EPF Educational Workshop on Pharmaceutical Incentives

Summary report

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1. Introduction

On 2 February 2018, EPF organised an educational workshop for patient representatives from our member organisations on the topic of pharmaceutical incentives. The half-day workshop was inspired by the need for more knowledge among patient organisations about this complex topic.

The EPF workshop focused on the complex technical dimensions of incentives such as data exclusivity or IP, rather than their political aspects. It provided an opportunity to better understand the complex, technical dimensions of incentives, including intellectual property. The workshop was also part of the training-offer of EPF to its members to build up knowledge and empower them to contribute meaningfully to the current EU political debate on the pharmaceutical incentives from a patient perspective.

EPF has only briefly touched on this issue in our paper on the pricing and value of innovative medicines, published in 2016; we welcomed emerging initiatives exploring alternative models for funding and incentivising pharmaceutical R&D which may be particularly relevant when it comes to addressing global health needs and health equity; however, EPF has not to date engaged in detailed discussions on incentives. Our 2016 paper put out a general call for the development of a "framework for fair access" which would address the affordability challenge but also maximise patient access and societal benefit derived from therapies. This was taken up by the European Parliament in its own initiative report in 2017, which EPF warmly welcomed and asked the Commission to follow up on its recommendation to set up High Level Strategic Dialogue to establish concrete and comprehensive strategies to achieve a framework for fair and equitable access in the short, medium and long term.

The workshop included an overview of the EU process by representatives of the European Commission (DG SANTE), a keynote by a legal expert, the patients' view, and the perspectives of both originator and generic medicines. Around 12 patient organisation leaders from the EPF community attended, representing diverse disease areas.

2. Background

The 2016 Council conclusions on "Strengthening the balance in the pharmaceutical systems in the EU and its Member States" asked the Commission to prepare "an evidence based analysis of the impact of the incentives (…) on innovation, as well as on the availability, inter alia supply shortages and deferred or missed market launches, and accessibility of medicinal products, including high priced essential medicinal products for conditions that pose a high burden for patients and health systems as well as availability of generic medicinal products." The Council asked for special attention to be given to the supplementary protection certificate (SPC)[1], the "Bolar" patent exemption[2], and the

[1] Supplementary protection certificates (SPCs) are an intellectual property right that serve as an extension to a patent right. They apply to specific pharmaceutical and plant protection products that have been authorised by regulatory authorities. The EU wishes to provide sufficient protection for these products in the interest of public health and to encourage innovation in these areas to generate smart growth and jobs.

[2] The principle behind the "Bolar" exemption is that generic companies should be in a position to take the necessary preparatory measures in order to be able to enter the market without delay once patent protection expires (article 10.6 of the Directive 2001/83/EC of 6 November 2001 on the Community code relating to medicinal products for human use).

incentives included in the EU Regulation on orphan medicines. The Council asked the Commission to conduct an investigation to provide:

"a. an overview of the current EU legislative instruments and related incentives that aim to facilitate the investment in the development of medicinal products and the marketing authorization of medicinal products given to the holders of a marketing authorisation as implemented within the EU: Supplementary Protection Certificates (Regulation EC 469/2009), medicinal products for human use (Directive 2001/83/EC and Regulation EC 726/2004), orphan medicinal products (Regulation EC 141/2000) and paediatrics (Regulation EC 1901/2006);

b. an evidence-based analysis of the impact of the incentives in these EU legislative instruments, as implemented, on innovation, as well as on the availability, inter alia supply shortages and deferred or missed market launches, and accessibility of medicinal products, including high priced essential medicinal products for conditions that pose a high burden for patients and health systems as well as availability of generic medicinal products. Among those incentives, particular attention should be given to the purpose of supplementary protection certificates as defined in the relevant EU legislative instrument and the use of the "Bolar" patent exemption, the data exclusivity for medicinal products and the market exclusivity for orphan medicinal products.

Where relevant, the analysis of impacts should also address - inter alia - the development of medicinal products and the effects of the pricing strategies of industry in relation to these incentives".

3. Summary

3.1 SETTING THE SCENE: THE EUROPEAN COMMISSION

In their presentation, Aude L'hirondel and Tidde Goldhoorn from the European Commission's DG SANTE presented the political context in which the work around incentives for pharmaceuticals operates. It is a cross-cutting issue that is dealt with by DG SANTE (responsible for health) and DG GROW (responsible for industry and internal market), giving follow-up to the Council Conclusions of 2016 on strengthening the balance in the pharmaceutical systems, and in accordance with the Better Regulation principles.

DG SANTE stressed the need to find an appropriate balance between:

- ✓ Adequate incentives for innovation,
- ✓ Equitable access to medicines for all,
- ✓ Sustainability of health systems.

The functioning of pharma systems indeed depends on delicate interactions between measures to promote innovation, pharmaceutical markets, HTA decisions and national pricing and reimbursement. This challenge was already highlighted in the Council Conclusions on innovation for the benefits of patients of 1 December 2014, and then in June 2016 Council Conclusions mentioned above. The European Parliament also took a strong stance on access to medicines in its resolution on EU options for improving access to medicines of 2 March 2017.

The Commission is engaged in collecting evidence and evaluating the existing EU legislation in order to guarantee a balance between all interests at stake. In terms of concrete recent and future actions, the following studies are being undertaken from the Commission's side.

A study on the "economic impact of the Paediatric Regulation, including its rewards and incentives" was published in October 2017. This report looks at different aspects of the Regulation including regulatory costs and economic value to the pharmaceutical industry as well as the direct and indirect social and economic benefits. The results of this study will feed into the evaluation of the legislation for children and rare diseases, to be carried out in 2018 and 2019.

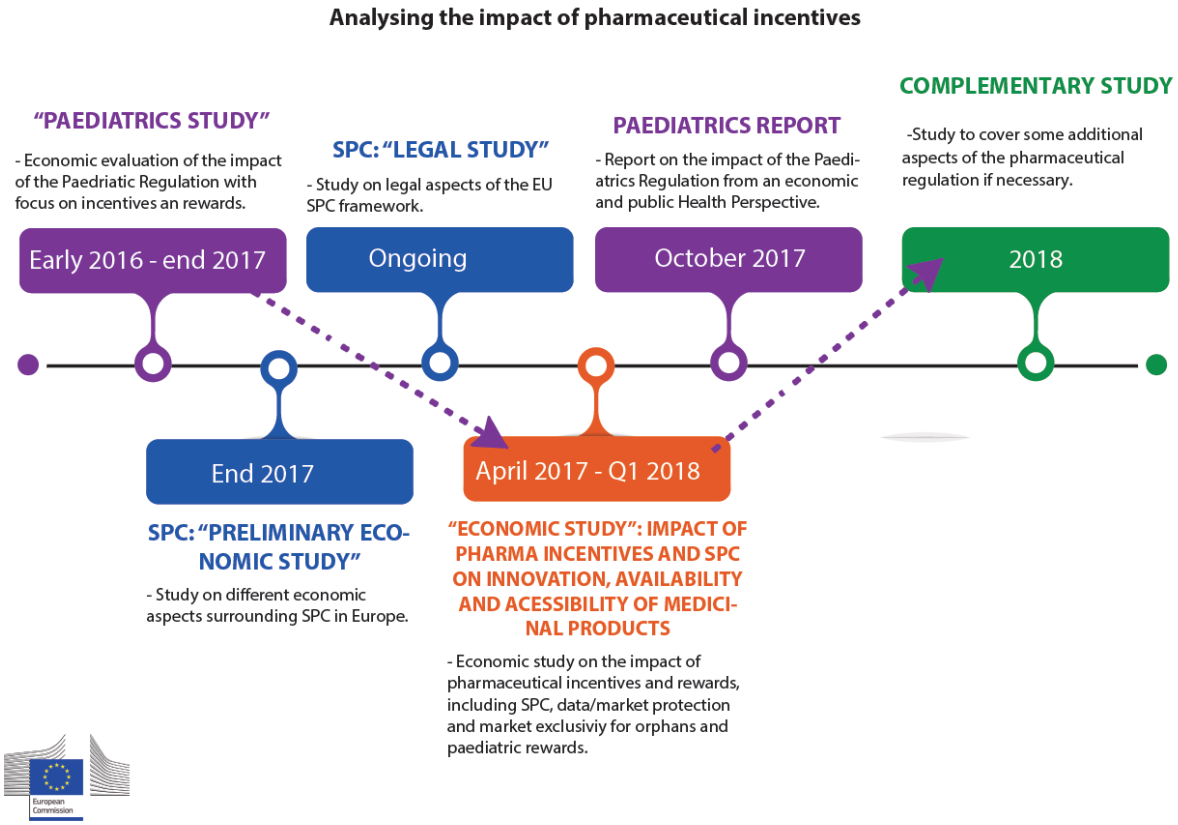
The other initiatives include:

1. A study on "the economic impact of supplementary protection certificates (SPCs), pharmaceutical incentives and rewards in Europe" is being conducted and will be completed by the summer of 2018 (orange part of the chart on page 4 below);
2. Study on the legal aspects of the supplementary protection certificates in the EU;
3. Gap analysis study for the evaluation of orphan medicines. In November 2017 a Roadmap was published along with a public consultation on the topic. During 2018 and 2019, this study will take place in consultation with various stakeholders.

The outcomes of the latter study will be used among others for the evaluation of the orphan medicines legislation.

In addition, the Commission is pursuing a gap analysis study for the evaluation of orphan medicines. In November 2017, a Roadmap was published along with a public consultation on the topic. During 2018-2019, the study will take place in consultation with various stakeholders. On the basis of this study, the evaluation will take place in 2019. In the area of Supplementary Protection Certificates (SPC), the Commission launched a 12-week public consultation looking at (1) the possibility of creating a "unitary" SPC title, (2) an update of the scope of the EU patent Bolar and research exemptions, and (3) the potential introduction of an SPC manufacturing waiver.

The chart on page 5 below provides an overview of the different ongoing and future initiatives from the Commission, including those of DG SANTE and DG GROW.



Source: European Commission

3.2 PRESENTATION BY LEGAL EXPERT CRISTIANO BACCHINI

Cristiano Bacchini, legal expert based in Italy, gave an overview of the legal framework surrounding incentives. There are two systems running in parallel. The first one relates to patents and patent law. This system offers **20 years of protection** to the producer of the product and can be **extended by an SPC[3] for a maximum of 5 years,** and in certain cases, with the possibility **for an extra 6 months** in the case of paediatric[4] research.

In this particular context Cristiano recalled a decision issued by the European Court of Justice in 2013 (case number C-443/12), according to which the SPC is designed simply to re-establish a sufficient period of effective protection of the basic patent by permitting the holder to enjoy an additional period of exclusivity on the expiry of his patent, which is intended to compensate, at least in part, for the delay to the commercial exploitation of his invention by reason of the time which has elapsed between the date on which the application for the patent was filed and the date on which the first marketing authorisation in the European Union was granted.

[3] Council regulation (EEC) no 1768/92 concerning the creation of supplementary protection certificate for medicinal products.

[4] Throughout this document, "paediatric" refers to the definition of the paediatric population given in the EU Regulation, that is, "that part of the population aged between birth and 18 years" (Art. 2 of the Paediatric Regulation).

The Paediatric Regulation[5] goes further than incentives for pharmaceutical companies, and it tried to make information on those medicines widely available and stimulate high quality paediatric research. This Regulation includes a set of obligations and rewards/incentives for industries to compensate the investment in paediatric development. The incentives for companies are threefold:

- (1) Scientific Advice and Protocol Assistance from the EMA;

  The advice might relate to the design and conduct of the various tests and studies necessary to demonstrate the quality, safety and efficacy of the medicinal product in the paediatric population. It might also relate to the design and conduct of pharmacovigilance and risk management systems. In both cases the advice is provided free of charge.

- (2a) Extension of the Supplementary Protection Certificate (SPC) for the duration of 6 months;

  This extension is provided if the company provides a study from a "paediatric investigation plan" (PIP). The results do not need to be positive. The reason this incentive is provided is to promote research of potential use in paediatric populations. In the exceptional case of an orphan drug being tested on a paediatric population, the SPC can have the complementary duration of 2 years.

- (2b) PUMA;

  Medicines developed specifically for children that are already authorised but are not protected by a patent or supplementary protection certificate are eligible for a Paediatric Use Marketing Authorisation (PUMA). If a PUMA is granted, the product will benefit from 10 years of market protection as an incentive.

- (3) A provision on EU funding into research leading to the development and authorisation of off-patent medicine for children.

The second system, applicable only to **orphan medicines**, is a parallel system with a different legal basis offering protection regardless of the patent system. This means that in the case a company focuses on developing orphan medicines, it can benefit from both systems. The following three instruments are key when it comes to orphan medicines:

- Regulation (EC) No 141/2000 of the European Parliament and of the Council on Orphan Medicinal Products of 16 December 1999
- Incentives Commission Regulation (EC) No 847/2000 of 27 April 2000
- Commission communication July 2003 (2003/C 178/02) Commission communication on art 8(1) and (3) (C(2008) 4077).

The *ratio legis* behind the orphan drug regulation was that patients suffering from rare conditions had to be entitled to the same quality of treatment as other patients. Orphan medicinal products are products that (1) treat a condition affecting not more than 5 in 10,000 persons in the EU, and (2) have no satisfactory method of diagnosis, prevention or treatment of the condition.

Orphan medicinal products benefit from access to the **centralised EMA marketing authorisation procedure**. Orphan medicinal products also benefit from **protocol assistance**. This means that the EMA can inform producers on types of studies needed to demonstrate the medicine's quality, benefits and risks, and information on the significant benefit of the medicine. Protocol assistance is available

[5] Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use, and Regulation (EC) No 1902/2006 amending regulation in which changes to the original text were introduced relating to decision procedures for the European Commission.

at a reduced charge for designated orphan medicines. Orphan medicinal products also benefit from a **10-year market exclusivity**. Because of the latter part of the definition of what an orphan drug is (point 2), as soon any product would exist that would guarantee a "satisfactory method of diagnosis, prevention or treatment", then no other product would be eligible to benefit from the same legal regime. Nevertheless, the legislation offers the possibility for derogations if certain cumulative conditions are met.

As far as the Italian system is concerned, Cristiano recalled the Balduzzi Decree which, among others, provides some incentives such as the evaluation by AIFA for the purposes of classification and reimbursement by the national health service giving priority to orphan drugs; also through extraordinary sessions of the competent Commissions, by granting a decision after 100 days instead of 180 days.

3.3 INDUSTRY PERSPECTIVES

Kristine Peers, speaking on behalf of EFPIA, the European Federation of Pharmaceutical Industries and Associations, as well as Sergio Napolitano, on behalf of Medicines for Europe, provided their respective views on the topic.

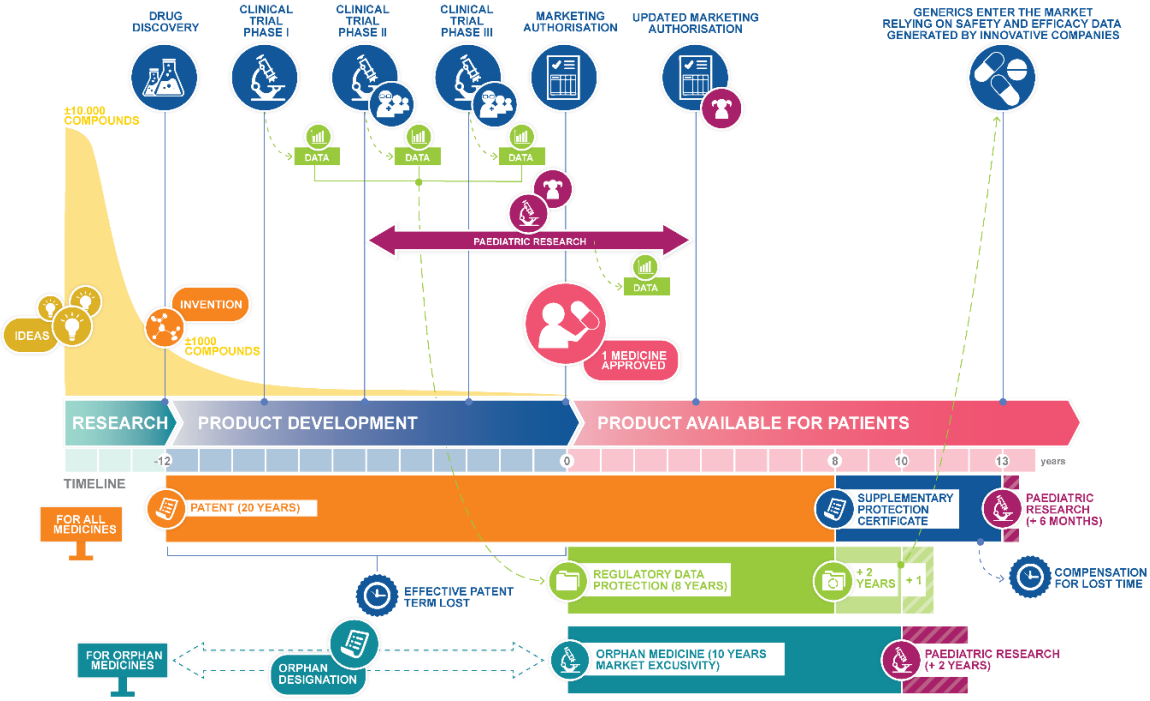
There was a general agreement that a lot of progress has been made over the last years and that pharmaceutical innovation has had a great impact on lives of patients. A patent application for a new potential treatment is filed very early in the R&D process. In general, out of the 20 years for which patent is granted, 10-12 years is spent in product development (clinical trials, marketing authorisation). The period that elapses between the filing of a patent application for a new medicinal product and the authorisation to place the medicinal product on the market makes the period of effective protection under the patent insufficient to cover the investment put into the research according to the industry (see illustration on page 8 below – larger version in annex).

To reflect the complexity around innovation, a sophisticated system of protections has been created in Europe in order to support and incentivise research:

- **Patents**: 20 years covering all possible innovative activities
- **Data + Market Exclusivity (DE+ME)**: 8 + 2 (+1 year for new indication with significant benefit) covers whole product (for a new chemical entity)
- **Data Exclusivity:** 1 year for new indication only (for well-established substance)
- **Data Exclusivity:** 1 year for changing classification (switch to over-the-counter)
- **Supplementary Protection Certificate (SPC)**: up to 5-year patent extension
- **Paediatric extension**: 6 months of SPC extension or 2-year market exclusivity if a Paediatric Investigation Plan (PIP) is completed for an orphan medicine or 10-year exclusivity for PUMA[6]
- **Orphan exclusivity**: 10-year data exclusivity
- **Second medical use patents**: 20-year patent protection for new indications

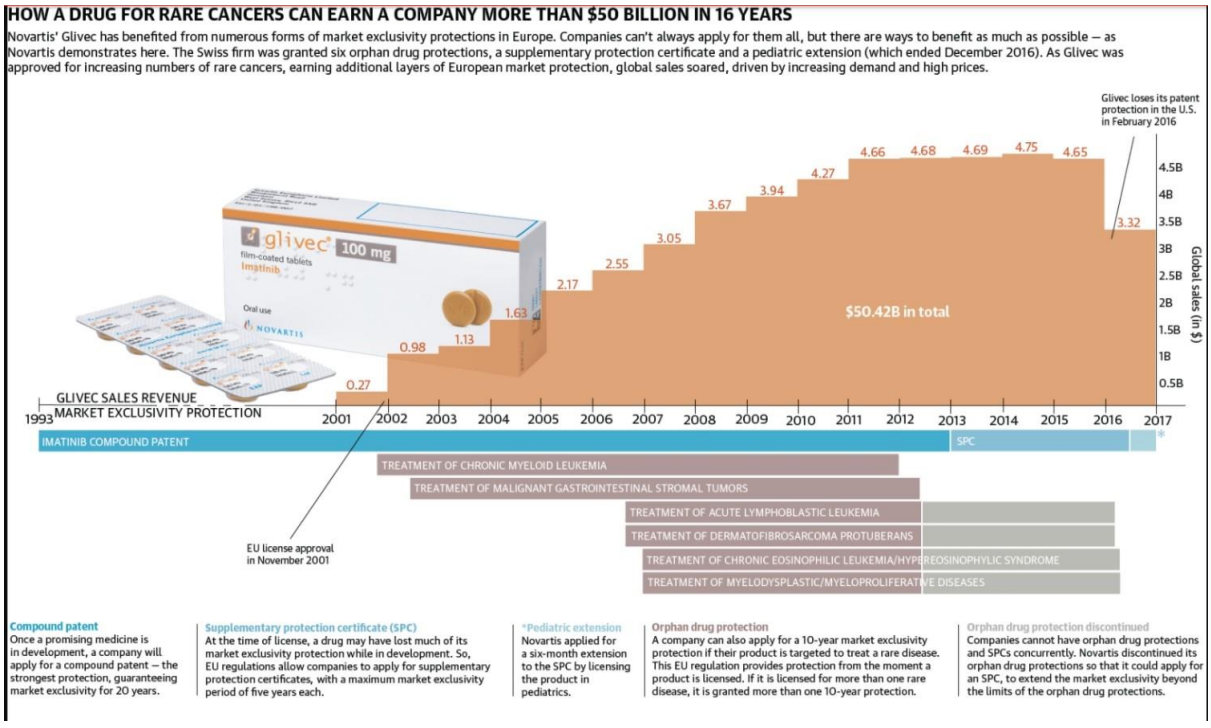
The challenge for governments related to the societal cost of new medicines derives partly from the increase of public expenditure on potentially important but costly niche medications treating small portions of the population, stretching healthcare budgets.

[6] Paediatric Use Marketing Authorisation



Source: EFPIA

As shown in the image below regarding a treatment for several cancers, the complex system of incentives can be used legitimately to maximise exclusivities, sometimes even beyond the original intention of the legislation, thus postponing market entry of generic competitors, or creating legal uncertainty for the whole industry, with an impact on patient access.



Source: Politico Research, source image by Novartis

At the same time, studies show that allowing other producers (generic and biosimilar companies) to enter the market after the expiry of exclusive rights of an innovator company and without delays, has lowered prices and increased patient access, even by doubling access to treatment without altering the public or private expenditure.

3.4 THE PATIENT PERSPECTIVE

Simone Boselli, on behalf of EPF's member organisation EURORDIS – Rare Diseases Europe, gave a view from the patients' perspective on the issue, focusing specifically on the orphan products and paediatric medicines regulation.

According to Simone, the current regulatory framework is working quite well, but some improvements are needed. The Regulation on Orphan Medicinal Products[7] is a success of EU action in support of entrepreneurship and industry. The current outlook is that this very positive trend is set to continue in the near future, with between 30 to 50 new orphan medicinal products coming to market per year by the year 2020. This is the fundamental backdrop against which the merits of any potential review of the legislation currently in place should be carefully considered.

However, the original ambitions laid out in the remain far from being fully achieved, especially when it comes to patient access to approved orphan medicinal products. Over 90% of the 6,000 recognised rare diseases do not have an authorised therapy, and for existing therapies, access is still problematic. The principle of EU market exclusivity applies today to a European market for orphan medicines which is far from being unified or complete, and across which access is still not structured with a common approach.

The Paediatric Regulation[8] has had a positive impact on both the number of new paediatric medicines authorised and the number of new paediatric indications for already authorised products, as well as on the information on the use of medicines in children, which has highly improved since the Regulation came into force. Nevertheless, progress in paediatrics is linked to development in adults and dependent on the companies' adult pipeline; therefore, only some therapeutic areas have been favoured while others remain neglected.

A combination of factors influences patients' access to innovative therapies. There is a potential for more treatments to be approved every year, but often the prices at which those treatments are offered are relatively high, while at the same time, uncertainties at time of marketing authorisation might be existing as to the effectiveness of the treatment. This poses affordability and sustainability questions to patients and healthcare systems, which individual countries are often not able to answer.

Simone concluded that the understanding of the regulatory frameworks for orphan and paediatric medicines should be improved. Incentives and rewards created to encourage development exist in areas that are generally overlooked and therefore are underused by pharmaceutical companies.

[7] Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products

[8] Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use

4. Next steps

The first meeting on the topic of incentives provided a useful overview of developments at European level, as well as insights on the perspectives of different stakeholders, particularly different industry actors, their complementarities and divergences.

This report gives an overview of these perspectives, without drawing specific conclusions. EPF envisages further dialogue with the wider membership, such as through a Breakfast Briefing highlighting the key issues, to be held in the next months, in order to provide opportunities for exchanges of views and to gain clarity on the members' views around these issues.

We are also active on topics related to questions around incentives: On Health Technology Assessment, we have published a position statement following the recent European Commission legislative proposal for a Regulation. We are also currently consulting its membership on a revision of our 2016 paper "Core Principles from the Patients' Perspective on the Value and Pricing of Innovative Medicines" in order to update it taking into account recent initiatives. An updated paper will be published later in 2018.

EPF will continue keep a close eye on developments in the area of pharmaceutical incentives at European level and engage actively when necessary, in consultation with the membership.

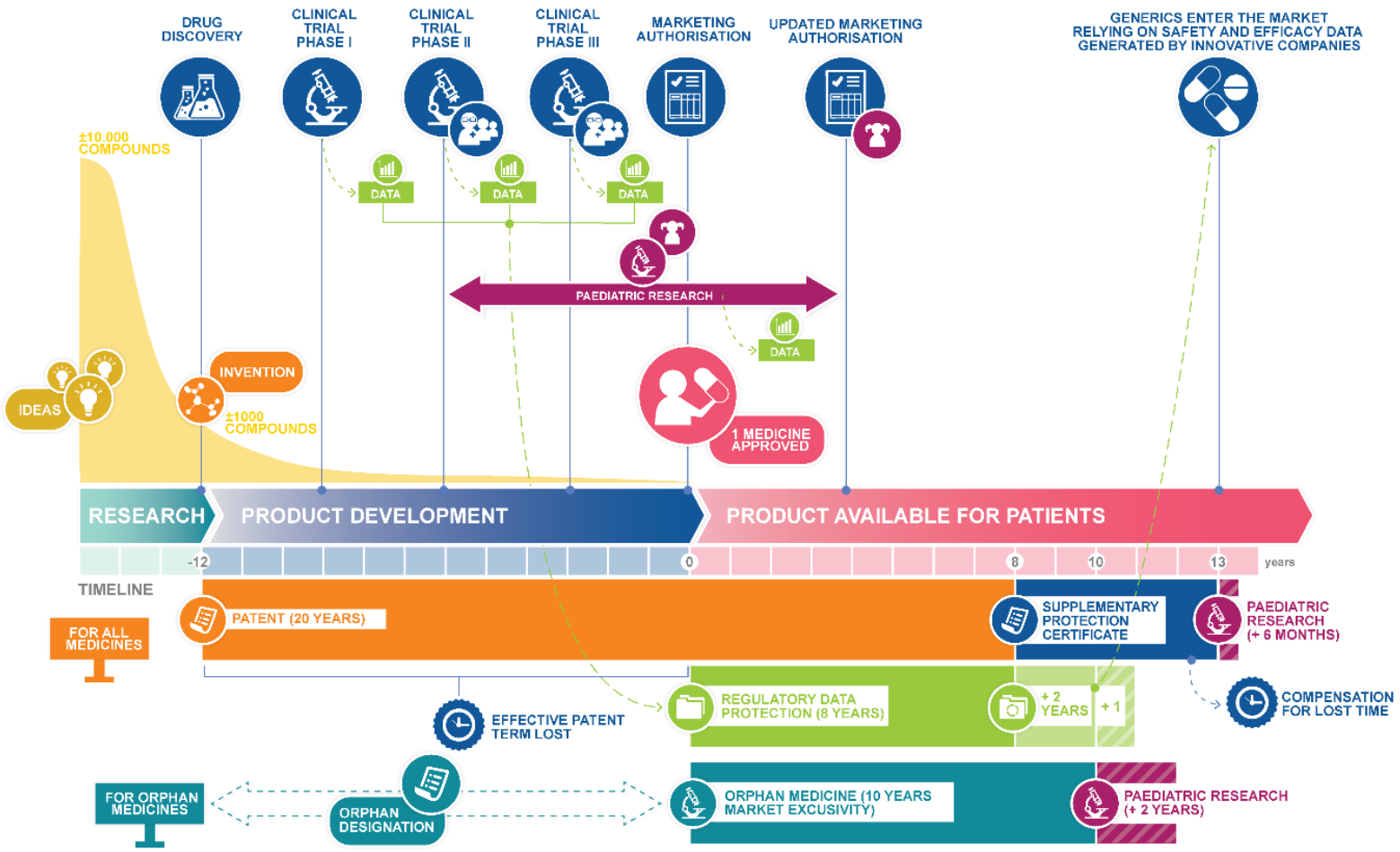
5. Annex – agenda

EPF Educational Workshop on Pharmaceutical Incentives

2 February 2018
EPF Office, Brussels

09:00-09.30	**Welcome coffee**
09:30-09.45	**Opening by Marco Greco, EPF President**
09:45-10.05	**Setting the scene** • *Olga Solomon, Representative of the European Commission*
10:05-10.30	**Keynote lecture** • *Cristiano Bacchini, Legal expert*
10:30-10.45	**Q&A**
10:45-11.15	**Coffee break**
11:15-11.35	**Overview from EFPIA** • *Kristine Peers, General Counsel*
11:35-11.50	**Overview from Medicines for Europe** • *Sergio Napolitano, Director Legal Affairs & Trade Policy*
11:50-12:10	**Q&A**
12:10-12:30	**Patient perspective** • *Simone Boselli, EURORDIS*
12:30-12:50	**Reflections from around the table**
12:50-13:00	**Conclusions**
13:00-14:00	**Lunch**

6. Annex – Product development timeline



Source: EFPIA