finalisation	Description and key concerns
D5.1	JCA/CA submission Dossier Template	4 July – 2 August 2022	4 November 2022	Updated JCA/CA Submission Dossier template, submission requirements and related guidance documents • The actual templates remain to be developed • There is a need for a procedure for dealing with label changes at time of CHMP opinion
D5.2	JCA/CA Assessment Report Template	1 – 30 August 2022	4 November 2022	Updated JCA/CA Assessment Report Template based on the recommendations of JA3 • The actual templates remain to be developed

Joint Scientific Consultations

ID	Deliverable	Public consultation	Finalisation	Description
D6.2/3	Template Briefing Book / Template JSC Report	1 – 31 August 2023	29 September 2023	• Update briefing book for parallel advice with EMA • Review and updated templates for application form, applicants response to List of Issues and others • Update JSC report for written recommendation (No consultation)
D6.4	Procedural Guidance JSC	1 – 31 August 2023	29 September 2023	• Review and optimise existing procedural guidance for JSC for all participants, HTA bodies, developers, patients and healthcare professionals (including both internal procedural guidance as well as guidance for industry, both on parallel JSC with EMA) • Update templates related to the procedure of JSC • If necessary, further templates to be developed • Establish checklist for quality assurance in accordance with the Quality Management System

Interactions with stakeholders and experts

ID	Deliverable	Public consultation	Finalisation	Description and key concerns
D7.1	Guidance for the interaction between HTD and HTA (for JCA and JSC)	20 July – 19 August 2022	30 September 2022	A practical guidance for HTA-HTD interaction, process for handling commercially sensitive data and procedure for the factual accuracy check. Definition of an incomplete Submission Dossier and procedure for managing incomplete submissions • General lack of points of communication and no scoping meeting with HTD to discuss draft PICO(s) • Discontinuation of the assessment should be possible, also without publication of submitted documents • Unrealistic timelines with no option of extension proposed for "grace period" (10 calendar days) in case of label changes and for HTD to respond to questions (5 calendar days) • An independent body (e.g. the JCA subgroup and EC) should decide on nature of factual accuracy check comments, not the Assessors • Redaction of commercially confident information must be possible in all cases

Excerpts from draft guideline D7.1 "Guidance for the interaction between HTD and HTA":

"we note that in May 2022 the International Committee of Medical Journal Editors 102 (ICMJE) has extended their recommendations stating that: 'The ICMJE does not consider results or data contained in assessment reports published by health technology assessment agencies, medical regulators, medical device regulators, or other regulatory agencies to be duplicate publication.'. Therefore, **it is no longer necessary to describe the handling of academic-in-confidence data for HTA production.".**

"As soon as the HTD has submitted their draft briefing book (for JSC) or the submission dossier (for JCA), **the process cannot be terminated by the HTD.** This means the documents submitted by the HTD cannot be withdrawn and **the JCA/CA or JSC process will continue also with publication of documents** as required for the JCA/CA or JSC procedure"

Interactions with stakeholders and experts

ID	Deliverable	Public consultation	Finalisation	Description and key concerns
D7.2/3	Guidance and template for the interaction with patient representative, healthcare professional and other experts	1 – 30 August 2022	4 November 2022	Guidance for the interaction with and involvement of patient representatives, HCP and other experts in JSC and JCA/CA and templates for patients and healthcare professionals input into JSC/JCA • No description of how experts/stakeholders input will be weighted in the overall report
D7.5	Guidance for identifying and handling conflicts of interest (COI) and declaration of interest (DOI) and EUnetHTA confidentiality agreement (ECA) forms	—	16 March 2022	• Continue the operations of the Conflict of Interest Committee based on previous joint work on already existing DOI and ECA procedures document templates and guidance • Revise the DOI procedure in order to fully cover the cases of (ultra) rare disease, where a potential conflict of interest may exist when involving clinical experts • Maintain the DOI database over the course of the activity, clear of any GDP concerns

The EUnetHTA 21 JCA pilot will serve to test the proposed new guidance documents

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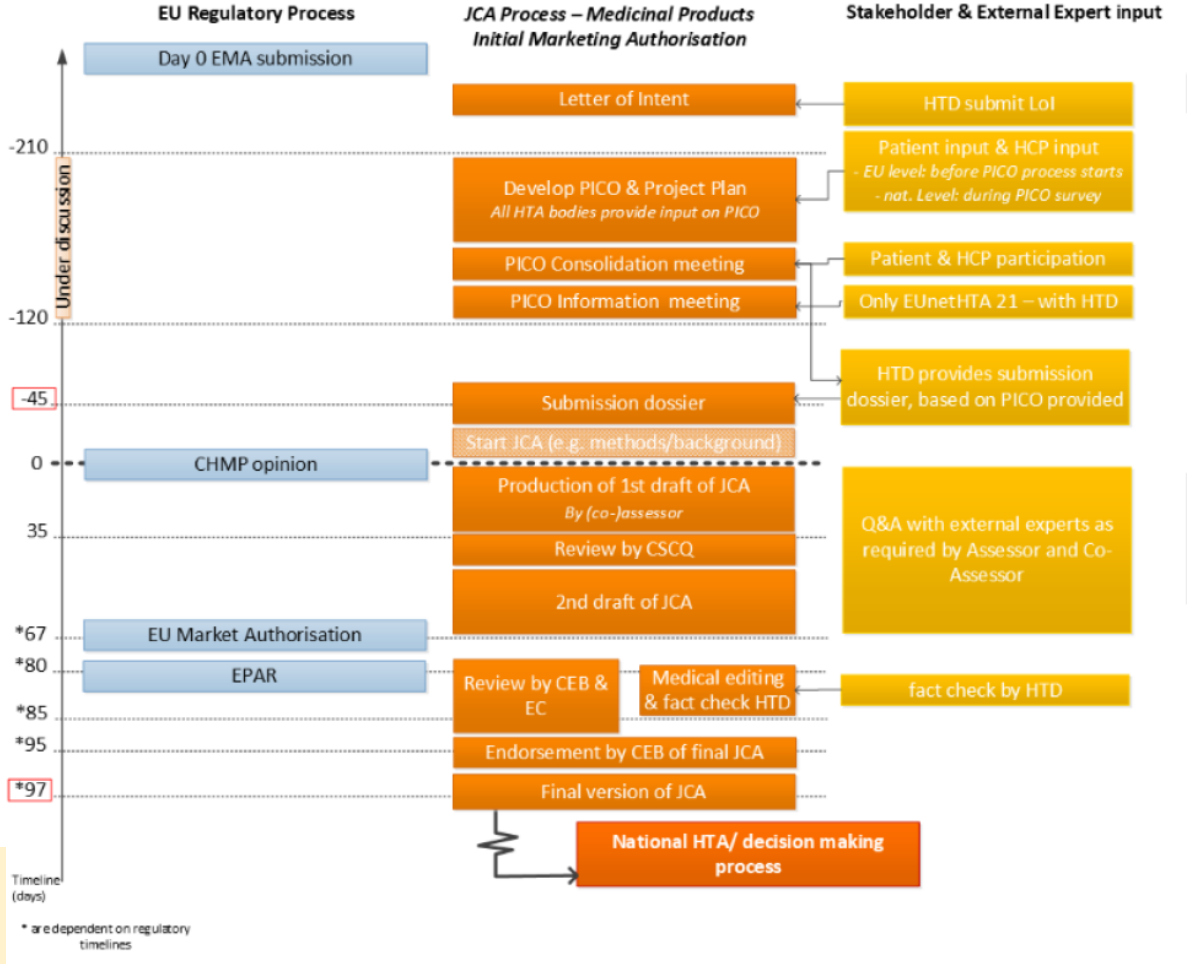
EUnetHTA 21 JCA production timelines *Medicinal Products JCA*

- Timelines are dependent on regulatory assessment timeline
  - Eligible products: initial marketing authorisation

Milestone	Month
Letter of Intent	August, 2022
Consolidated PICO	26 October, 2022
Submission Dossier	9 January, 2023 *45 days before CHMP opinion, as per HTA Regulation*
CHMP opinion	February, 2023 *Last CHMP meeting day = 23 Feb*
Publication JCA report	31 May, 2023 *Allowing 4-5 months for EUnetHTA21 to revise and update their deliverables before closing in September 2023*

**timelines for earlier or later start can be discussed bilaterally*



- EUnetHTA 21 originally proposed around 50 days for preparation of the dossier from the time the PICO(s) were communicated to the HTD, but this has now been extended to 75 days
- A "PICO information meeting" will be arranged with the HTD as part of the pilot, but has not been recommended for the EU HTA procedure

EUCOPE is actively communicating our views to EU decisionmakers and stakeholders

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European Confederation of Pharmaceutical Entrepreneurs AISBL

POLITICOPRO

HEALTH TECHNOLOGY ASSESSMENT

CONCERN OVER HTA METHODOLOGY FOR RARE DISEASE DRUGS: For those health technology assessment (HTA) wonks with an ear to the ground on the progress on the implementation of the EU HTA regulation, the latest tranche of consultations is out. Helen caught up with Matias Olsen of EUCOPE, the lobby group for smaller pharmaceutical and biotech firms, often developing orphan drugs, to get its take. And one draft has got them especially worried.

Clinical trials: To developers of drugs to treat rare diseases, real-world evidence is an essential way of showing the value of a treatment over time in a small patient group. In addition, given the very small patient numbers, single-arm, unblinded trials are often the only approach for evidence generation. But the current plans to allow these trials are disappointing, said Olsen.

The draft takes a statistical theoretical approach, he said: EU HTA will "dismiss evidence" that falls below certain statistical thresholds, both in tightly controlled clinical settings, such as randomized controlled clinical trials (RCTs), as well as in the real-world setting. "To maximize both of those is not really possible," Olsen said. "They're sort of opposed concepts."

Help me? As with all things HTA, it's technical. But ultimately, if you generate data in a very tightly controlled setting, this is not going to reflect the real-world setting. The draft states that it would be "methodologically inappropriate to take into account … the impossibility of blinding," Olsen said. "But there are ethical and practical issues around organizing trials for rare disease [therapies]; randomization or assigning a control group becomes impossible."

What's the solution? EUCOPE wants EU HTA to accept wider forms of evidence, as regulators do for rare disease drugs. "When it comes to single-arm trials, you can have historic controls, you can use real-world evidence, you can have registry-based studies," he said. Regulators accept that these studies provide enough initial evidence to move forward, with the knowledge that additional evidence will come as the therapies are used more.

Why it matters: So-called advanced therapy medicinal products (ATMPs) including cancer drugs and orphan therapies are going to be the first medicines to be assessed under the new EU HTA regulation. If the assessment doesn't work for these types of therapies, patients could be looking at even longer waits for potentially life-changing drugs.

POLITICOPRO

DRIVING THE DAY

CRUNCH TIME FOR EU HTA DECISIONS: It may be summer, but work has not stopped on the implementation of the EU's health technology assessment regulation. In fact, there are currently six consultations out, covering a total of 10 draft guidance documents. These will dictate the rules by which drug developers and Europe's health technology assessors will operate when determining the added value of a new therapy to existing clinical practice.

Why it matters: The outcomes of these assessments will be considered by EU countries when they negotiate a final price for the therapy. EU countries can choose to carry out their own duplicate assessment, but the aim is to develop an assessment that keeps all countries happy, avoiding the need for repeating a similar process 27 times. Helen caught up with the European Confederation of Pharmaceutical Entrepreneurs (EUCOPE), which largely represents small companies developing advanced therapy medicinal products (ATMPs), often for rare diseases. For EUCOPE, there are some concerns in these drafts.

Let's get together: One document sets out the guidelines for interactions between the drug developers and the HTA bodies, via the secretariat and the assessors. "Currently, this guideline proposes very limited interaction," said Matias Olsen, public affairs and policy manager. "When it comes to ATMPs, you would need a bit more of an interactive process to capture the complexities of the disease and the technologies to avoid any misunderstandings," he added.

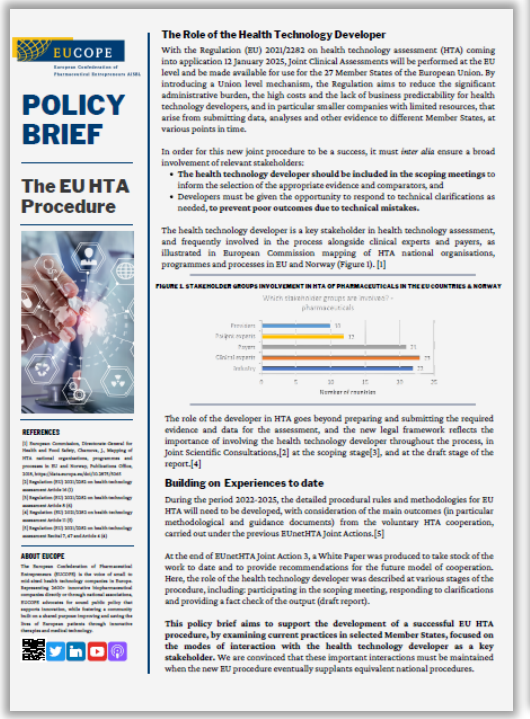
Whoa, wait up: When a new medicine is submitted to the European Medicines Agency for review, it's not uncommon for the final authorized indication to differ from the developer's application. Quite often, the EMA can restrict the therapy to a smaller patient population, and sometimes it can even allow its use in a broader patient group. When this happens, the HTA dossier also needs to be updated, to reflect the authorized use. One draft consultation proposes 10 days for this update. EUCOPE wants 45.

It's "not an easy thing to do," said Secretary-General Alexander Natz. "You have to bring in your own data to show that there is efficacy and cost-effectiveness in those new types of patient groups," he explained, pointing out that this affected half of the products approved in the first half of 2021.

Go compare: Building on an earlier document, draft guidance on the use of comparators for assessing the added value of a new therapy fails to "go far enough in accepting alternative methods" of data collection, Olsen said. For rare diseases, it can be impractical and/or unethical to carry out randomized controlled trials, he pointed out. "There really needs to be overall a stronger recognition that evidence that is generated outside of randomized, controlled trial settings … should be accepted and can bring really relevant information for the HTA procedure," he added.

There is also currently no planned guidance for the choice of appropriate comparators. Using the wrong clinical practice to compare a new therapy to, could result in market failure. "For me, it's one of the most important things," said Natz. "We need to have guidance, what is an appropriate comparator?"

The feedback deadline for these drafts is August 30.


EUCOPE

POLICY BRIEF

The EU HTA Procedure

The Role of the Health Technology Developer

With the Regulation (EU) 2021/2282 on health technology assessment (HTA) coming into application 12 January 2025, Joint Clinical Assessments will be performed at the EU level and be made available for use for the 27 Member States of the European Union. By introducing a Union level mechanism, the Regulation aims to reduce the significant administrative burden, the high costs and the lack of business predictability for health technology developers, and in particular smaller companies with limited resources, that arise from submitting data, analyses and other evidence to different Member States, at various points in time.

In order for this new joint procedure to be a success, it must *inter alia* ensure a broad involvement of relevant stakeholders:

- **The health technology developer should be included in the scoping meetings** to inform the selection of the appropriate evidence and comparators, and
- Developers must be given the opportunity to respond to technical clarifications as needed, **to prevent poor outcomes due to technical mistakes.**

The health technology developer is a key stakeholder in health technology assessment, and frequently involved in the process alongside clinical experts and payers, as illustrated in European Commission mapping of HTA national organisations, programmes and processes in EU and Norway (Figure 1). [1]

FIGURE 1. STAKEHOLDER GROUPS INVOLVEMENT IN HTA OF PHARMACEUTICALS IN THE EU COUNTRIES & NORWAY

The role of the developer in HTA goes beyond preparing and submitting the required evidence and data for the assessment, and the new legal framework reflects the importance of involving the health technology developer throughout the process, in Joint Scientific Consultations,[2] at the scoping stage[3], and at the draft stage of the report.[4]

Building on Experiences to date

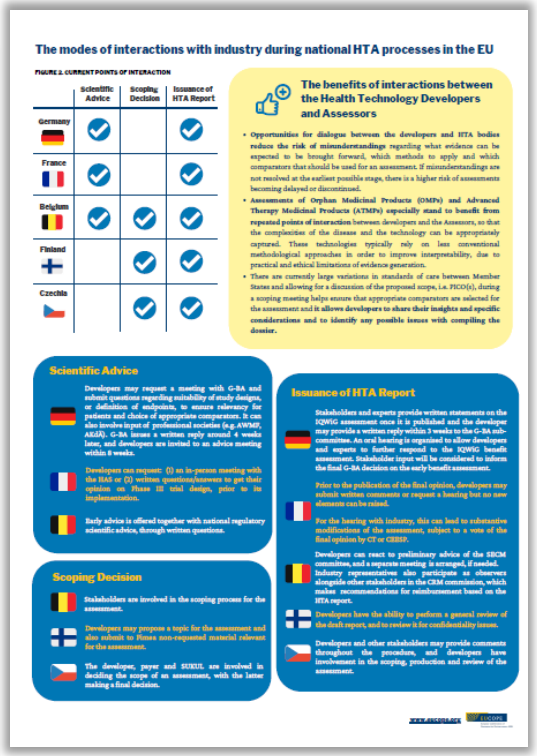
During the period 2022-2025, the detailed procedural rules and methodologies for EU HTA will need to be developed, with consideration of the main outcomes (in particular methodological and guidance documents) from the voluntary HTA cooperation, carried out under the previous EUnetHTA Joint Actions.[5]

At the end of EUnetHTA Joint Action 3, a White Paper was produced to take stock of the work to date and to provide recommendations for the future model of cooperation. Here, the role of the health technology developer was described at various stages of the procedure, including: participating in the scoping meeting, responding to clarifications and providing a fact check of the output (draft report).

This policy brief aims to support the development of a successful EU HTA procedure, by examining current practices in selected Member States, focused on the modes of interaction with the health technology developer as a key stakeholder. We are convinced that these important interactions must be maintained when the new EU procedure eventually supplants equivalent national procedures.

REFERENCES

ABOUT EUCOPE



- **Policy Brief:** Description of the benefits of interactions with HTDs at various stages of the HTA procedure and an overview of the current interactions at Member State level, in selected countries.

VII. AOB