



Universiteit
Leiden
The Netherlands

Development of medicines for rare diseases and inborn errors of metabolism: Ttward novel public-private partnerships

Rosenberg, N.; Stolwijk, N.N.; Berg, S. van den; Heus, J.J.; Wel, V. van der; Gelder, T. van; ... ; Hollak, C.E.M.

Citation

Rosenberg, N., Stolwijk, N. N., Berg, S. van den, Heus, J. J., Wel, V. van der, Gelder, T. van, ... Hollak, C. E. M. (2023). Development of medicines for rare diseases and inborn errors of metabolism: Ttward novel public-private partnerships. *Journal Of Inherited Metabolic Disease*. doi:10.1002/jimd.12605

Version: Publisher's Version

License: [Creative Commons CC BY 4.0 license](#)

Downloaded from: <https://hdl.handle.net/1887/3594489>

Note: To cite this publication please use the final published version (if applicable).

REVIEW



WILEY

Development of medicines for rare diseases and inborn errors of metabolism: Toward novel public–private partnerships

Noa Rosenberg^{1,2} | Nina N. Stolwijk^{1,2} | Sibren van den Berg^{1,2} |
 Joris J. Heus³ | Vincent van der Wel^{1,4} | Teun van Gelder⁵ |
 Annet M. Bosch⁶ | Saco J. de Visser^{1,7} | Carla E. M. Hollak^{1,2}

¹Medicines for Society (Medicijn voor de Maatschappij), Platform at Amsterdam UMC - University of Amsterdam, Amsterdam, The Netherlands

²Department of Endocrinology and Metabolism, Amsterdam UMC, Amsterdam Gastroenterology Endocrinology Metabolism (AGEM) Research Institute, Expertise Center for Inborn Errors of Metabolism, MetabERN, University of Amsterdam, Amsterdam, The Netherlands

³Innovation eXchange Amsterdam (IXA) Office Amsterdam UMC, Amsterdam, The Netherlands

⁴Orfenix B.V., Leiden, The Netherlands

⁵Department of Clinical Pharmacy & Toxicology, LUMC, Leiden University Medical Center, Leiden, The Netherlands

⁶Department of Pediatrics, Division of Metabolic Diseases, Emma Children's Hospital, Amsterdam Gastroenterology Endocrinology Metabolism (AGEM), Amsterdam UMC location University of Amsterdam, Amsterdam, The Netherlands

⁷Centre for Future Affordable & Sustainable Therapy development (FAST), The Hague, The Netherlands

Correspondence

Carla E. M. Hollak, Department of Endocrinology and Metabolism, Amsterdam UMC, Amsterdam Gastroenterology Endocrinology Metabolism (AGEM) Research Institute, Expertise center for inborn errors of Metabolism, MetabERN, University of Amsterdam, P. O. BOX 22660, 1100 DD Amsterdam, The Netherlands.
 Email: c.e.hollak@amsterdamumc.nl

Funding information

Nationale Postcode Loterij

Communicating Editor: Georg Hoffmann

Abstract

Medicine development for rare diseases, including inborn errors of metabolism (IEMs) is challenging. Many academic innovations fail to reach the patient, either by stranding in the translational stage or due to suboptimal patient access related to pricing or uncertain effectiveness. Expanding and solidifying the role of the academic in public–private partnerships (PPPs) may present an innovative solution to help overcome these complexities. This narrative review explores the literature on traditional and novel collaborative approaches to medicine development for rare diseases and analyzes examples of PPPs, with a specific focus on IEMs. Several academic institutions have introduced guidelines for socially responsible licensing of innovations for private development. The PPP model offers a more integrative approach toward academic involvement of medicine development. By sharing risks and rewards, failures in the translational stage can be mutually absorbed. If socially responsible terms are not included, however, high pricing can impede patient access. Therefore, we propose a framework for socially responsible PPPs aimed at medicine development for metabolic disorders. This socially responsible PPP framework could stimulate successful and accessible medicine development for IEMs as well as

Noa Rosenberg and Nina N. Stolwijk contributed equally to the manuscript and should be considered as joint first authors.

This is an open access article under the terms of the [Creative Commons Attribution](https://creativecommons.org/licenses/by/4.0/) License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

© 2023 The Authors. *Journal of Inherited Metabolic Disease* published by John Wiley & Sons Ltd on behalf of SSIEM.

other rare diseases if the establishment of such collaborations includes terms securing joint data ownership and evidence generation, fast access, and socially responsible pricing.

KEYWORDS

medicine development, orphan medicinal products, public–private partnerships, rare diseases, socially responsible pricing

1 | INTRODUCTION

Medicine development for rare diseases can be challenging, as illustrated by the fact that, at present, appropriate medicinal treatments only exist for an estimated 5% of rare disorders.¹ To boost pharmacological development in this sphere, the European Commission (EC) introduced the “Orphan Regulation” in 2000, offering incentives to developing medicines targeting rare diseases (defined as a prevalence <1:2000 in the EU), known as orphan medicinal products (OMPs).² Since its introduction, the number of approved OMPs has been steadily rising.^{3–5} Historically, medicine development for rare diseases has relied on key contributions from academia. However, academic innovations often fail to bridge the gap from research to successful therapy benefitting patients, stranding in the so-called valley of death.⁶ Even if novel OMPs are successfully introduced, limited access due to high pricing, reimbursement issues or uncertain (long-term) effectiveness can still reduce patient benefit.^{7,8} Redefining the role of academia in the development process offers the potential to address pressing impediments to successful and accessible medicine development for rare diseases.^{9,10}

In traditional medicine development, the role of academia has mainly been at its start, propelling innovation—for instance by elucidating pathophysiological pathways and identifying early-stage (repurposed) medicine candidates.^{10–12} The translational stage of development that follows is commonly privatized, which sometimes includes commissioning academics to perform late-stage trials.^{10,13} More recently, academic centers of expertise, alone or as networks, commenced initiatives such as the INTEGRATE-ATMP or MLDi projects, to collect real-world evidence via registries to investigate outcomes of novel therapies.^{14–16} Data collected via such networks is increasingly used in regulatory approval and reimbursement decisions, in particular for the rarest diseases.¹⁷

Apart from this, a novel approach to medicine development is the formation of public–private partnerships (PPPs), wherein private parties and academic partners, or European Reference Networks, are forged to address a specific public health need.¹⁸ Currently, these PPPs are scattered across different stages of the medicine development

process, including identifying novel drug targets, describing natural history cases, determining meaningful clinical endpoints, collecting real world evidence, and conducting post-authorization safety studies.^{19–25} By involving academics as dedicated participants throughout all stages of medicine development, the risk of innovation stranding can be reduced, while their ability to exert influence on actual access to their invention will increase.^{26,27} The incorporation of socially responsible terms in novel PPPs could help ensure that academic endeavors ultimately benefit patients and society better.

This collaborative approach to (orphan) medicine development is especially relevant to the field of inborn errors of the metabolism (IEMs), where treatment options are often limited.²⁸ In 2020, only two-thirds of authorized OMPs for IEMs were actually accessible for patients.²⁹ Prioritizing integrative collaboration and socially responsible terms in PPPs in this field can leverage strengths of both academic and private parties and improve outcomes for medicine development.

In this review, we aim to describe the developments that led to the PPP model and provide multiple PPP examples. Based on our findings we propose a framework for integrative socially responsible PPPs, which include terms for data ownership and evidence generation, fast access, and socially responsible pricing. The proposed socially responsible PPP framework can stimulate delivering novel treatments to patients by facilitating academic involvement in all stages of medicine development, reducing costs, and expanding risk-sharing for public and private entities, as well as securing patient access goals.

2 | METHODS

We performed a narrative review on the traditional role of academia in PPPs for medicine development for rare diseases including IEMs, with a specific focus on social responsibility. To this end, we retrieved purposively sampled scientific literature from the PubMed database using keywords “knowledge transfer offices,” “university–industry collaborations,” “public–private partnerships” in combination with “social responsibility” or “socially

responsible” and “rare disease” or “orphan medicine.” Only English articles were considered. Literature that did not pertain to the role of the public and/or academia in medicine development was excluded. Additionally, we included policy documents and position papers known to the authors that were deemed relevant to this article.

We illustrate challenges and lessons learned of PPPs for medicine development through a number of selected cases (well-known PPPs in the global health space and PPPs relating to IEMs). The data on these cases were obtained by searching “the name of the PPP” and “the name of the active substances” or “trade name of the medicinal product” in combination with “collaboration” or “public–private partnership” in the PubMed database. We excluded any literature that did not address PPPs. To gain a broader understanding, we also collected English newspaper articles using a similar search strategy in the NexisLexis database.

Last, we propose a framework consisting of crucial elements for socially responsible PPPs with the aim of developing accessible medicinal treatments for metabolic patients.

2.1 | The traditional role of academics in medicine development

Historically, researchers–clinicians involvement in medicine development has been fragmented. Academia has been at the root of many therapeutic developments fueled by fundamental and translational research on pathology and the identification of novel therapeutic targets.¹⁰ Additionally, academic researchers have been involved in identifying novel applications for existing medicinal products (i.e., drug repurposing), an approach which is deemed especially relevant for rare diseases like IEMs.^{29,30} In fact, the majority of medicinal products repurposed for rare diseases in the EU were found to originate in academia.¹¹

Following the identification of promising therapeutic compounds, academia traditionally needed to involve pharmaceutical or biotech companies for the further development and commercialization of its inventions to pharmaceutical or biotech companies.¹² This process is facilitated by the academic institute's knowledge transfer offices (KTOs). KTOs are responsible for identifying inventions that could benefit society and patients. They take care of the patenting process and the subsequent out-licensing or transfer of these patents to industrial parties, involving a monetary return in the form of royalties, milestone payments, and/or shares in spin-off companies.^{31–33} In the sporadic case that an academic invention leads to a successful product, these returns can be substantial for universities and researchers.³⁴

Besides, KTOs may support academic institutions in starting spin-off companies to further their inventions

with private investments.³⁵ Starting a spin-off may seem logical, but comes with the risk of losing control over pricing and access due to the company's high cost of capital and commercial interests of its shareholder.³⁶ An example is the development of alipogene tiparvovec (Glybera), a gene therapy targeted at lipoprotein lipase deficiency (OMIM no. 238600).³⁷ The initial treatment was invented by the University of British Columbia and further developed by spin-off company Amsterdam Molecular Therapeutics (AMT, now uniQure).³⁸ When finally approved, the price setting exceeded \$1 million per treatment which—at the time—was the most expensive medicine in the world.^{38,39} Subsequent reimbursement issues resulted in limited usage, which led to the decision to withdraw the authorization.^{38,40–42} Despite their pivotal role in commencing development of this treatment, the initially involved researchers were unable to influence the pricing and subsequent patient access.³⁸

Apart from fostering novel therapeutic concepts and identifying early-stage medicine candidates, researcher–clinicians are often engaged in later stages of commercial medicine development. This can encompass involvement in industry-led pre- and post-marketing studies, for instance by consultation regarding relevant endpoints in (pivotal) trial design—although the value of such academic input has often been overlooked.

In these phases, disease registries that are usually used for natural history or post-authorization safety studies may also play a role by benefitting regulatory evaluation and reimbursement decisions.⁴³ Enzyme replacement therapy (ERT) for Fabry disease (OMIM no. 301500), for example, was only reimbursed in Canada on the condition of additional evidence generation in an independent registry.⁴⁴ OMPs for metabolic indications potentially have an increased need for registry data. These products are more often authorized under exceptional circumstances (meaning acceptance of inevitably lower evidence for safety and efficacy), which can impact reimbursement outcomes negatively.⁴⁵ Registry data can help establish real-world effectiveness and support reimbursement decisions.^{43,44} The role of academia in metabolic medicine development is thus already changing. This presents an opportunity to restructure academic involvement and in doing so, academics can help address roadblocks to successful and accessible medicine development that have persisted in the traditional model.

2.2 | Academic integration in collaborative medicine development

The broader societal shift toward “corporate social responsibility” (i.e., all business practices aiming to benefit society) has also impacted the pharmaceutical

industry.^{46,47} Increasingly, a similar discourse has emerged in academia, with several national organizations and academic institutions introducing initiatives for social terms in the traditional model of out-licensing.⁴⁸ In the United Kingdom, for instance, several universities including University College London and University of Oxford have incorporated “socially responsible licensing” terms, particularly aimed at affordable access in developing countries.⁴⁹ In the Netherlands and Belgium, university associations have established principles for socially responsible licensing to ensure scientific insights remain of benefit to society.^{50,51} One of the Dutch principles addresses the access aspect, stating that a license should ensure that pricing of the final product may not endanger availability. A toolkit is available online that can be used to integrate these principles in contracts.^{52,53} These local policy documents outline a modernized version of the classical academic out-licensing model.

A more drastic shift from out-licensing to the PPP model might offer more substantial and impactful solutions to the complexities in medicine development for rare diseases. PPPs are, in essence, structures for public-private collaboration to reach a mutual goal, wherein efforts and rewards are shared.^{54,55} The major players within PPPs are the pharmaceutical industry (small, medium, and large pharma), academic institutions, governmental funding programs, and private investors. More recent stakeholders in PPPs include patient organizations, regulatory agencies, health technology assessment bodies, health insurance companies, IT-companies, and European Reference Networks.⁵⁶ Governance structures that balance perspectives of all stakeholders should include scientific and auditing committees, financial administrators, and management or coordinators.^{57,58} Such structures can support the mitigation of conflicts of interest.⁵⁹

The PPP model has the potential to bridge the valley of death through shared public-private financial commitments and cost- and risk-saving strategies.^{26,27} Direct cost-saving can be achieved by executing academic endeavors for cost price and limiting marketing activities. Lower costs also lead to the reduction of cost of capital (i.e., the cost of funds required to finance a development project). As a result, the project is less likely to strand in the valley of death (due to financial reasons). Expanding the positive impact of PPPs can be achieved by including innovative ideas or approaches, such as transparent processes, open communication with the public,⁵⁷ and creating a revolving fund with the rewards from collaborations to invest in future research and development.⁶⁰

In return for embracing risk-sharing and cost-saving strategies, PPPs aimed at medicine development should

ensure their benefit to patients as well as society by including socially responsible terms. As Laplane and Mazzucato suggest in their framework for such collaborations,⁶⁰ it is imperative to ensure that innovation that has been publicly co-funded must remain affordable and accessible to avoid taxpayers paying for both the funding as well as high pricing.⁶¹ In the next section we explore existing PPPs aimed at medicine development and/or patient access, both to illustrate the potential of this approach and to demonstrate the shortcomings.

2.3 | Lessons learned from PPPs: The need for socially responsible terms

Currently, involvement of academia or European Reference Networks in PPPs is fragmented and appears in different stages of medicine development. The implementation of PPPs in the public health field coincided with the pursuit of social responsibility, since early PPPs primarily aimed to improve access to medicines in low and middle income countries.⁶² They emerged in the 1990s, when rising research and development (R&D) costs led to pharmaceutical companies focusing on projects with the most potential for profitable return on investments. PPPs were subsequently proposed as a way to realize less profitable projects in low-income countries—which, by definition, offer less potential for return on investment.^{63,64} One well-known example is the access-focused “Mectizan® Donation Program” in which pharmaceutical company Merck works with partners in over 45 countries and facilitates access to ivermectine (Mectizan) for the treatment of river blindness and lymphatic filariasis.^{65,66} Although such philanthropic collaborations differ significantly from product development PPPs for IEMs, these PPPs have successfully achieved significant impact on public health.^{63,64}

More recently, PPPs in the global health space have also incorporated development goals, as demonstrated by the not-for-profit Pediatric Praziquantel Consortium.^{67–69} This consortium developed a suitable pediatric formulation of arpraziquantel for the treatment of schistosomiasis and now aims to obtain marketing authorization for this product and provide affordable access.^{70,71} Global health PPPs thus illustrate the adaptability of these collaborations, as well as their potential toward alleviating unmet medical needs.

Our understanding of this potential has deepened following the response to the unprecedented COVID-19 pandemic, which propelled a rapid increase in PPPs that proclaimed philanthropic motives.⁷² However, these claims were not always fully fulfilled. One example is the Oxford–AstraZeneca COVID-19 vaccine, which was based on proprietary technology jointly owned by the University of

Oxford and its spin-off company Vaccitech and developed further following a partnership with the pharmaceutical company AstraZeneca.^{73,74} Although this collaboration resulted in rapid and successful vaccine development, concerns regarding AstraZeneca's profit margin have arisen as the fulfillment of pledges regarding global equitable vaccine distribution lagged behind.⁷³ This illustrates the need to incorporate socially responsible terms, including transparency on price build-up, when establishing such product development PPPs to ensure that the ultimate goal of patient access is achieved.

Although the COVID-19 pandemic accelerated public-private collaborations for a large population in an emergency setting, similar PPPs for IEMs remain rare, due to the unique challenges for medicine development in this field—including (extremely) low disease prevalence.⁷⁵ In other words, there is a very small market potential makes the field of IEMs uninteresting for companies to invest in. Despite these difficulties, there are several striking examples of collaborations in different stages of development,^{76,77} yet (to the best of our knowledge) lacking the necessary socially responsible elements to guarantee patient access and public investments benefitting society.

One of these scant examples is the Urea Cycle Disorders Consortium (UCDC). The UCDC is an academic research consortium that organized a large longitudinally studies cohort: a resource for natural history and a potential cost-decreasing tool.¹⁹ Regarding this cohort, the UCDC formed multiple early-stage partnerships seeking to develop treatments, which eventually led to the installment of an industry relations committee to guard transparency and conflicts of interests.⁷⁸ Albeit no socially responsible pricing terms are embedded, the UCDC positions itself to accord a paramount importance to ensuring access and will not pursue profit.^{78,79}

The UCDC did not only collaborate with commercial parties in the pre-competitive space but also ventured beyond that. The UCDC, as well as the N-carbamylglutamate consortium (NCGC), interacted with industry for trials with N-carbamylglutamate (Carbaglu, Orphan Europe, later Recordati Rare Diseases) for multiple IEMS, including N-acetylglutamate synthase deficiency (NAGSD, OMIM no. 237310), propionic academia (PA, OMIM no. 606054), methylmalonic aciduria (MMA), ornithine transcarbamylase deficiency (OTCD, OMIM no. 311250), and carbamylphosphate synthetase 1 deficiency (CPS1D, OMIM no. 237300).^{19,20} Carbaglu is dubbed one of the most pricey medicines in the world,⁸⁰ demonstrating that academia should look beyond the publication horizon and embrace objectives that benefit patients and society.

Apart from partnerships in pre-marketing stages, collaboration in the rare disease arena occasionally happens

in later stages too, such as for post-authorization safety studies. This can be initiated in coordination with the regulators to comply to post-authorization measures,^{21,81} as was the case for betaine anhydrous (Cystadane, Orphan Europe SARL, later Recordati Rare Diseases) for the treatment of homocystinuria (OMIM no. 23600) and glycerol phenylbutyrate (Ravicti®, Immedica Pharma AB) for urea cycle disorders.^{22,82} In these instances, the registry initiatives E-HOD and E-IMD formed a PPP with the respective marketing authorization holder and utilized a multicenter registry that helped to introduce the treatment on the market and minimized the impact on patients by reusing existing data.²² However, engagement in such settings might have limited potential for the implementation of socially responsible terms and necessitates a more unified allegiance from the inception of drug development.

The DevelopAKUre Consortium highlights the possibility for innovation in this space. This consortium is a patient organization-initiated collaboration of patient advocates, industry partners, and academic researchers and clinicians, with the aim of developing nitisinone for the treatment of alkaptonuria (AKU, OMIM no. 203500).²³ Nitisinone has been available as a treatment for hereditary tyrosinaemia type 1 (OMIM no. 276700), a disorder of the tyrosine metabolism similar to AKU, in the United States since 2002 and the EU since 2005.²³ The consortium was essential to the subsequent EU market authorization of this treatment for AKU in 2020 and features some important factors that contributed to its success. These include early interaction with regulators (improving regulatory alignment before trials were executed), the development of an information network parallel to clinical development (expediting timelines and organizing data collection) as well as valorization of the scientific contributions to this project to collect funding.²³

Although the consortium was successful in introducing the first registered medicine for AKU in the EU, a 2021 study found that 20% of treatment centers clinicians reported that nitisinone was not available for prescription to their patients.²⁹ This illustrates that registration does not always equal patient access, which may be related to the product's pricing.⁷ The DevelopAKUre consortium did not include socially responsible terms to secure accessibility, despite extensive public funding (including a nearly €6 million contribution of the European Commission),⁸³ jeopardizing patient access and potentially leading to (excessive) private rewards following public investments. This underlines the importance of incorporating socially responsible terms like transparent pricing agreements to realize the ultimate goal of patient access.

3 | PROPOSING A FRAMEWORK FOR SOCIALLY RESPONSIBLE PPPs AIMED AT TREATMENT DEVELOPMENT FOR RARE DISEASES, INCLUDING INBORN ERRORS OF THE METABOLISM

Increased and integrative academic involvement in PPPs throughout all medicine development stages has the potential to improve treatment development for rare diseases while simultaneously securing patient access goals. The aim of the expansion of academic involvement is to reduce the gap from innovation to successful medicinal product by lowering costs through risk-sharing and the integration of existing scientific knowledge and resources along the development chain. The inclusion of socially responsible terms in these PPPs is imperative to ensure that public contributions to these collaborations ultimately benefit patients and society. To achieve these goals, we propose a framework for establishing such PPPs by defining socially responsible terms for shared data ownership and evidence generation, fast and controlled access, and transparent socially responsible pricing (Table 1, Figure 1).

3.1 | Data ownership and evidence generation

In a PPP, clear agreements should be made to guarantee that (partly) publicly funded academic research outcomes will benefit society, that is, in the form of scientific publications, education, and affordable access to new medicines. To reach this goal, (in)angible assets such as data and knowledge should be available to stakeholders and should be compliant to GDPR regulation and FAIR data principles. This way, joint efforts can benefit scientific advancement as well as regulatory evidence generation, for instance by collaborating through European Reference Networks and ensuring that pivotal trials include scientifically and clinically relevant end-points. Ideally, evidence generation is streamlined via international multipurpose disease registers that can be used for research, marketing approval, reimbursement, and post-marketing evaluation.^{24,25}

3.2 | Socially responsible pricing

The combination of uncertain effectiveness and prices frequently exceeding national reimbursement thresholds, which can negatively impact access.⁷ Since the goal of (partially) publicly funded PPPs should be developing a

TABLE 1 Framework for PPPs under socially responsible terms.

Topic	Socially responsible term
Data ownership and evidence generation	1. Data and other knowledge will be available to stakeholders, while being compliant to the GDPR regulation and FAIR data principles.
Socially responsible pricing	2. Investment and pricing breakdown shall be disclosed. 3. Pricing will be based on actual costs plus a reasonable profit margin. 4. Adaptations will be made after sufficient return on investments. 5. Public revenues will benefit a revolving fund for new projects. 6. Clinical trials at academic centers will be executed for cost price. 7. Marketing activities will be limited to a minimum. 8. Risks will be shared.
Fast access	9. All parties are committed to bringing the product to patients. 10. Termination or pausing of development is prohibited when there is sufficient evidence for patient benefit and a positive business case. 11. Inventions will not be sold to third parties without consent of all stakeholders. If all stakeholders provide consent, selling or out-licensing will only occur on these socially responsible terms.

product that is accessible to patients, there is a clear need for socially responsible pricing. In our view, this means pricing should be transparent and reflect actual costs while maintaining a suitable profit margin for contributing private parties for the entrepreneurial risk taken. When academia and industry partners commit to a project, this should therefore include disclosure of all investments—both public and private—to ensure accountability of pricing via a clear cost breakdown. After sufficient return on investments, adaptations can be made to lower the price. A relevant profit margin to stimulate industry participation should be implemented when reasonable in relation to the entrepreneurial risk taken. The collaboration participants can negotiate a reasonable surplus and accommodate a revolving fund for new projects.

In striving for affordability and access, effort should be made to drastically reduce development costs—which

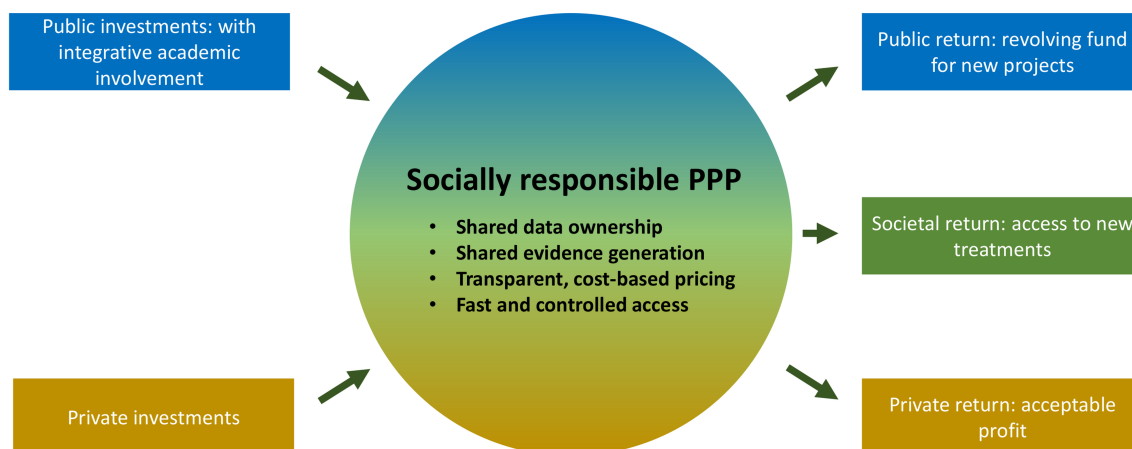


FIGURE 1 Illustration of a framework for a socially responsible PPP. The PPP consists of both public and private investments, including integrative academic involvement. The PPP is built on the socially responsible terms for shared data ownership and evidence generation, socially responsible pricing (via a transparent and cost-based method), and fast and controlled access. This way, society and patients can access new treatments, private returns will follow via an acceptable profit margin, and public rewards will benefit a revolving fund for new projects.

lowers pricing when using a cost-based pricing calculation. Academic partners can contribute to achieving this goal by executing trials at academic centers based on actual costs and industry partners can assist by diminishing marketing activities. Reduced costs also result in a decrease of cost of capital (thus lowering the need for investment capital demanding higher returns). Besides reducing costs, de-risking makes a project more appealing for commercial parties.⁸³ Sharing risks and responsibility further decreases the investment risks and lowers the chance of the project stranding in the valley of death. In conclusion, sharing costs, risks, and rewards can help propel development through the translation phase.

3.3 | Fast access

Medicine development can take notoriously long, with clinical development time spans of ~10 years.⁸⁴ This is especially difficult if no other therapeutic options are available yet—as is the case for many IEMs. To ensure fast development and eventual access to meet these medical needs, all parties should commit to bringing the product to patients as soon as possible. Additionally, termination or pausing the project should not be allowed as long as there is sufficient evidence for clinical benefit as well as a financially manageable project. To protect the social arrangement, transfer or out-licensing of the asset should only be accepted when all parties agree—under the preservation of identical socially responsible terms into the new collaborations.

4 | CONCLUSION

Medicine development for rare diseases has been impeded by long-standing complexities, including the lack of commercial interest to develop medicines for rare diseases, the failure of promising projects in the so-called valley of death and access and reimbursement issues. The effects of these issues are apparent in the field of IEMs, where many unmet medical needs persist due to the lack of treatment options or access.²⁹

Over the past decades, a shift in the traditional model of medicine development has become discernible. Academia-driven initiatives and PPPs are emerging in various medicine development stages with a relatively small number actually realizing the authorization of medicinal products for IEMs.^{23,39,58,85} Recent examples that did not lead to sustainable and equal access for all, such as the Glybera case, highlight the need to include socially responsible terms for patient access in collaborations.^{23,29,39,41,42} A paradigm shift from traditional out-licensing and PPPs solely operating in a single medicine development stage (such as for post-authorization safety studies) to the integrative socially responsible PPP framework that includes terms on data sharing, pricing, and fast access, might be essential to expedite successful and accessible medicine development, especially for rare diseases such as IEMs.

To help realize this, we proposed a framework for PPPs under socially responsible terms, primarily aimed at academics. This can serve as a reference in the establishment of such collaborations to ensure their foundation aligns with public interest. The framework is based on

the crucial elements of (1) data-sharing and evidence generation, (2) socially responsible pricing, and (3) fast access. Practical PPP experience and/or future research can further refine this proposal.

Although this framework is applicable to medicine development for rare diseases in general, the metabolic field may be particularly amenable to this novel approach, as there is ample knowledge in concentrated centers of expertise, frequently equipped with resources such as databases, registries, and biobanks. By valorizing and employing this pre-existing knowledge base as well as strong clinical networks such as the MetabERN network, academic contributions to the development process can be efficiently expanded with the ultimate goal of alleviating persisting unmet medical needs in patients afflicted by IEMs.

CONFLICT OF INTEREST STATEMENT

Noa Rosenberg, Nina N. Stolwijk, Sibren van den Berg is part of the Round table for orphan drugs at the Dutch Healthcare Institute, and Annet M. Bosch have no competing interests to declare. Carla E.M. Hollak is involved in premarketing studies in the field of lysosomal storage disorders with Idorsia and Sanofi for which financial arrangements are made through AMC Research BV. Carla E. M. Hollak is part of the Advisory Committee to the Package, Round table for orphan drugs and Horizonscan medicines at the Dutch Healthcare Institute. Vincent van der Wel is owner of Orfenix B.V. Teun van Gelder received grants from the Dutch Ministry of Health and ZonMw. Teun van Gelder's institution received consulting fees from Aurinia Pharma, Roche Diagnostics, CSL Behring, and Thermo Fisher Scientific and payment or honoraria from Astellas. Teun van Gelder received support for attending meetings and/or travel from Astellas. Teun van Gelder is part of the Dutch Central Committee for Research on Human Subjects. Joris J. Heus has shares of total value less than 50 euros in Pharming N.V. and is a volunteer for Healthy Ideas, Healthy Returns. Saco J. de Visser is part of the Board of Governors of European infrastructure for translational medicine (EATRIS) and board member of the Federation for Innovative Drug Research Netherlands (FIGON).

DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the findings of this study are available within the article.

ETHICS STATEMENT

IRB approval or patient consent was not applicable for this study.

ORCID

Noa Rosenberg  <https://orcid.org/0000-0002-9586-6135>

Sibren van den Berg  <https://orcid.org/0000-0001-8908-3858>

Carla E. M. Hollak  <https://orcid.org/0000-0003-0464-1078>

REFERENCES

1. Nguengang Wakap S, Lambert DM, Olry A, et al. Estimating cumulative point prevalence of rare diseases: analysis of the Orphanet database. *Eur J Hum Genet.* 2020;28(2):165-173. doi: [10.1038/s41431-019-0508-0](https://doi.org/10.1038/s41431-019-0508-0)
2. Regulation (EC) No 141/2000 of the European Parliament and of the Council of December 16, 1999 on orphan medicinal products. 2000. Official Journal L018, p. 1. Accessed December 21, 2022. <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A02000R0141-20190726>
3. European Medicines Agency. Orphan Medicinal Product Designation Overview 2000–2021. Accessed December 7, 2022. https://www.ema.europa.eu/en/documents/other/orphan-medicines-figures-2000-2021_en.pdf
4. European Medicines Agency. Orphan Medicines in the EU. Accessed December 7, 2022. https://www.ema.europa.eu/en/documents/leaflet/leaflet-orphan-medicines-eu_en.pdf
5. Technopolis Group & Ecorys. *Study to Support the Evaluation of the EU Orphan Regulation.* European Commission; 2019.
6. Hudson J, Khazragui HF. Into the valley of death: research to innovation. *Drug Discov Today.* 2013;18(13-14):610-613. doi: [10.1016/j.drudis.2013.01.012](https://doi.org/10.1016/j.drudis.2013.01.012)
7. Detiček A, Locatelli I, Kos M. Patient access to medicines for rare diseases in European countries. *Value Health.* 2018;21(5):553-560. doi: [10.1016/j.jval.2018.01.007](https://doi.org/10.1016/j.jval.2018.01.007)
8. Onakpoya IJ, Spencer EA, Thompson MJ, Heneghan CJ. Effectiveness, safety and costs of orphan drugs: an evidence-based review. *BMJ Open.* 2015;5(6):e007199. doi: [10.1136/bmjopen-2014-007199](https://doi.org/10.1136/bmjopen-2014-007199)
9. KNAW. Efficiency Gains Through Innovation in Medicines Development: How Can Science Contribute? Accessed December 21, 2022. <https://storage.knaw.nl/2022-06/20211005-Advies-Efficiency-through-innovation-web.pdf>
10. Loregian A, Palù G. How academic labs can approach the drug discovery process as a way to synergize with big pharma. *Trends Microbiol.* 2013;21(6):261-264. doi: [10.1016/j.tim.2013.03.006](https://doi.org/10.1016/j.tim.2013.03.006)
11. Silber BM. Driving drug discovery: the fundamental role of academic labs. *Sci Transl Med.* 2010;2(30):30cm16. doi: [10.1126/scitranslmed.3000169](https://doi.org/10.1126/scitranslmed.3000169)
12. van den Berg S, de Visser S, Leufkens HGM, Hollak CEM. Drug repurposing for rare diseases: a role for academia. *Front Pharmacol.* 2021;12:746987. doi: [10.3389/fphar.2021.746987](https://doi.org/10.3389/fphar.2021.746987)
13. Jorgensen WL. Challenges for academic drug discovery. *Angew Chem Int ed Engl.* 2012;51(47):11680-11684. doi: [10.1002/anie.201204625](https://doi.org/10.1002/anie.201204625)
14. Schoenmakers DH, Beerepoot S, van den Berg S, et al. Modified Delphi procedure-based expert consensus on endpoints for an international disease registry for metachromatic leukodystrophy: the European Metachromatic Leukodystrophy Initiative

- (MLDi). *Orphanet J Rare Dis.* 2022;17(1):48. doi:10.1186/s13023-022-02189-w
15. European Medicines Agency. A Vision for Use of Real-World Evidence in EU Medicines Regulation. Accessed February 9, 2023. <https://www.ema.europa.eu/en/news/vision-use-real-world-evidence-eu-medicines-regulation>
 16. Gemeinsamer Bundesausschuss. INTEGRATE-ATMP – Integrierte Versorgung Neuer Therapien durch Telemedizin, Empowerment, Gentherapie, Registeretablierung, Arzneimittelsicherheit, Therapiepfaden und Erstattung. Accessed February 9, 2023. <https://innovationsfonds.g-ba.de/projekte/neue-versorgungsformen/integrate-atmp-integrierte-versorgung-neuer-therapien-durch-telemedizin-empowerment-gentherapie-tika-registeretablierung-arzneimittelsicherheit-therapiepfaden-und-erstattung.510>
 17. Naumann-Winter F, Wolter F, Hermes U, et al. Licensing of orphan medicinal products-use of real-world data and other external data on efficacy aspects in marketing authorization applications concluded at the European Medicines Agency between 2019 and 2021. *Front Pharmacol.* 2022;13:920336. doi:10.3389/fphar.2022.920336
 18. Yassany DM, Anason AP, Barrett DH. Mitigating ethical risks in public-private partnerships in public health. *J Public Health Manag Pract.* 2021;27(4):E177-E182. doi:10.1097/PHH.0000000000001031
 19. Seminara J, Tuchman M, Krivitzky L, et al. Establishing a consortium for the study of rare diseases: the urea cycle disorders consortium. *Mol Genet Metab.* 2010;100:S97-S105. doi:10.1016/j.ymgme.2010.01.014
 20. Ah Mew N, Cnaan A, McCarter R, et al. Conducting an investigator-initiated randomized double-blinded intervention trial in acute decompensation of inborn errors of metabolism: lessons from the N-carbamylglutamate consortium. *Transl Sci Rare Dis.* 2018;3(3-4):157-170. doi:10.3233/TRD-180031
 21. Mofid S, Bolisli WR, Kühler TC. Real-world data in the postapproval setting as applied by the EMA and the US FDA. *Clin Ther.* 2022 Feb;44(2):306-322. doi:10.1016/j.clinthera.2021.12.010
 22. Mütze U, Gleich F, Garbade SF, et al. Postauthorization safety study of betaine anhydrous. *J Inher Metab Dis.* 2022;45(4):719-733. doi:10.1002/jimd.12499
 23. Rudebeck M, Scott C, Rhodes NP, et al. Clinical development innovation in rare diseases: lessons learned and best practices from the DevelopAKUre consortium. *Orphanet J Rare Dis.* 2021;16(1):510. doi:10.1186/s13023-021-02137-0
 24. Hollak CEM, Sirrs S, van den Berg S, et al. Registries for orphan drugs: generating evidence or marketing tools? *Orphanet J Rare Dis.* 2020;15(1):235. doi:10.1186/s13023-020-01519-0
 25. Kölker S, Gleich F, Mütze U, Opladen T. Rare disease registries are key to evidence-based personalized medicine: highlighting the European experience. *Front Endocrinol.* 2022;13:832063. doi:10.3389/fendo.2022.832063
 26. Fagnan DE, Gromatzky AA, Stein RM, Fernandez JM, Lo AW. Financing drug discovery for orphan diseases. *Drug Discov Today.* 2014;19(5):533-538. doi:10.1016/j.drudis.2013.11.009
 27. Bogaerts J, Sydes MR, Keat N, et al. Clinical trial designs for rare diseases: studies developed and discussed by the international rare cancers initiative. *Eur J Cancer.* 2015 Feb; 51(3):271-281. doi:10.1016/j.ejca.2014.10.027
 28. Talele SS, Xu K, Pariser AR, et al. Therapies for inborn errors of metabolism: what has the orphan drug act delivered? *Pediatrics.* 2010;126(1):101-106. doi:10.1542/peds.2009-3246
 29. Heard JM, Vrinten C, Schlender M, et al. Availability, accessibility and delivery to patients of the 28 orphan medicines approved by the European Medicine Agency for hereditary metabolic diseases in the MetabERN network. *Orphanet J Rare Dis.* 2020;15(1):3. doi:10.1186/s13023-019-1280-5
 30. Kort E, Jovinge S. Drug repurposing: claiming the full benefit from drug development. *Curr Cardiol Rep.* 2021;23(6):62. doi:10.1007/s11886-021-01484-5
 31. Sun W, Zheng W, Simeonov A. Drug discovery and development for rare genetic disorders. *Am J Med Genet A.* 2017; 173(9):2307-2322. doi:10.1002/ajmg.a.38326
 32. van Norman GA, Eisenkot R. Technology transfer: from the research bench to commercialization: part 1: intellectual property rights-basics of patents and copyrights. *JACC Basic Transl Sci.* 2017;2(1):85-97. doi:10.1016/j.jacbts.2017.01.003
 33. van Norman GA, Eisenkot R. Technology transfer: from the research bench to commercialization: part 2: the commercialization process. *JACC Basic Transl Sci.* 2017;2(2):197-208. doi:10.1016/j.jacbts.2017.03.004
 34. Leute K. Patenting and licensing of university-based genetic inventions: a view from experience at Stanford University's Office of Technology Licensing. *Community Genet.* 2005;8(4): 217-222. doi:10.1159/000087958
 35. Bains W. How academics can make (extra) money out of their science. *J Commer Biotechnol.* 2005;11(4):353-363. doi:10.1057/palgrave.jcb.3040137
 36. Heus JJ, de Pauw ES, Mirjam L, Margherita M, Michael RH, Michal H. Importance of intellectual property generated by biomedical research at universities and academic hospitals. *J Clin Transl Res.* 2017;3(2):250-259. doi:10.18053/jctres.03.201702.005
 37. Gupta Strategists. The Cost of Opportunity: A Study on Pharmaceutical R&D Costs. Accessed December 15, 2022. <https://gupta-strategists.nl/storage/files/The-cost-of-opportunity-Gupta-Strategists.pdf>
 38. Bryant LM, Christopher DM, Giles AR, et al. Lessons learned from the clinical development and market authorization of Glybera. *Hum Gene Ther Clin Dev.* 2013;24(2):55-64. doi:10.1089/humc.2013.087
 39. Crowe K. The Million-Dollar Drug. CBC News. Accessed December 7, 2022. <https://newsinteractives.cbc.ca/longform/glybera>
 40. Morrison C. \$1-million price tag set for Glybera gene therapy. *Nat Biotechnol.* 2015;33(3):217-218. doi:10.1038/nbt0315-217
 41. Senior M. After Glybera's withdrawal, what's next for gene therapy? *Nat Biotechnol.* 2017;35(6):491-492. doi:10.1038/nbt0617-491
 42. Crowe K. Canadian Breakthrough That Became the World's Most Expensive Drug, Then Vanished, Gets Second Chance CBC News. Accessed February 8, 2023. <https://www.cbc.ca/news/health/glybera-lpld-rare-drug-orphan-disease-nrc-cbc-price-1.5312177>
 43. European Medicines Agency. Guideline on Registry-Based Studies: Draft. Accessed December 21, 2022. <https://www.ema>

- europa.eu/en/documents/scientific-guideline/guideline-registry-based-studies_en.pdf
44. Sirrs SM, Arthus MF, Bichet DG, et al. Independent registries are cost-effective tools to provide mandatory postauthorization surveillance for orphan medicinal products. *Value Health*. 2021;24(2):268-273. doi:10.1016/j.jval.2020.10.006
 45. Malinowski KP, Kawalec P, Trabka W, Sowada C, Pilc A. Reimbursement of orphan drugs in Europe in relation to the type of authorization by the European Medicines Agency and the decision making based on health technology assessment. *Front Pharmacol*. 2018;9:1263. doi:10.3389/fphar.2018.01263
 46. Barney JB, Ketchen DJ, Wright M, McWilliams A, Siegel DS. Creating and capturing value: strategic corporate social responsibility, resource-based theory, and sustainable competitive advantage. *J Manage*. 2011;37(5):1480-1495. doi:10.1177/0149206310385696
 47. Bruyaka O, Zeitzmann HK, Chalamon I, Wokutch RE, Thakur P. Strategic corporate social responsibility and orphan drug development: insights from the US and the EU biopharmaceutical industry. *J Bus Ethics*. 2013;117:45-65. doi:10.1007/s10551-012-1496-y
 48. Nguyen T-Y, Shahzad M, Veras J. Les Nouvelles February 2019 Article of the Month: Recent Experiences in Policy Implementation of Socially Responsible Licensing in Select Universities Across Europe And North America: Identifying Key Provisions to Promote Global Access to Health Technologies. Licensing Executives Society International. Accessed December 7, 2022. <https://www.lesi.org/publications/les-nouvelles/les-nouvelles-article-of-the-month/les-nouvelles-article-of-the-month-february-2019>
 49. Gotham D, Meldrum J, Nageswaran V, et al. Global health equity in United Kingdom university research: a landscape of current policies and practices. *Health Res Policy Syst*. 2016;14(1):76. doi:10.1186/s12961-016-0148-6
 50. NFU. Ten Principles of Socially Responsible Licensing. Accessed December 7, 2022. https://www.nfu.nl/sites/default/files/2020-08/19.4511_Ten_principles_for_Socially_Responsible_Licensing_v19-12-2019.pdf
 51. VLIR. Principles of Socially Responsible Licensing. Accessed December 7, 2022. https://vlir.be/wp-content/uploads/2022/01/02_2021_Principles_of_socially_responsible_licensing.pdf
 52. NFU. Socially Responsible Licensing Toolkit. Accessed December 15, 2022. https://www.nfu.nl/sites/default/files/2020-10/News_MVL-toolkit_27082020NEW2.pdf
 53. NFU. Patent Licence Toolkit. Accessed December 15, 2022. <https://www.nfu.nl/sites/default/files/2020-08/MVLToolkit2020%28pdf%29.pdf>
 54. Reich MR. Public-private partnerships for public health. *Nat Med*. 2000;6(6):617-620. doi:10.1038/76176
 55. Strasser S, Stauber C, Shrivastava R, Riley P, O'Quin K. Collective insights of public-private partnership impacts and sustainability: a qualitative analysis. *PLoS One*. 2021;16(7):e0254495. doi:10.1371/journal.pone.0254495
 56. de Vruhe RLA, de Vlieger JSB, Crommelin DJA. Editorial: public-private partnerships as drivers of innovation in healthcare. *Front Med*. 2019;6:114. doi:10.3389/fmed.2019.00114
 57. Torcel-Pagnon L, Bauchau V, Mahy P, et al. Guidance for the governance of public-private collaborations in vaccine post-marketing settings in Europe. *Vaccine*. 2019;37(25):3278-3289. doi:10.1016/j.vaccine.2019.04.073
 58. Díez-Domingo J, Torcel-Pagnon L, Carmona A, et al. The value of public-private collaborative real-world evidence platforms to monitor vaccine performance post authorization: DRIVE - a European initiative. *Expert Rev Vaccines*. 2022;21(12):1701-1710. doi:10.1080/14760584.2022.2137144
 59. Davis AM, Engkvist O, Fairclough RJ, Feierberg I, Freeman A, Iyer P. Public-private partnerships: compound and data sharing in drug discovery and development. *SLAS Discov*. 2021;26(5):604-619. doi:10.1177/2472555220982268
 60. Laplane A, Mazzucato M. Socializing the risks and rewards of public investments: economic, policy, and legal issues. *Res Policy*. 2020;49S:100008. doi:10.1016/j.repolx.2020.100008
 61. Alperovitz G, Daly L. Who is really 'Deserving'? inequality and the ethics of social inheritance. *Dissent*. 2019;54(4):88-91. doi:10.1353/dss.0.0085
 62. Barr DA. Ethics in public health research: a research protocol to evaluate the effectiveness of public-private partnerships as a means to improve health and welfare systems worldwide. *Am J Public Health*. 2007;97(1):19-25. doi:10.2105/AJPH.2005.075614
 63. Pastakia SD, Tran DN, Manji I, et al. Framework and case study for establishing impactful global health programs through academia - biopharmaceutical industry partnerships. *Res Social Adm Pharm*. 2020;16(11):1519-1525. doi:10.1016/j.sapharm.2020.07.018
 64. Widdus R. Public-private partnerships: an overview. *Trans R Soc Trop Med Hyg*. 2005;99(Suppl 1):S1-S8. doi:10.1016/j.trstmh.2005.06.005
 65. The Mectizan Donation Program. Accessed December 7, 2022. <https://mectizan.org/>
 66. Merck. 35 Years: The Mectizan® Donation Program. Accessed December 7, 2022. <https://www.merck.com/stories/mectizan/>
 67. The Pediatric Praziquantel Consortium. The Pediatric Praziquantel Consortium. Accessed December 22, 2022. <https://www.pediatricpraziquantelconsortium.org/>
 68. The Pediatric Praziquantel Consortium. Vision & Mission. Accessed December 22, 2022. <https://www.pediatricpraziquantelconsortium.org/about-us/vision-mission>
 69. The Pediatric Praziquantel Consortium. Where We Stand. Accessed December 22, 2022. <https://www.pediatricpraziquantelconsortium.org/where-we-stand>
 70. The Pediatric Praziquantel Consortium. Development & Registration Program. Accessed December 22, 2022. <https://www.pediatricpraziquantelconsortium.org/what-we-do/development-and-registration-program>
 71. The Pediatric Praziquantel Consortium. Access Program. Accessed December 22, 2022. <https://www.pediatricpraziquantelconsortium.org/what-we-do/access-program>
 72. Bloom DE, Cadarette D, Ferranna M, Hyer RN, Tortorice DL. How new models of vaccine development for COVID-19 have helped address an epic public health crisis. *Health Aff (Millwood)*. 2021;40(3):410-418. doi:10.1377/hlthaff.2020.02012
 73. Cross S, Rho Y, Reddy H, et al. Who funded the research behind the Oxford-AstraZeneca COVID-19 vaccine? *BMJ Glob Health*. 2021;6(12):e007321. doi:10.1136/bmjgh-2021-007321
 74. University of Oxford. Oxford University Announces Landmark Partnership With AstraZeneca for the Development and Potential Large-Scale Distribution of COVID-19 Vaccine Candidate. Accessed December 7, 2022. <https://www.ox.ac.uk/news/2020-04-30-oxford-university-announces-landmark-partnership-astra-zeneca-development-and>

75. Putzeist M, Mantel-Teeuwisse AK, Wied CC, Hoes AW, Leufkens HG, de Vruet RL. Drug development for exceptionally rare metabolic diseases: challenging but not impossible. *Orphanet J Rare Dis*. 2013;8:179. doi:[10.1186/1750-1172-8-179](https://doi.org/10.1186/1750-1172-8-179)
76. Wood J, Sames L, Moore A, Ekins S. Multifaceted roles of ultra-rare and rare disease patients/parents in drug discovery. *Drug Discov Today*. 2013;18(21-22):1043-1051. doi:[10.1016/j.drudis.2013.08.006](https://doi.org/10.1016/j.drudis.2013.08.006)
77. Litterman NK, Rhee M, Swinney DC, Ekins S. Collaboration for rare disease drug discovery research. *F1000Res*. 2014;3:261. doi:[10.12688/f1000research.5564.1](https://doi.org/10.12688/f1000research.5564.1)
78. Berry SA, Coughlin CR 2nd, McCandless S, et al. Developing interactions with industry in rare diseases: lessons learned and continuing challenges. *Genet Med*. 2020 Jan;22(1):219-226. doi:[10.1038/s41436-019-0616-9](https://doi.org/10.1038/s41436-019-0616-9)
79. Urea Cycle Disorders Consortium. Industry Collaboration Policy and Procedures. 2016.
80. Staton T. The World's Most Pricey Drugs, From a \$1.2M Gene Therapy to a \$450K Lymphoma Med. Fierce Pharma. Accessed February 8, 2023. <https://www.fiercepharma.com/marketing/world-s-most-pricey-drugs-from-a-1-2m-gene-therapy-to-a-450k-lymphoma-med>
81. European Medicines Agency. Post-Authorisation Safety Studies (PASS). Accessed February 9, 2023. <https://www.ema.europa.eu/en/en/human-regulatory/post-authorisation/pharmacovigilance/post-authorisation-safety-studies-pass-0>
82. European Medicines Agency. European Network of Centers for Pharmacoepidemiology and Pharmacovigilance. EUPAS registration number: EUPAS17267. Accessed February 13, 2023. <https://www.encepp.eu/encepp/viewResource.htm?id=30377>
83. Schmidt L, Sehic O, Wild C. EU FP7 research funding for an orphan drug (Orfadin[®]) and vaccine (hep C) development: a success and a failure? *J Pharm Policy Pract*. 2021;14(1):37. doi:[10.1186/s40545-021-00317-8](https://doi.org/10.1186/s40545-021-00317-8)
84. Brown DG, Wobst HJ, Kapoor A, Kenna LA, Southall N. Clinical development times for innovative drugs. *Nat Rev Drug Discov*. 2022;21(11):793-794. doi:[10.1038/d41573-021-00190-9](https://doi.org/10.1038/d41573-021-00190-9)
85. Innovative Medicines Initiative. Europe's Partnership for Health. Accessed February 15, 2025. <https://www.imi.europa.eu/>

How to cite this article: Rosenberg N, Stolwijk NN, van den Berg S, et al. Development of medicines for rare diseases and inborn errors of metabolism: Toward novel public-private partnerships. *J Inherit Metab Dis*. 2023;1-11. doi:[10.1002/jimd.12605](https://doi.org/10.1002/jimd.12605)