Guidance for Searching and Finding Public contributions to pharmaceutical R&D

December 2025

Daniel Fabian
Claudia Wild

This project has received funding from the European Union's Horizon Europe research and innovation programme under Grant Agreement No: 101095593

HTA Austria
Austrian Institute for Health Technology Assessment GmbH

I-PRIX

Guidance for Searching and Finding Public contributions to pharmaceutical R&D

Publication date: December 2025

This report has been written by Daniel Fabian (AIHTA) and Claudia Wild (AIHTA) for the Horizon Europe project Health Innovation Next Generation Payment & Pricing Models (HI-PRIX).

AIHTA

The Austrian Institute of Health Technology Assessment (AIHTA) is the national HTA-unit and publicly funded by public payers (Ministry of Health, Health Funds of the nine Regions and of the Federation of the Social Insurances) of the Austrian healthcare system.

Contact:
Josefstädterstraße 39
1080 Vienna
Austria
Phone: +43(0)1-2368119-0
E-mail: office@aihta.at
Website: https://aihta.at/

HI-PRIX

The HI-PRIX project aims at accelerating access to high-quality, affordable health innovation by fostering the adoption of new pricing and payment models fit to address the challenges posed by high-priced health technologies, in an effort to ultimately balance sustainability of health innovation with sustainability of healthcare systems.

Website: https://hiprixhorizon.eu/

Project Report No. 179: https://eprints.aihta.at/1595

Acknowledgements:

The research took place from January 2023 to December 2025 and sought to analyse public contributions to pharmaceutical research and developments (R&D). Connected to the proposed revision of the European pharmaceutical directive (Article 57) and World Health Assembly (WHA) resolution 72.8 on increasing transparency and to provide governments with recommendations for its future implementation.

Contents

Tables

Figures

Executive summary

The narrative that high drug prices are justified by development costs of up to several billion dollars per approved medicines hides the extensive public investment underlying pharmaceutical innovation.

Despite substantial public investments, including direct funding, clinical trial infrastructure, regulatory support, current pricing mechanisms fail to account for public contributions. This results in taxpayers "paying twice": first through research funding, then through premium drug prices. The absence of standardised reporting enables this warped understanding of innovation, where the pharmaceutical industry is portrayed as the sole inventor while public contributions remain invisible.

This handbook presents the HI-PRIX framework for systematically identifying and documenting public contributions to pharmaceutical R&D across eight categories spanning basic research through post-market evidence generation. Our analysis reveals that the public is not a part of the innovation ecosystem but the main driver of it.

The proposed European pharmaceutical directive's Article 57 represents a critical step toward transparency, but effective implementation requires standardised reporting frameworks, comprehensive tracking systems, and integration of public contribution data into pricing negotiations. Without such systematic transparency, breakthrough therapies will remain increasingly unaffordable despite their fundamental dependence on public investment, threatening healthcare sustainability across Europe and beyond.

Figure 1: Public money at all stages of pharmaceutical development

Abbreviations

AIHTA ..... Austrian Institute for Health Technology Assessment GmbH
AMR ..... Antimicrobial Resistance
ATMP ..... advanced therapy medicinal product
CAR-T ..... chimeric antigen receptor T-cell
CHMP ..... Committee for Medicinal Products for Human Use
COC ..... Cost of Capital
CORDIS ..... Community Research and Development Information Service
CRADA ..... Cooperative Research and Development Agreement
CRO ..... Clinical Research Organisations
DNDi ..... Drugs for Neglected Diseases initiative
EBMT ..... European Society for Bone Marrow Transplantation
EC ..... European Commission
ECRIN ..... European Clinical Research Infrastructure Network
EIB ..... European Investment Bank
EIC ..... European Innovation Council
EISMEA ..... Executive Agency for Small and Medium-sized Enterprises
EFPIA ..... European Federation of Pharmaceutical Industries and Associations
EHDS ..... European Health Data Space
EMA ..... European Medicines Agency
ESMA ..... European Securities and Markets Authority
ERDF ..... European Regional Development Fund (ERDF)
ERN ..... European Reference Networks
FDA ..... U.S. Food & Drug Administration
GDP ..... Gross Domestic Product
HTA ..... Health Technology Assessment
M&A ..... Mergers and Acquisition
INSERM ..... Institut national de la santé et de la recherche médicale
IMI ..... Innovative Medicines Initiative
NIH ..... National Institutes of Health
NMEs ..... New Molecular Entities
OECD ..... Organisation for Economic Cooperation and Development
PDP ..... Public Private Development Partnerships
RoI ..... Return of Investment
RWE ..... Real World Evidence
R&D ..... Research and Development
SEC ..... Security and Exchange Commission
SME ..... Small and Medium-sized Enterprise
WIPO ..... World Intellectual Property Organisation

1. The Challenge of Innovation Pricing in Healthcare

The current pharmaceutical landscape presents a fundamental paradox that increasingly challenges the sustainability of healthcare systems worldwide. While the industry continues to develop novel therapies that promise benefits for patients suffering from previously untreatable conditions, the pricing of these innovations has reached levels that strain even the most robust social security systems. This tension between therapeutic advancement and financial accessibility represents more than a simple market dynamic; it reflects a deeper structural imbalance in how pharmaceutical innovation is conceptualized, financed, and ultimately valued in modern healthcare economies.

The escalation of pharmaceutical prices, particularly for novel therapies targeting rare diseases (orphans), and Advanced Therapy Medicinal Products (ATMPs), has become a defining characteristic of the current innovation ecosystem system [1]. Gene therapies with prices exceeding three million dollars per treatment [2] orphan drugs with annual costs in the hundreds of thousands, and even incremental innovations bearing premium price tags have become commonplace. This pricing trajectory occurs against a backdrop of increasing healthcare expenditure constraints and growing demands. The result is a situation where potentially beneficial therapies remain financially out of reach for many patients who could benefit from them, while healthcare systems face impossible choices between fiscal responsibility and therapeutic access.

The pharmaceutical industry has consistently defended these pricing practices by invoking the substantial costs and risks associated with drug development. Figures suggesting that bringing a new molecular entity to market requires investments ranging from hundreds of millions [3] to several billion dollars [4], with development timelines spanning over a decade and failure rates that doom the vast majority of investigational compounds. The narrative of high risk demanding high reward has become deeply embedded in policy discussions, with the narrative that premium pricing for successful products is necessary to recoup investments not only in those specific therapies but also in the numerous failed attempts that never reach patients.

However, a critical examination of contemporary pharmaceutical business practices reveals a more complex reality that challenges this straightforward narrative. The industry's financial allocations tell a story that diverges significantly from the image of companies primarily focused on reinvesting revenues into research and development (R&D). Share buyback programs, which return capital to shareholders rather than investing in new discoveries, have reached unprecedented levels among major pharmaceutical companies [5]. These financial engineering practices often exceed actual R&D expenditures, raising fundamental questions about corporate priorities and the validity of claims that high prices are necessary to sustain innovation.

The merger and acquisition (M&A) landscape further complicates the traditional understanding of pharmaceutical innovation. Rather than developing new therapies internally through comprehensive research programs, large pharmaceutical companies increasingly operate as acquirers of late-stage assets developed by smaller biotechnology firms, academic institutions, or through public-private partnerships [5]. This "search and development" [6] model, sees major companies purchasing promising compounds after much of the scientific risk has been mitigated, often through publicly funded research [1] . The financialisation of these transactions, where assets change hands multiple times with substantial monetary values increases at each transfer, adds layers of cost that ultimately manifest in final product pricing without necessarily reflecting an additional contribution to the actual innovation or novel pharmaceutical therapies [7].

Perhaps most significantly, the current pharmaceutical innovation ecosystem benefits heavily from public sector contributions that remain largely invisible in pricing discussions. Academic institutions conducting basic research, government grants supporting translational studies, publicly funded clinical trial infrastructure, and tax benefits for research activities all represent substantial public investments in the drug development process [1]. These public contributions extend beyond mere financial support to encompass the entire knowledge infrastructure upon which private sector innovation builds. The phenomenon of "paying twice" [8]– where taxpayers fund the research that enables drug discovery and then pay premium prices for the resulting therapies – has emerged as a central critique of current pricing models.

Understanding this public-private innovation ecosystem requires mapping the complex web of contributions across the entire development pipeline. From the earliest stages of target identification and validation, typically occurring in academic institutions with public funding, through preclinical development often supported by governmental grants and conducted using publicly funded infrastructure, to clinical trials that leverage public hospital systems and patient populations, the public sector's role is pervasive. This extends to the regulatory phase, where public agencies provide scientific advice, expedited review pathways, and market exclusivity provisions that significantly enhance commercial value.

The support mechanisms employed can be broadly categorised as push and pull incentives [9]. Push mechanisms include direct research grants, tax credits for R&D activities, subsidised use of research infrastructure, and support for high-risk early-stage research that private capital typically avoids [10]. Pull mechanisms encompass

extended market exclusivity periods, priority review vouchers, guaranteed purchase agreements, and regulatory flexibility for certain therapeutic categories [9]. These interventions fundamentally alter the risk-reward calculus of pharmaceutical development, yet their value is hardly ever acknowledged in pricing decisions or public discourse about innovation costs.

This introduction sets the stage for a comprehensive examination of these interconnected issues. The following chapters will delve deeper into the empirical evidence surrounding R&D costs, analyse the various forms of public contribution to pharmaceutical innovation, introduce a framework for capturing these contributions, and ultimately propose pathways toward a more equitable and transparent system. The goal is not to diminish the genuine challenges and investments required for pharmaceutical innovation, but rather to develop a more complete understanding of the true ecology of drug development. One that acknowledges all stakeholders' contributions and proposes mechanisms for ensuring that the fruits of collective investment remain accessible to those who need them.

The urgency of addressing these issues cannot be overstated. As therapeutic possibilities expand through advances in genomics, cell therapy, and individualized medicine, the current trajectory of pricing threatens to create a two-tier system where potentially beneficial treatments become only accessible by the wealthy while public health systems struggle to provide potentially disease-altering or disease-alleviating therapies. Resolving this tension requires moving beyond simplistic narratives about innovation costs and actors to engage with the complex realities of modern pharmaceutical development. Only by striving for greater transparency in the interaction between stakeholders can we hope to reshape the social contract in a way that reconciles the legitimate need for incentives for innovation with the fundamental necessity of access to therapies.

2. Deconstructing R&D Economics

The question of how much it truly costs to bring a new medicine to market has become an issue in pharmaceutical policy debates. The academic literature presents a bewildering array of estimates that span from hundreds of millions to several billion dollars per approved drug [1, 11]. This extraordinary variability in cost assessments is not merely an academic curiosity; it fundamentally shapes policy discussions about drug pricing, innovation incentives, and the allocation of public resources. Understanding the sources of this variability and the methodological choices that drive different estimates is essential for any meaningful engagement with questions of pharmaceutical economics and access.

The most frequently cited studies in this domain have emerged from the Tufts Center for the Study of Drug Development, particularly the work of Joseph DiMasi and colleagues [4, 12, 13]. Their longitudinal analyses have documented what appears to be a continuous escalation in development costs over time. The 1991 study estimated capitalized costs at $594 million (in 2022 dollars) [12], rising to $1.368 billion by 2003 [13], and reaching $3.295 billion in the 2016 analysis [4]. This trajectory suggests that drug development costs have increased at rates far exceeding inflation, doubling approximately every decade. Yet these figures stand in stark contrast to other analyses. At the lower end of the spectrum, the Drugs for Neglected Diseases Initiative (DNDi) reports development costs of merely $4-63 million for their portfolio of treatments [3].

The sources of this variability become clearer upon examining the methodological choices embedded in different studies. Cost estimates fundamentally depend on several key parameters: the definition of what constitutes R&D activities, the point at which cost accounting begins, the treatment of failed projects (attrition rates), assumptions about cost of capital (COC), and the time horizons considered. Studies using project-level data [3, 4, 11-24], from confidential industry surveys tend to produce higher estimates than those relying on aggregate financial data [25-28] or a combination of both [29, 30]. The inclusion or exclusion of basic research costs, the treatment of opportunity costs, and assumptions about appropriate discount rates can shift estimates by hundreds of millions of dollars.

Perhaps most critically, the role of attrition rates – the proportion of investigational compounds that fail to reach market approval – serves as a major amplifier of cost estimates. Studies report overall success rates ranging from a pessimistic 0.7% [31] to a more optimistic 34% [29], with profound implications for per-approval cost calculations. However, the literature reveals a troubling opacity around the nature of these failures. None of the cost studies differentiate between scientific attrition (compounds that fail due to lack of efficacy or unacceptable safety profiles) and commercial attrition (projects abandoned for market-related reasons despite technical success) [1]. We have visualized how per product R&D costs are calculated in Figure 2.

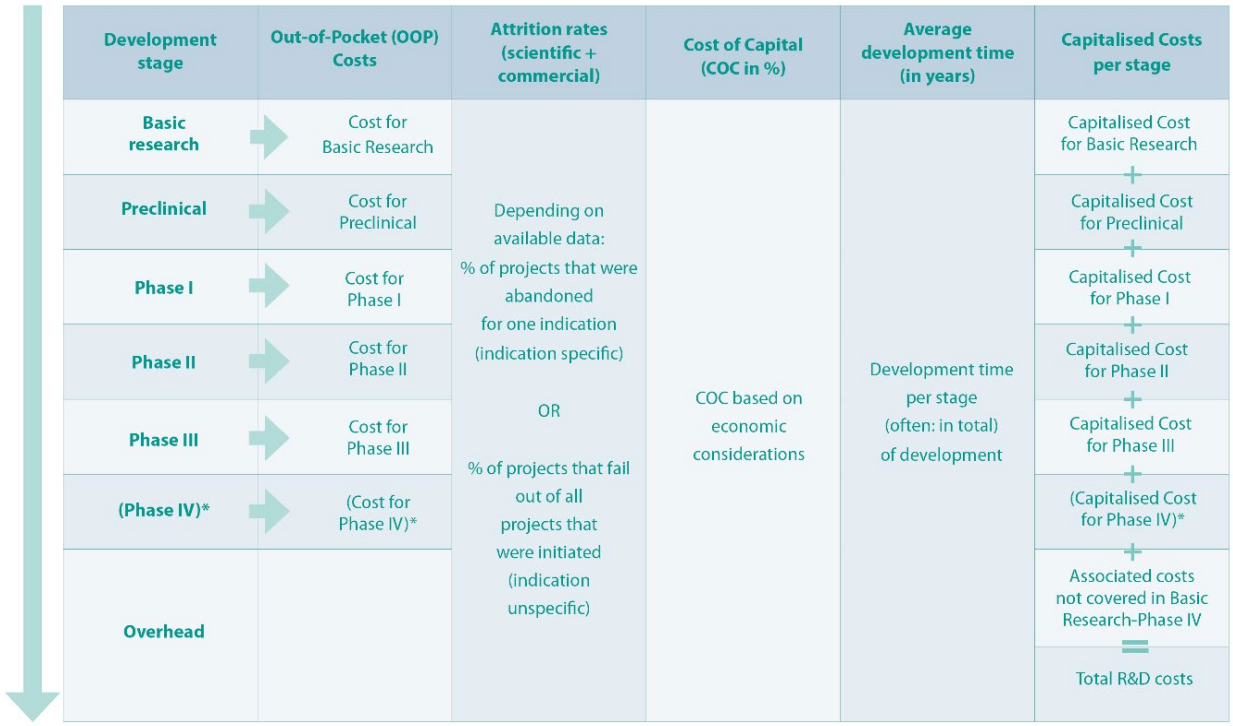

Figure 2: Calculation method of the total R&D costs per product

This distinction is far from trivial. Economic considerations have become an increasingly prominent factor in development decisions [11], with companies terminating programs not because clinical trials have failed but because the anticipated return of investment (RoI) do not justify continued investment. When a company abandons a potentially effective therapy for a disease due to limited commercial prospects, including these costs in estimates for blockbuster drug development creates a distorted picture of the true costs associated with R&D. The conflation of scientific necessity with commercial strategy in cost estimates serves to inflate apparent development costs while obscuring the role of business decisions in shaping therapeutic availability.

The development pathway itself introduces another layer of complexity. The "traditional" model of fully integrated pharmaceutical companies conducting all research internally has given way to a complex ecosystem of licensing, acquisitions, and collaborative arrangements. Research by Cleary et al. shows that every U.S. Food and Drug Administration (FDA)-approved drug between 2000 and 2016 received some form of U.S. public health funding for R&D [32], with development timelines often truncated through strategic partnerships or acquisitions. These externally sourced compounds typically demonstrate higher success rates, partly due to pre-acquisition screening and risk mitigation. Yet cost studies struggle to account for this reality, with some focusing exclusively on self-originated compounds while others attempt to aggregate costs across diverse development models, each with distinct risk profiles and resource requirements.

The fundamental challenge in assessing pharmaceutical development costs lies not only in methodological differences but also in a lack of transparency that prevents independent verification of industry claims. Many cost studies [4, 11-13] rely on proprietary data voluntarily provided by pharmaceutical companies, with researchers bound by confidentiality agreements that prevent disclosure of underlying information. This creates a problem: the primary source of data on development costs comes from entities with clear financial incentives to present high-cost estimates, yet independent researchers lack access to information that would enable critical evaluation of these claims.

The opacity extends beyond simple data availability to encompass definitional ambiguities that complicate any attempt at standardised assessment. The pharmaceutical industry operates without universally accepted definitions of what constitutes R&D expenditure. Activities ranging from basic molecular research to post-marketing studies designed to expand market share may be classified as R&D. The inclusion of M&A costs, licensing fees, and the allocated overhead of corporate operations further decreases reliability of the presented average costs. Tax incentive structures in various jurisdictions create additional motivations for expansive R&D definitions, as these expenditures often qualify for favourable treatment.

Current cost estimation methods suffer from several critical limitations that bias results. The use of aggregate financial data requires researchers to make assumptions about the relationship between total corporate R&D spending and per-product costs, often relying on simple division by the number of approvals without accounting for pipeline composition or development stage distribution. Project-based approaches face the challenge of selection bias, where companies may selectively share data on particularly expensive programs while withholding information on cheaper product developments. The treatment of opportunity costs through capitalization at market rates rather than government borrowing rates can double or triple apparent costs, yet this methodological choice often goes unexamined in policy discussions.

The temporal dimension adds another layer of complexity. Drug development timelines spanning a decade or more mean that cost aggregation must account for changing economic conditions, evolving regulatory requirements, and technological advances that may dramatically alter development economics. Studies analysing drugs approved in 2020 include development costs incurred as early as 2005, yet the relevance of these historical costs to contemporary development decisions remains questionable. The backward-looking nature of cost analyses provides limited insight into current developments or future trends.

Most troublingly, the absence of transparency prevents any meaningful assessment of public contributions to development costs. While industry-sponsored studies meticulously account for private sector investments, they systematically exclude or undervalue public sector contributions ranging from basic research funding to clinical trial infrastructure, regulatory support, and tax incentives. This asymmetric accounting creates an inflated impression of private sector investment while rendering invisible the substantial public resources that enable pharmaceutical innovation. The result is a distorted narrative that serves to justify high prices while obscuring the true ecology of drug development.

The need for comprehensive transparency extends beyond mere data disclosure to encompass standardised reporting frameworks that enable meaningful comparison across companies, therapeutic areas, and development models. Such transparency must include not only direct development expenditures but also the full spectrum of public support received, the rationale for development discontinuations, and the relationship between development costs and pricing decisions. Without such transparency, policy discussions about pharmaceutical innovation and access will continue to rely on incomplete and potentially misleading information, perpetuating a system where claims about development costs serve more as negotiating positions than empirical foundations for evidence-based policy.

The establishment of mandatory, standardised reporting requirements for both public and private R&D investments represent a critical first step toward

meaningful transparency. This must be coupled with independent oversight mechanisms capable of verifying reported information and methodological standards that ensure comparability across different analyses. Only through such systematic transparency can we move beyond the current impasse where wildly divergent cost estimates fuel ideological debates rather than inform practical solutions to the challenge of balancing innovation incentives with therapeutic access. We aim at providing such standardised reporting and have created a framework for assessing public contributions to pharmaceutical R&D.

3. Public Investment in Pharmaceutical Innovation

The landscape of public contributions to pharmaceutical R&D encompasses both direct and indirect forms that operate at all stages of the development path and through various institutional channels.

Public sector contributions include basic scientific research, direct funding mechanisms in forms of grants, scientific infrastructure, technology transfers, human capital development, tax systems, technology transfer units and data systems [33].

3.1 Direct Public Contributions

Basic Research and Knowledge Foundation

At the most basic level, public sector institutions provide the basic scientific knowledge upon which pharmaceutical novelty builds upon. Universities and health research institutes generate the understanding of disease mechanisms, molecular targets, and biological pathways that form the essential foundation for drug discovery. This basic research, while often conducted without immediate commercial applications in mind, creates the knowledge that private sector actors subsequently use for product development.

Direct Funding Mechanisms

Beyond basic science, public contributions work through multiple direct funding mechanisms. Government grants support translational research that bridges the gap between discoveries and potential therapeutic applications. Public institutions fund pre-clinical studies, support early-stage (and increasingly late-stage) clinical trials, and provide resources for proof-of-concept investigations that de-risk projects before private capital becomes interested. Analyses reveal that 42% of all biologicals and up to 90% of drug target research are associated with public sector institutions. For first-in-class drugs with novel targets, public funding amounts to $839 million to $1.44 billion per approval [34].

National funding agencies provide additional support through targeted programs, while public venture capital and innovation support mechanisms offer grants and equity investments for early-stage biotechnology companies.

Infrastructure and Resources

Public hospitals provide clinical trial infrastructure, offering facilities, patient populations, clinical expertise, and research protocols. Academic medical centres maintain research facilities including biobanks, imaging centres, and specialized laboratories. The European Reference Networks (ERNs) for rare diseases provide coordinated clinical networks facilitating patient recruitment and monitoring for orphan drug development [35, 36].

Clinical trial networks like the European Clinical Research Infrastructure Network (ECRIN) reduce costs and complexity while ensuring high-quality data collection [37]. Public investment in health data systems, patient registries, and real-world evidence (RWE) platforms creates resources for target identification through post-market surveillance.

Data infrastructure represents an increasingly critical public contribution as drug development becomes

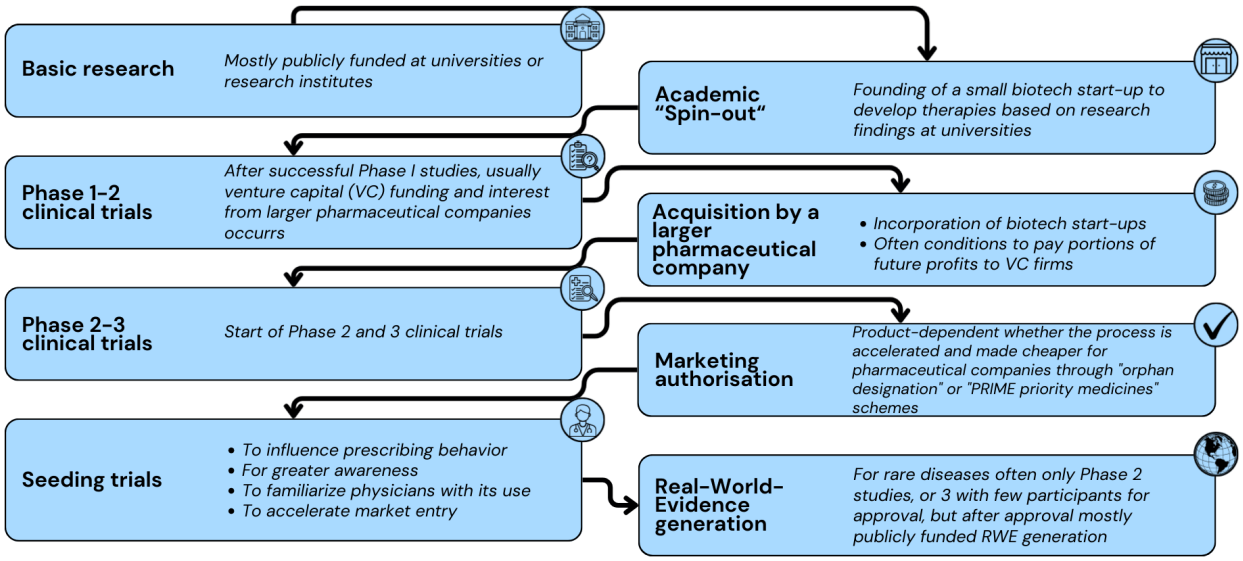

Figure 3: Identified trend of pharmaceutical development pathways

more data intensive. Public investment in health data systems, patient registries, and RWE platforms creates resources that pharmaceutical companies utilise for everything from target identification to post-market surveillance. The European Health Data Space (EHDS) exemplifies efforts to create interoperable data resources that can support innovation while protecting patient privacy, representing a massive public investment in digital infrastructure that will underpin future pharmaceutical development [38].

3.2 Indirect Public Contributions

Academic Environment and Collaboration

Universities provide environments where interdisciplinary collaboration enables cross-pollination of ideas leading to breakthrough discoveries. The relationship between academic research and pharmaceutical development has evolved toward complex arrangements involving ongoing collaboration and joint appointments. Public funding supports both research and institutional mechanisms facilitating productive academic-industry collaboration [38].

Public universities maintain technology transfer offices that identify discoveries, file patents, and negotiate licensing agreements. These offices reduce transaction costs and facilitate commercialization [39]. University spin-offs, supported through public seed funding and incubator programs, advance early-stage discoveries to attract private investment.

Philanthropic-Public Contributions

Philanthropic contributions, while not strictly public funding, often operate in conjunction with government support to advance research in areas of high medical need but limited commercial interest. Disease-focused foundations provide funding for basic research, support young investigators, and sometimes directly fund clinical trials. The interplay between philanthropic and public funding creates synergies, with foundation support often catalysing subsequent government investment or demonstrating proof-of-concept that attracts public funding for larger-scale efforts. The Spinal Muscular Atrophy Foundation's investment of $150 million, complementing public research funding, exemplifies how philanthropic and public contributions combine to enable therapeutic breakthroughs [40, 41].

Human Capital Development

The public sector trains scientists, clinicians, and technical personnel through public education budgets and research grants to doctoral and postdoctoral programs. This creates a skilled workforce upon which pharmaceutical innovation depends, representing a massive public subsidy as companies recruit trained researchers without bearing full education costs.

Regulatory support

The public sector's contribution to pharmaceutical innovation infrastructure extends far beyond the provision of research facilities. Regulatory capabilities, developed and maintained by agencies like the European Medicines Agency (EMA), create frameworks and methodologies that enable efficient drug development and approval. Public investment in regulatory science includes developing guidelines for novel therapeutic modalities, establishing biomarker qualification processes, and creating adaptive regulatory pathways that reduce development timelines and costs. These contributions, while less visible than direct research funding, fundamentally shape the innovation landscape by determining what types of evidence are required and how development programs should be structured.

Furthermore, EMA maintains special programs (PRIME: priority medicines, orphan designation and accelerated approval) which provide regulatory support [42, 43].

Gaps in Existing Evaluation Methods

There is no unanimously agreed upon methodology for evaluating public contributions to pharmaceutical innovation. The temporal dimension poses particular challenges for evaluation, as public contributions may occur decades before commercial products emerge. Basic research conducted in the 1990s may underpin drugs approved in the 2020s, yet accounting methods struggle to trace these long-term connections. The non-linear nature of innovation, where insights from multiple research streams combine in unexpected ways, further complicates attribution of public contributions to specific commercial outcomes. However, these issues can be accounted for when distinguishing research in direct and indirect contributing to the product.

Need for Comprehensive Assessment Tools and Framework

The development of a comprehensive assessment tool for public contributions must address multiple objectives while remaining practically implementable. Such a tool needs to capture as much of the spectrum of public contributions across the development continuum as possible, from basic research through post-market evidence generation- while relying entirely on publicly accessible data. It must accommodate different types of contributions, including financial investments, in-kind support and regulatory facilitation. Assessment frameworks must enable retrospective analysis of public contributions.

Standardization represents a critical requirement for meaningful assessment. Common taxonomies for categorizing public contributions, standardised reporting for-

mats, and consistent definitions would enable aggregation and comparison across different jurisdictions. The framework must be sufficiently flexible to accommodate national variations while maintaining enough structure to permit meaningful analysis.

The proposed European pharmaceutical legislation's requirement for transparency regarding public financial support represents an important step toward systematic assessment, yet significant gaps remain. The focus on direct financial support excludes many important categories of public contribution, while the limitation to individual products misses portfolio effects and shared infrastructure investments. Moving forward, the creation of robust analytical frameworks for assessing public contributions should serve multiple purposes. For policymakers, such tools would enable evidence-based decisions about research funding allocation and the design of innovation incentives. For the public, comprehensive assessment would shine light on the true nature of pharmaceutical innovation as a collective enterprise. For industry, transparent accounting of public contributions could facilitate more productive partnerships while providing factual grounding for pricing and access discussions. In the next chapter we present a framework for systematically searching public contributions for individual products.

4. The HI-PRIX Framework for analysing public contributions to pharmaceutical R&D

The imperative to systematically capture and evaluate public contributions to pharmaceutical R&D has evolved from academic curiosity to policy necessity. As the proposed European pharmaceutical legislation advances toward implementation, with Article 57 mandating disclosure of direct public financial support received for R&D activities, the need for a comprehensive analytical framework becomes increasingly urgent [44]. This chapter presents the HI-PRIX framework structured methodology developed to identify, categorise, and assess the spectrum of public sector contributions to medical novelty across the entire development pathway.

The framework emerges from recognition that existing approaches to documenting public investment suffer from fundamental limitations that obscure the true ecology of pharmaceutical development. While supranational funding agencies such as the EC and the national institutes of health maintain transparent reporting systems, the fragmented nature of national, regional, and institutional contributions creates a mosaic of investment that resists simple aggregation. Moreover, the focus on direct financial transfers fails to capture the extensive infrastructure, human capital, and regulatory support that constitutes much of the public sector's contribution to pharmaceutical innovation. However, such public contributions cannot be attributed to specific products and are excluded in the following framework but not forgotten.

Mapping the Anatomy of Public Investment

The development of any pharmaceutical product proceeds through distinct yet overlapping phases, each characterised by different risk profiles, resource requirements, and stakeholder involvement. Our framework divides this continuum into four primary stages: basic and translational research, early-stage development in biotechnology enterprises, late-stage development in corporate settings, and the market authorization and post-launch evidence generation phase. This temporal segmentation provides the fundament upon which eight categories of public contribution can be systematically mapped and evaluated.

The identification of these categories emerged through an iterative process combining targeted literature review with insights from seventeen stakeholder interviews conducted across the pharmaceutical ecosystem [6]. Representatives from policy advocacy Organisations, pharmaceutical industry associations, public infrastructure providers, non-profit developers, regulatory agencies, and academic institutions contributed perspectives that revealed the multifaceted nature of public support mechanisms. This multi-stakeholder approach proved essential in uncovering contributions that might otherwise remain invisible in traditional accounting frameworks.

Eight Categories of Public Support

1. Basic, Applied, and Translational Research Support

The foundation of pharmaceutical innovation rests upon decades of accumulated scientific knowledge generated primarily through public investment. In 2022, European Union member states devoted 0.74% of GDP (€117.4 billion) to government allocations for R&D, with 35.5% directed to basic research at public universities and an additional 8.3% supporting applied health research [45]. This investment creates the knowledge infrastructure—understanding of disease mechanisms, identification of therapeutic targets, development of research tools—upon which all subsequent pharmaceutical development builds.

The European Framework Programs exemplify the scale and scope of this foundational investment. Framework Programme 7 (2007-2013) contributed €5.6 billion to health-related projects, generating 174 biotechnology projects that yielded 107 patents and 15 spin-off companies. Horizon 2020 (2014-2020) expanded this investment to €9.8 billion, supporting 6,571 projects in personalized medicine, infectious diseases, and digital health transformation. While establishing direct causality between specific public investments and individual products remains methodologically challenging, case studies of orphan drugs and antibiotics demonstrate clear pathways from public research to commercial therapeutics [46, 47].

2. Pre-competitive Applied Research Infrastructure

The Innovative Medicines Initiative and its successor, the Innovative Health Initiative, represent Europe's largest public-private partnership in pharmaceutical research, with combined public contributions exceeding €3.8 billion across three funding periods [48]. These initiatives have generated methodological innovations, practical tools, and research infrastructure that benefit the entire pharmaceutical sector. The European Lead Factory, for instance, created a compound library of 550,000 small molecules available for screening—a resource that individual companies could not economically justify developing independently [49].

3. Technology Transfer and Academic Entrepreneurship

The translation of academic discoveries into commercial development often proceeds through university spin-offs supported by extensive public infrastructure. Technology transfer offices, funded through institutional budgets and often supplemented by public grants, provide the legal, business, and technical expertise necessary to navigate

the complex transition from academic research to commercial viability. Oxford University alone reports generating £2.5 billion in income through its spin-outs since 2010 [50], while Berkeley College of Chemistry received $100 million from a single gene therapy spin-out—figures that suggest both the value of academic innovation and the returns that escape public accounting [51].

4. Business Support and Public Venture Capital

Public institutions increasingly function as direct investors in pharmaceutical innovation, providing capital at critical junctures where private markets prove reluctant or absent. This role extends from early-stage grants for proof-of-concept studies to substantial equity investments in later-stage development, effectively socializing the risks that private venture capital often avoids in high-uncertainty therapeutic areas.

The European Innovation Council exemplifies the public sector's role as venture investor, providing up to €2.5 million in grants for early-stage development and up to €15 million for later-stage projects, with the option to take equity stakes up to 25% in promising companies [52, 53]. National and regional programs offer additional layers of support, from pre-seed funding to growth capital, often in therapeutic areas where private investment proves insufficient. These public venture investments represent high-risk capital deployed where market failures would otherwise prevent development of potentially valuable therapies.

5. Changes in Ownership Architecture

The financialisation of pharmaceutical development—whereby products change hands multiple times with substantial value increases at each transfer—obscures the public sector's foundational contributions. Analysis of the eighteen ATMPs approved in Europe and the United States as of September 2023 reveals that nearly all originated from public research institutions or publicly funded research programs [54, 55]. The escalating valuations through successive ownership changes reflect not additional innovation but rather the progressive de-risking achieved through public investment in clinical development and regulatory science.

6. Clinical Trial Infrastructure and Support

Academic medical centres and public hospitals provide the essential infrastructure for clinical trials, offering not merely physical facilities but access to patient populations, clinical expertise, and established research protocols. While pharmaceutical companies pay per-patient fees, these payments rarely cover the full costs of maintaining specialized facilities, trained personnel, and administrative systems. Analysis of FDA-approved biologics reveals that between 25% [54] and 40% [55] of new drugs received public financial support for late-stage development, with this proportion rising to 80-91% [56, 57] for CAR-T cell therapies when academic sponsorship is considered.

7. Regulatory Science and Market Authorization Support

The development of regulatory frameworks, methodological guidelines, and expedited approval pathways represents a massive public investment in the innovation ecosystem. The EMA budget of €600.2 million (2025), while 91.5 industry-funded through fees, supports the development of regulatory science that fundamentally shapes development strategies across the industry [58]. Priority review designations, orphan drug incentives, and adaptive pathways—all developed and maintained through public investment—can reduce development timelines by years and costs by hundreds of millions.

8. Post-launch Evidence Generation Infrastructure

The shift toward conditional approvals based on limited clinical evidence has created extensive requirements for post-market data collection, largely conducted through publicly funded registries and RWE platforms.
The European Bone Marrow Transplantation CAR-T registry operates with a €12.7 million budget partly derived from public sources, while initiatives like DARWIN EU create the data infrastructure necessary for ongoing safety and efficacy monitoring [60].

We visualized the framework of the eight categories and four stages of development in Figure 4.

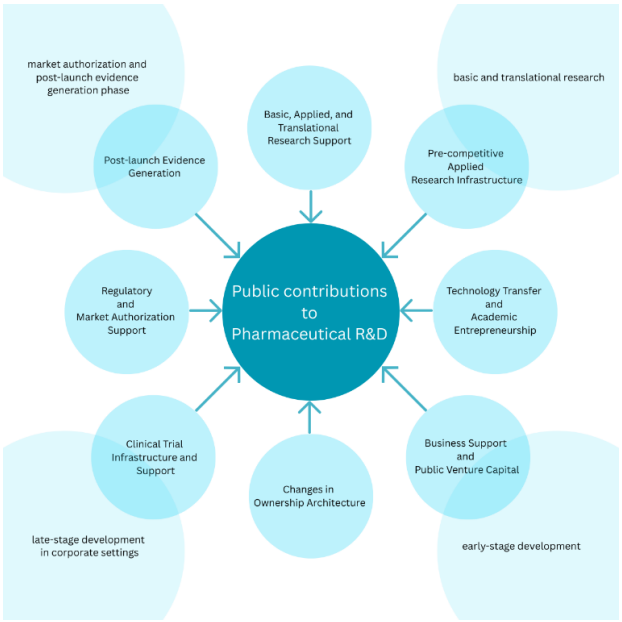

Figure 4: Categories of public contributions and stages of development

Limitations to the framework

The framework focuses on direct research grants while unable to include infrastructure, human capital development, regulatory facilitation, and opportunity costs of public resources. The tendency to examine individual products or programs in isolation misses network effects and knowledge spillovers that amplify the impact of public investment. Furthermore, the framework only counts successful products while ignoring public investment in failed projects that nonetheless generated valuable knowledge or capabilities.

Additionally, the lack of transparency of reporting public contributions in Europe leads to European pharmaceutical contributions being underrepresented. Funding details in Europe often are surface level but often don't report funding amounts.

From Framework to Practice

The transformation of this analytical framework into actionable intelligence requires more than methodological rigor; it demands institutional commitment to transparency and standardization. The absence of universally accepted definitions for R&D expenditure allows both public and private actors to present selective accountings that serve their respective narratives. The pharmaceutical industry's inclusion of M&A costs, licensing fees, and marketing-related studies within R&D budgets inflates apparent development costs, while public sector accounting often excludes indirect support through tax incentives, infrastructure provision, and opportunity costs.

Standardised reporting requirements must encompass both direct and indirect contributions, with sufficient granularity to enable product-specific analysis while protecting legitimate commercial confidentiality. The framework must be flexible enough to accommodate diverse national contexts while maintaining sufficient structure to permit meaningful comparison and aggregation. Integration with existing reporting systems, rather than creation of entirely new requirements, could facilitate adoption while minimizing administrative burden.

The systematic application of this framework reveals pharmaceutical innovation as fundamentally dependent on public investment across multiple dimensions. From the basic science that identifies therapeutic targets through the clinical infrastructure that enables definitive testing, public contributions permeate every aspect of drug development. This reality challenges the prevailing narrative of pharmaceutical companies as primary risk-takers deserving unlimited returns on their investments.

For policymakers, comprehensive assessment of public contributions enables evidence-based decisions about appropriate pricing, access provisions, and benefit-sharing arrangements. The framework provides the analytical foundation for implementing "fair pricing" principles that acknowledge public investment while maintaining incentives for continued innovation. It supports the development of contractual mechanisms—such as reasonable pricing clauses, profit-sharing arrangements, and public rights in intellectual property—that ensure public return on public investment.

The urgency of implementing such frameworks extends beyond individual products to the sustainability of the entire innovation ecosystem. As therapeutic possibilities expand through advances in genomics, cell therapy, and personalized medicine, the current trajectory of pricing threatens to create a system where breakthrough treatments remain accessible only to the wealthy while public health systems struggle to provide basic care. The HI-PRIX framework offers a pathway toward rebalancing this equation, providing the transparency necessary for informed negotiation and equitable access.

Yet the framework's ultimate value depends not on its analytical sophistication but on the political will to employ it. Without commitment from both public authorities and private companies to engage with the full complexity of pharmaceutical innovation, transparency requirements risk becoming mere compliance exercises rather than catalysts for systemic change. The challenge lies not in documenting public contributions—the evidence is overwhelming—but in translating this evidence into policies that recognize pharmaceutical innovation as the collective enterprise it has always been.

5. Evidence Collection and Analysis

This chapter presents a structured framework for evidence collection that moves from the initial characterization of pharmaceutical products through progressively detailed investigations of public sector involvement across multiple jurisdictions and institutional levels. The following tables include relevant Organisations, databases etc. and are not exhaustive.

Establishing the Product Foundation

The investigation of public contributions begins with establishing a comprehensive profile of the pharmaceutical product under examination. This foundational work requires using the EMA or FDA database to extract essential regulatory and therapeutic characteristics. The approval status, including any revocations or positive Committee for Medicinal Products for Human Use (CHMP) opinions, provides initial context for understanding the product's development. The therapeutic classification system, which encompasses medical specialty, pharmacotherapeutic group, and therapeutic area, offers insights into the likely research pathways and funding that may have supported development.

Special regulatory designations must be included as they often correlate with specific public support mechanisms. Orphan medicine status, for instance, typically indicates eligibility for various public incentives designed to address market failures in rare disease drug development. Similarly, accelerated assessment or PRIME (Priority Medicines) designation suggests recognition of significant public health need, often accompanied by enhanced regulatory support and potentially increased public sector interest in the product's development. Furthermore, ATMPs and orphan drugs tend to receive substantial public contributions.

Table 1: Marketing Authorization Authorities

Marketing Authorization Organisation	Link
EMA	https://www.ema.europa.eu/
FDA	https://www.fda.gov/

The identification of all product designations represents a critical early step that enables comprehensive searching across databases and repositories. Pharmaceutical products typically accumulate multiple identifiers throughout their development journey, from initial alphanumeric research codes through International non-proprietary names to eventual brand names. Databases from AdisInsight or the International Horizon Screening Initiative (IHSI) provide consolidated listings of these alternative designations, which prove essential for tracking products across their often decades-long development trajectories. The failure to identify all relevant nomenclature can result in significant gaps in the evidence base, particularly when products have changed ownership.

Table 2: Product Identification

Database to identify all product identifiers	Link
AdisInsight	https://adisinsight.springer.com/
IHSI	https://ihsi-horizonscandb.ecri.org/

Mapping the Scientific Literature and Clinical Development Landscape

Scientific publications provide insight in institutional involvement and funding relationships throughout the development process and the conflict-of-interest statements in the studies. Searches of medical databases, particularly PubMed, using all identified product names reveal involvement of academic and public sector. The institutional affiliations of authors on key publications often reveal a complex development story. When academic institutions or publicly funded research centres appear prominently in early publications, this typically indicates substantial public sector contributions to basic research.

The clinical trials registry ecosystem offers complementary insights into the practical development pathway and associated funding streams. The ClinicalTrials.gov database, maintained by the U.S. National Library of Medicine, provides standardised reporting of trial sponsors, collaborators, and funding sources for studies conducted globally. This resource proves particularly valuable for identifying public sector involvement in pivotal trials that may have been sponsored by commercial entities but conducted using public infrastructure or with public co-funding. The European Union Clinical Trials Register and its successor, EU Clinical Trials Information System (CTIS), provide similar data for trials conducted within European jurisdictions, though with varying levels of detail regarding funding arrangements.

The World Health Organisation's International Clinical Trials Registry Platform (ICTRP) aggregates data from national and regional trial registries worldwide, providing a global perspective on product development that may reveal public contributions from non-traditional sources. This proves particularly valuable for products developed through international collaborations or those targeting diseases of particular relevance to low- and middle-income countries, where public and philanthropic funding often plays a dominant role.

Patent databases offer another crucial dimension of evidence, revealing both the intellectual property landscape and potential public sector contributions to foundational innovations. The World Intellectual Property Organisation (WIPO) Patent Database, google patents and the

Orange Book database maintained by the FDA provides detailed patent information for approved products, including composition, method of use, and process patents. Analysis of patent assignees and inventors can reveal academic institutions or public research Organisations that contributed to key innovations, even when these contributions have been subsequently licensed or acquired by commercial entities.

Table 3: Clinical Trial registries

Clinical Trial registries and patent databases	Link
PubMed	https://pubmed.ncbi.nlm.nih.gov/
NIH Clinicaltrials.gov	https://clinicaltrials.gov/
EU Clinical Trials Information System (CTIS)	https://euclinicaltrials.eu/
EU Clinical Trials Register	https://www.clinicaltrialsregister.eu
International Clinical Trials Registry Platform (ICTRP)	https://trialsearch.who.int/
FDA Orange Book	https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm
World Intellectual Property Organisation (WIPO) Patent Database	https://patentscope.wipo.int/search/de/search.jsf
Google Patents	https://patents.google.com/

Corporate Documentation and Strategic Intelligence

Company websites and corporate communications, while requiring critical evaluation for promotional content, provide valuable insights into development partnerships and funding relationships. The news sections of company websites often contain press releases announcing grants, collaborations with academic institutions, or participation in public-private partnerships. These announcements, particularly when cross-referenced with other sources, can reveal public contributions that may not be captured in scientific databases.

When products have been acquired or licensed rather than developed internally, investigation must extend to previous owners and development partners. This "archaeological approach" to corporate history often reveals layers of public investment that become obscured through subsequent commercial transactions. Small biotechnology companies that originated as university spin-offs, for instance, may have benefited from substantial public investment before being acquired by larger pharmaceutical companies. These earlier contributions remain relevant to understanding the full public investment in the final product, even when separated by multiple ownership changes.

Publicly traded firms, regardless of their sector, have an obligation to, depending on the jurisdiction, publish reports quarterly or annually. They include a comprehensive business overview, financial updates, major events or changes and proxy statements (Shareholder meeting info and executive compensation). This ensures transparency, helping investors make informed decisions about public companies. These reports provide information of acquisitions, licensing agreements with milestone payments etc. and are a valuable source of information when identifying public contributions.

Table 4: Corporate communication and market regulators

Corporate Communications and regulators for markets	Link
Originator and Developer Company	n.a.
U.S. Securities and Exchange Commission	https://www.sec.gov/
European Securities and Markets Authority	https://www.esma.europa.eu/

Public Funding Authorities: Supranational, national, regional and local

Supranational Mechanisms

The EU's research and innovation funding architecture represents one of the world's largest sources of public support for pharmaceutical development. Specialized European agencies provide targeted support for different stages of pharmaceutical development. The European Institute of Innovation and Technology, through its Health Knowledge and Innovation Community, supports entrepreneurship and innovation in life sciences, including pharmaceutical development. The Executive Agency for Small and Medium-sized Enterprises (EISMEA) administers various programs supporting biotechnology companies, often providing crucial early-stage funding for innovative pharmaceutical development. The European Innovation Council offers both grants and equity investments for breakthrough innovations, including novel therapeutic approaches, while the European Investment Bank provides loans and guarantees for life sciences companies, representing a form of public support through favourable financing terms.

The CORDIS database, documenting European Union research and development projects, represents an essential resource for identifying public contributions. This repository captures not only direct product development support but also platform technologies, methodological innovations, and basic research that may have enabled subsequent pharmaceutical development. The temporal scope of CORDIS, spanning multiple Framework Programmes, allows researchers to trace public investments that may have occurred years or even decades before product approval.

The Innovative Medicines Initiative and its successor, the Innovative Health Initiative, explicitly structure public-private partnerships in pharmaceutical research, with public funds from the EU matched by industry contributions. While these initiatives emphasize their leveraging of private investment, the public contribution often extends beyond direct funding to include access to public research infrastructure, patient populations, and regulatory expertise.

Table 5: Supranational public contributors

Supranational public contribution institution/ Organisation	Link
EU Community Research and Development Information Service	https://cordis.europa.eu/
Horizon Europe/ Horizon 2020/	https://research-and-innovation.ec.europa.eu/funding/funding-opportunities/funding-programmes-and-open-calls/horizon-europe_en /https://wayback.archive-it.org/12090/20220124075100/https:/ec.europa.eu/programmes/horizon2020/
Executive Agency for Small and Medium-sized Enterprises (EISMEA)	https://eismea.ec.europa.eu/index_en
European Investment Bank (EIB)	https://www.eib.org/
European Innovation Council (EIC)	https://eic.ec.europa.eu/
Innovative Medicines Initiative (IM)	https://www.ihi.europa.eu/
European Regional Development Fund (ERDF)	https://ec.europa.eu/regional_policy/funding/erdf_en

National Funding Landscapes

All EU member states provide varying forms of funding for the pharmaceutical industry. The EC Competition website documents such state aid decisions that may include support for pharmaceutical development, particularly for companies developing products addressing significant public health needs. These decisions often contain detailed information about the nature and extent of public support, including both direct grants and purchase agreements.

National funding systems exhibit considerable diversity in structure, scope, and transparency, necessitating country-specific investigation strategies. The United States maintains perhaps the most transparent and comprehensive system for tracking public biomedical research investments through the National Institutes of Health RePORTER database. This system allows detailed searches linking specific products or companies to federal research support, often revealing decades of cumulative public investment underlying supposedly private sector innovations. The Small Business Innovation Research and Small Business Technology Transfer programs provide additional support specifically designed to bridge academic research and commercial development, with detailed award information publicly available.

The clinical trial infrastructure maintained by academic medical centres and public hospitals represents a massive public subsidy to pharmaceutical development. While companies typically pay per-patient fees for trial participation, these payments rarely cover the full costs of maintaining the specialized facilities, trained personnel, and administrative systems required for clinical research. The existence of this infrastructure, built and maintained primarily through public healthcare and research budgets, enables the clinical development that constitutes the most expensive phase of bringing new medicines to market.

The United Kingdom's research funding landscape, coordinated through UK Research and Innovation, encompasses multiple research councils with distinct but overlapping remits in biomedical research. The Medical Research Council provides traditional research grants, while Innovate UK focuses on translational and commercial development support. The UK system demonstrates particular strength in supporting early-stage biotechnology companies through various schemes that combine grant funding with business development support.

Continental European countries maintain diverse approaches to pharmaceutical research support, often combining national programs with regional initiatives. To name a few examples, Germany's federal research ministry coordinates multiple funding streams accessible through the centralized Förderkatalog portal, though additional support may flow through state-level programs and specialized agencies. France combines direct research funding through institutions like Institut national de la santé et de la recherche médicale (INSERM) with substantial tax incentives for research and innovation, creating a complex landscape of public support that requires investigation across multiple administrative levels. The Netherlands coordinates life sciences innovation support through Health~Holland, a public-private partnership that exemplifies the Dutch approach to strategic sector development.

In our studies we found national funding authorities as well as websites documenting them and have grouped them in Table 6, however this list is not exhaustive and other national funding authorities for the countries listed may exist.

Table 6: National funding authorities

Country	Funding authority + website
USA*	https://www.sbir.gov/ https://reporter.nih.gov/ https://www.nsf.gov/
UK*	https://www.ukri.org/
Canada*	https://www.nserc-crsng.gc.ca/ase-oro/index_eng.asp
China*	https://english.cas.cn/
Austria	https://www.ffg.at/
Belgium	https://www.frs-fnrs.be/fr/
Bulgaria	https://www.chistera.eu/bnsf https://fni.bg/
Croatia	https://hrzz.hr/ https://mzom.gov.hr/
Cyprus	https://www.research.org.cy/
Czechia	https://gacr.cz/en/ https://tacr.gov.cz/
Denmark	https://innovationsfonden.dk/da
Estonia	https://etag.ee/ https://eis.ee/
Finland	https://www.aka.fi/ https://www.businessfinland.fi/suomalaisille-asiakkaille/etusivu
France	https://www.bpifrance.com/ https://www.inserm.fr/en/home/ https://entreprendre.service-public.fr/vosdroits/F35494#:~:text=Le%20cr%C3%A9dit%20d'imp%C3%B4t%20innovation,PME%20%3A%20Petite%20et%20moyenne%20entreprise%20
Germany	https://foerderportal.bund.de/ https://www.foerderdatenbank.de/FDB/DE/Home/home.html
Greece	https://www.elidek.gr/
Hungary	https://nkfih.gov.hu/palyazoknak https://mta.hu/
Ireland	https://www.ucc.ie/en/apc/
Italy	https://www.aifa.gov.it/ https://www.cnr.it//
Latvia	https://www.lzp.gov.lv/lv
Lithuania	https://mita.lrv.lt/
Luxembourg	https://www.lih.lu/de/
Malta	https://xjenzamalta.mt/
Netherlands	https://www.health-holland.com/.
Poland	https://ncn.gov.pl/en https://www.gov.pl/web/ncbr
Portugal	https://www.fct.pt/ https://ani.pt/
Romania	https://uefiscdi.gov.ro/
Slovakia	https://www.apvv.sk/ https://www.sav.sk/
Slovenia	https://www.gov.si/
Spain	https://www.isciii.es/en/ https://www.cdti.es/
Sweden	https://www.vr.se/ https://forte.se/ https://www.vinnova.se/

*in colour highlighted fields are non-European countries with significant pharmaceutical industry/ research capabilities

Regional and Institutional Contributions

Sub-national public contributions often escape systematic documentation despite their potential significance in pharmaceutical development. Regional governments, particularly in strong federal systems, may provide substantial support through economic development programs, research infrastructure investments, or tax incentives designed to attract life sciences companies. The European Regional Development Fund channels significant resources through regional authorities for innovation support, including pharmaceutical development, yet these contributions rarely appear in product-level analyses of public investment.

Philanthropic and Hybrid Funding Models

There are two types of philanthropic funders: either a foundation that funds relevant research or indication/ disease specific foundations. Foundations like the Gates Foundation have a set of rules for funding that need to be met to receive funds instead of being disease- specific.

Major disease-focused foundations often co-fund research with government agencies, creating synergistic investments that accelerate therapeutic development. These partnerships prove particularly important in areas of high medical need but limited commercial interest, such as neglected tropical diseases or rare paediatric conditions.

Organisations like the Drugs for Neglected Diseases Initiative operate through complex funding arrangements combining governmental support, philanthropic contributions, and in-kind contributions from both public institutions and private companies. These models challenge traditional categorizations of public versus private investment while demonstrating the essential role of public and philanthropic funding in addressing market failures in pharmaceutical development.

Table 7: Philanthropic funders

Philanthropic or not-for-profit Organisation	Link
Gates Foundation	https://www.gatesfoundation.org/
DNDi	https://dndi.org/
Fisevi	https://fisevi.com/en/home/
The Mark Foundation for Cancer Research	https://themarkfoundation.org/
The Jon Moulton Charity Trust	https://www.perscitusllp.com/moulton-charity-trust/

Media and Alternative Intelligence Sources

The pharmaceutical press and investment media provide documentation of funding announcements, partnership formations, and strategic developments that may not yet appear in academic or regulatory databases. Specialized publications maintain extensive archives that can reveal funding relationships, particularly for products in active development. These sources prove particularly valuable for understanding recent developments and emerging funding trends that will only appear in official databases after considerable delay.

General news media occasionally report on significant public investments in pharmaceutical development, particularly when these involve large sums or politically sensitive disease areas. While requiring careful

verification, media reports can provide leads to public contributions that might otherwise escape notice, particularly those involving regional or novel funding mechanisms.

Table 8: News outlets/ Investor news

News Outlet	Link
Forbes	https://www.forbes.com/
Reuters	https://www.reuters.com/
Science	https://www.science.org/
cafepharma	https://www.cafepharma.com/
Livescience	https://www.livescience.com/
BioSpace	https://www.biospace.com/
BioWorld	https://www.bioworld.com/
BioPharma Dive	https://www.biopharmadive.com/
pharmaphorum	https://pharmaphorum.com/
PharmaTimes	https://pharmatimes.com/
Pharmafile	https://pharmafile.com/
Fierce Pharma	https://www.fiercepharma.com/
Fierce Biotech	https://www.fiercebiotech.com
BioCentury	https://www.biocentury.com
businesswire	https://www.businesswire.com/
Business Insider	https://www.businessinsider.com/
STAT news	https://www.statnews.com/
yahoo!finance	https://finance.yahoo.com
GlobeNewswire	https://www.globenewswire.com
La Presse	https://www.lapresse.ca
Newswire	https://www.newswire.ca/

Quality Assurance and Synthesis

The synthesis of evidence from these diverse sources requires systematic Organisation and critical evaluation. The application of the standardised categorization framework enables comparison across products and identification of patterns in public contribution.

The development of artificial intelligence offers both opportunities and challenges for comprehensive evidence collection. These systems can rapidly scan vast quantities of text to identify potential funding relationships or institutional connections that might escape manual review. However, current systems may mistake similar-sounding entities, misinterpret company structures, or generate plausible but fictitious funding arrangements. At the current state of AI, we strongly discourage the use of it in identifying public contributions.

The robustness of our analytical framework has been validated through systematic application across diverse pharmaceutical products and company portfolios, enabling both verification of its comprehensiveness and identification of areas requiring refinement. Our initial testing on orphan drugs and vaccines revealed the framework's capacity to capture public contributions across the full development spectrum, though it highlighted the need for greater granularity in distinguishing between direct research grants and indirect infrastructure support. For details of five analysed products see Appendix 1. The analysis of antibiotics development through SMEs proved particularly valuable in refining our categorization system, as it revealed the prominence of public-private partnerships and regional funding mechanisms that required addition as distinct categories within the framework [46].

Application to major pharmaceutical company portfolios provided critical insights into the framework's scalability and consistency. The examination of Novartis and Novo Nordisk products approved between 2014 and 2024 demonstrated that the framework could effectively capture public contributions regardless of whether products were developed in-house or acquired [59]. This comparative analysis necessitated expansion of the "changes in ownership" category to better account for the complex pathways through which publicly funded innovations transition to private control via licensing agreements, acquisitions, and spin-out formations.

Through iterative application across these varied contexts, we identified consistent gaps in capturing late-stage public contributions, particularly regulatory support and post-market evidence generation infrastructure. Each case study contributed methodological refinements: the antibiotics analysis expanded our source identification protocols to include investor communications, the company portfolio studies revealed the importance of tracking university technology transfer offices, and the ATMP investigations highlighted the need to trace multi-generational ownership changes. This progressive refinement through empirical testing has produced a framework that maintains structural consistency while accommodating the full complexity of modern pharmaceutical development pathways.

Experience from the evidence collection process reveals the pharmaceutical innovation system as fundamentally dependent on public investment across all stages of development. From the basic science that identifies therapeutic targets through the clinical infrastructure that enables definitive testing, public contributions are in every aspect of drug development. The challenge lies not in finding evidence of public contribution but in systematically documenting and valuing these contributions in a manner that can inform policy discussions and price negotiations about appropriate pricing, access provisions, and benefit sharing arrangements. Only through comprehensive evidence collection can we move beyond simplistic narratives about pharmaceutical innovation to engage with the complex reality of drug development as a fundamentally collective enterprise requiring and deserving collective benefit.

6. From Local Investment to Global Pricing

Bridging Geographic Disparities to Facilitate Impact on Price Negotiations

The analysis of public contributions to the development of medical products as a field of research began about a decade ago and has gained momentum in recent years [60]. However, until now, a standardised methodology has been lacking. Our research aimed to address this issue by providing a structured and systematic framework for data collection [6, 46]. First, we divided product development into phases. With the help of targeted interviews with experts in the field, we then searched the published literature for categories of public contributions. We identified eight categories, including both direct and indirect public funding.

While supranational funding organisations (e.g. the EC and the NIH) report their R&D expenditure transparently, national expenditure data is not available in such a structured form (i.e. funding recipient, expenditure type and amount). The lack of standardised reporting on public R&D spending and its results, measured in key performance indicators (KPIs) such as patents, licences, sales and revenue, is part of the problem of opacity that the pharmaceutical industry exploits to perpetuate the myth that it is the sole innovator and spends vast sums on R&D.

This lack of a systematic approach to reporting on public and private investments makes it difficult to shed light on the respective (private and public) contributions to innovation and to quantify the opportunity costs of risky public investments, especially in early-stage research. While new price records for the most expensive drugs are broken every year, the public sector lacks sufficient data to substantiate direct and indirect public contributions to basic, applied, and translational research, as well as methodological research to achieve lower prices in negotiations.

Our findings demonstrate how product development works in practice, primarily through research partnerships with public research institutions and small biotech start-ups. Large pharmaceutical companies have access to a high level of 'business intelligence', such as patent scouts who support key decisions regarding the purchase of promising product developments. Pharmaceutical companies compensate researchers based on defined milestones. Globally active pharmaceutical companies then take responsibility for final approval and market launch.

The public sector can learn from this 'business intelligence'. Investing in the International Horizon Scanning Initiative (IHSI, https://ihsi-health.org/) and supporting “fair pricing” [61-63] through data is a step towards increasing public 'business intelligence'.

There is ample evidence of public and philanthropic contributions to drug development, and the need for transparent reporting is clear. It is crucial to have a coordinated public policy that promotes transparency in R&D investments across geographical jurisdictions. Some countries, such as Italy, France, Japan [64] and, more recently, Austria [65], are pioneering the implementation of transparency requirements.

The development history and public contributions to every new (high-priced) drug seeking reimbursement must be disclosed. However, implementation remains ineffective without clear definitions of direct versus indirect contributions or sanctions for violations. Effective implementation requires transparent data on direct public contributions leading to products, as well as high-quality information on indirect funding, including tax breaks, preliminary work, and contributions to methodology, tools, and techniques, such as big data processing, databases on target molecules, and CRISPR gene editing.

Last but not least, it is crucial to communicate using the same vocabulary. While the private sector talks about venture capital, 'sunk costs' for abandoned or failed projects, and the cost of capital, these technical terms are never used for public investments, even though they are equally valid.

Exploring Policy Options to Unlock the Potential of Increased Transparency and Accountability: Recommendations.

There is a great deal of scepticism that the call for greater transparency in development spending is merely a political statement with no tangible effect. In order to address this justified scepticism surrounding the lack of practical implications, and therefore the lack of relevance, of the proposed reporting system, we would also like to present some ideas and suggestions.

Rather than asking why we need to consider public contributions, we should be asking how we can capture the considerable public funds, especially from European and American public institutions. The proposed directive sets out the transparency requirements. However, the conditions that enable verification and monitoring are currently insufficient. As shown here, though, indirect public contributions are just as relevant as direct ones.

- **Uniform reporting on public contributions** for R&D and innovation support from local, regional, national and supranational agencies is necessary to verify the information provided by the pharmaceutical industry. A website with easily accessible information on all direct subsidies is needed at the national and EU levels. This standardised disclosure of all public and

non-profit contributions must also cover the **results from university spinouts sold** to industry or to companies´ spin-offs, thus enabling more detailed insights into the subsidised projects and their return on investment. All licence agreements, patent sales, M&A and collaborations between universities and pharmaceutical companies must be disclosed.

- The need to set up **a monitoring and control system** in the EMA and to reflect on sanctions in cases when the rules of Article 57 are violated or ignored (e.g. clock stop of approval procedure) is obvious as is the establishment and strengthening of national transparency laws to further implement Art 57 on the national level.
- To date, only a few countries have introduced **transparency requirements for reimbursement applications** [64]. However, these remain voluntary as long as no sanctions, such as deferrals until data is submitted, are imposed. Compliance with these requirements will become mandatory due to the implementation of the new EU Medicines Regulation. It can be assumed that other countries will also want to **use the information in price negotiations**.
- Similar to the **exchange of experiences** on Managed Entry Agreements (MEAs), an exchange of experiences should be organised as “communities of practice” to accelerate the operationalisation of the transparency clause.

As the pharmaceutical industry has so far declared its expenditure without a standardised definition of R&D, a definition that can be applied universally is necessary to compare public and private R&D expenditures. The Organisation for Economic Co-operation and Development's (OECD) Frascati Manual provides a broad definition of R&D as 'creative and systematic work undertaken to increase the stock of knowledge, including knowledge of humanity, culture and society, and to devise new applications of available knowledge' [66].

- **Binding requirements** for R&D reporting in industry, with clearly defined inclusion and exclusion criteria, are recommended to improve comparability between public and private R&D expenditure. A clarification is needed whether the purchase of knowledge through M&A or licensing costs can be declared as R&D expenditure [59], or whether 'seeding trials' to increase market share are considered R&D.
- The development of **a methodology is a public-private endeavour** to arrive at transparent calculations of R&D incorporating cost-drivers, capital costs, and scientific failure (attrition) rates. DNDi can function as role model and starting point [67]. These R&D reports must be publicly available: those provided by pharmaceutical companies must be made accessible to the public in a format that allows the data to be easily filtered and edited, making it easier for users/researchers to download, analyse and review the files.

It is necessary to have detailed contractual options for the conditions and requirements for public funding of R&D [68]. The conditions attached to public contributions have not been given sufficient consideration and must be addressed as a key policy measure.

- **Contractual agreements and conditions** can stipulate a fair price via a 'fair price clause', open access to intellectual property rights (an open access pool for academic research results, for example, to promote genuine competition instead of monopolistic marketing), or profit sharing and repayment of the initial investment upon reaching sales thresholds.

Finally, the importance of political decision-makers using transparent information about public contributions must be emphasised. It is essential to incorporate the public contributions in the fair-pricing calculator [69, 70]. Otherwise, the transparency clause will remain ineffective and will fail to promote a paradigm shift. As the pharmaceutical industry now bases prices on market value, as determined by financial markets and their investors (often referred to euphemistically as 'value-based pricing' [71]), it is essential to dispel the myth that commercial companies are the only innovators.

- The further development or **revitalisation of public infrastructure** for the research, development and approval of medicines is now widely discussed [72] as a means of countering the powerful position of the pharmaceutical industry and the market's failure to provide essential medicines such as antibiotics. This would enable public institutions to act as confident innovators.

The fractured social contract between governments, organisations and private economic actors needs to be healed and revised [73]: Public and private funding of drug development are complementary activities based on a division of labour, and both involve high levels of risk capital. Public R&D spending has macroeconomic effects on gross domestic product (GDP) and microeconomic effects on corporate revenues. However, the strategic objectives of public R&D in health, life sciences and biotechnology must prioritise public health over economic interests.

This complementarity is based on an implicit agreement, or 'social contract', between governments, citizens, organisations, and private economic actors, whereby the contracting parties have mutual obligations to one another. In the context of medicines (and other medical products), companies commit to bringing medicines to market that meet health needs, in exchange for profits that compensate for their investments. The role of governments within this social contract is to create the legal and regulatory framework. If therapies are unavailable

due to unaffordable prices, this system of complementarity must be considered a failure.

Transparency of public (and private) investments in R&D is not an end in itself but provides arguments and visibility towards a new business model that needs to be implemented. The development of vaccines and drugs for the treatment of SARS-CoV-2 can serve as a role model for some, but not all, aspects of the system. Rights and responsibilities must be delinked along the value chain, and the 3Rs principles must be employed: The way forward is a dynamic mix of public–private partnerships that share resources, risks and rewards [74], not only for antibiotics.

7. References

[1] Wild C. and Fabian D. Role of Public Contributions to the Development of Health Innovations and its Integration in Value Assessment and Pricing/Reimbursement Decisions. 2024 Report No. HTA-project report 158. Available from: https://eprints.aihta.at/1499/1/HTA-Projektbericht_Nr.158.pdf.

[2] Myshko D. Updated: FDA Approves $3.5 million Gene Therapy Hemgenix for Hemophilia B. Formulary Watch. 2022:NA-NA.

[3] Drugs for Neglected Diseases Initiative (DNDi). 15 Years of Needs-Driven Innovation for Access: Key Lessons, Challenges, and opportunities for the Future. 2019.

[4] DiMasi J. A., Grabowski H. G. and Hansen R. W. Innovation in the pharmaceutical industry: new estimates of R&D costs. Journal of health economics. 2016;47:20-33.

[5] Angelis A., Polyakov R., Wouters O. J., Torreele E. and McKee M. High drug prices are not justified by industry's spending on research and development. BMJ. 2023;380:e071710. Epub 20230215. DOI: 10.1136/bmj-2022-071710.

[6] Wild C., Sehic O., Schmidt L. and Fabian D. Public contributions to R&D of medical innovations: A framework for analysis. Health Policy. 2025;152:105235. Epub 20241212. DOI: 10.1016/j.healthpol.2024.105235.

[7] Lazonick W., Tulum Ö., Hopkins M., Sakinç M. E. and Jacobson K. Financialisation of the US pharmaceutical industry. Institute for New Economic Thinking. 2019;2.

[8] Hyman D. and Silver C. Are We 'Paying Twice' for Pharmaceuticals? The use of prizes could resolve concerns that drugmakers receive improper rents for their discoveries. CATO Journal, an interdisciplinary Journal for Public Policy Analysis. 2020;12:14-18.

[9] Mueller-Langer F. Neglected infectious diseases: are push and pull incentive mechanisms suitable for promoting drug development research? Health Economics, Policy and Law. 2013;8(2):185-208.

[10] Matthey M. A. and Hollis A. Pull me–push you? The disparate financing mechanisms of drug research in global health. Globalization and Health. 2024;20(1):14.

[11] Mestre-Ferrandiz J., Sussex J. and Towse A. The R&D cost of a new medicine. Monographs. 2012.

[12] DiMasi J. A., Hansen R. W., Grabowski H. G. and Lasagna L. Cost of innovation in the pharmaceutical industry. Journal of health economics. 1991;10(2):107-142.

[13] DiMasi J. A., Hansen R. W. and Grabowski H. G. The price of innovation: new estimates of drug development costs. Journal of health economics. 2003;22(2):151-185.

[14] Hansen R. and Chien R. The pharmaceutical development process: estimates of current development costs and times and the effects of regulatory changes. Issues in Pharmaceutical Economics. Lexington Books, Lexington, MA; 1979.

[15] Paul S. M., Mytelka D. S., Dunwiddie C. T., Persinger C. C., Munos B. H., Lindborg S. R., et al. How to improve R&D productivity: the pharmaceutical industry's grand challenge. Nature reviews Drug discovery. 2010;9(3):203-214.

[16] Jayasundara K., Hollis A., Krahn M., Mamdani M., Hoch J. S. and Grootendorst P. Estimating the clinical cost of drug development for orphan versus non-orphan drugs. Orphanet journal of rare diseases. 2019;14:1-10.

[17] DiMasi J. A., Hansen R. W., Grabowski H. C. and Lasagna L. Research and development costs for new drugs by therapeutic category: a study of the US pharmaceutical industry. PharmacoEconomics. 1995;7:152-169.

[18] Global Alliance for TB Drug Development. The economics of TB drug development: New data for new research: Global Alliance for TB Drug Development; 2001.

[19] DiMasi J. A., Grabowski H. G. and Vernon J. R&D costs and returns by therapeutic category. Drug Information Journal. 2004;38(3):211-223.

[20] DiMasi J. A. and Grabowski H. G. Economics of new oncology drug development. J Clin Oncol. 2007;25(2):209-216.

[21] Chit A., Parker J., Halperin S. A., Papadimitropoulos M., Krahn M. and Grootendorst P. Toward more specific and transparent research and development costs: the case of seasonal influenza vaccines. Vaccine. 2014;32(26):3336-3340.

[22] Falconi A., Lopes G. and Parker J. L. Biomarkers and receptor targeted therapies reduce clinical trial risk in non–small-cell lung cancer. Journal of Thoracic Oncology. 2014;9(2):163-169.

[23] Prasad V. and Mailankody S. Research and development spending to bring a single cancer drug to market and revenues after approval. JAMA internal medicine. 2017;177(11):1569-1575.

[24] Årdal C., Baraldi E., Theuretzbacher U., Outterson K., Plahte J., Ciabuschi F., et al. Insights into early stage of antibiotic development in small-and medium-sized enterprises: a survey of targets, costs, and durations. Journal of pharmaceutical policy and practice. 2018;11(1):1-10.

[25] Wouters O. J., McKee M. and Luyten J. Estimated research and development investment needed to bring a new medicine to market, 2009-2018. Jama. 2020;323(9):844-853.

[26] Gilbert J., Henske P. and Singh A. Rebuilding big pharma's business model. IN VIVO-NEW YORK THEN NORWALK-. 2003;21(10):73-80.

[27] Schuhmacher A., Hinder M., und Stein A. v. S., Hartl D. and Gassmann O. Analysis of pharma R&D productivity–a new perspective needed. Drug discovery today. 2023:103726.

[28] Sertkaya A., Eyraud J. T., Birkenbach A., Franz C., Ackerley N., Overton V., et al. Analytical framework for examining the value of antibacterial products. Submitted to the US Department of Health and Human Services. 2014:14-25.

[29] Adams C. P. and Brantner V. V. Estimating the cost of new drug development: is it really 802 million dollars?

Health Aff (Millwood). 2006;25(2):420-428. Epub 2006/03/09. DOI: 10.1377/hlthaff.25.2.420.

[30] Adams C. P. and Brantner V. V. Spending on new drug development 1. Health economics. 2010;19(2):130-141.

[31] Thomas D. W. Clinical development success rates 2006–2015. BIO Industry Anal. 2016;1:16.

[32] Cleary E. G., Beierlein J. M., Khanuja N. S., McNamee L. M. and Ledley F. D. Contribution of NIH funding to new drug approvals 2010-2016. Proc Natl Acad Sci U S A. 2018;115(10):2329-2334. Epub 20180212. DOI: 10.1073/pnas.1715368115.

[33] Wild C. and Fabian D. The Role of Public Contributions to the Development of Health Innovations. HTA-Projektbericht_Nr1582023.

[34] Cleary E. G., Jackson M. J., Zhou E. W. and Ledley F. D. Comparison of Research Spending on New Drug Approvals by the National Institutes of Health vs the Pharmaceutical Industry, 2010-2019. JAMA Health Forum: American Medical Association; 2023. p. e230511-e230511.

[35] European Commission, Health D.-G. f. and Food Safety. European Reference Networks – Working for patients with rare, low-prevalence and complex diseases – Share, care, cure: Publications Office of the European Union; 2023.

[36] European Commission (EC). European Reference Networks. 2025 [cited 13.10]. Available from: https://health.ec.europa.eu/rare-diseases-and-european-reference-networks/european-reference-networks_en.

[37] European Clinical Research Infrastructure Network (ECRIN). Supporting clinical studies across borders. 2025. Available from: https://ecrin.org/clinical-trials.

[38] Good M., Knockaert M., Soppe B. and Wright M. The technology transfer ecosystem in academia. An Organisational design perspective. Technovation. 2019;82:35-50.

[39] Siegel D. S. and Wright M. University technology transfer offices, licensing, and start-ups. Chicago handbook of university technology transfer and academic entrepreneurship. 2015;1(40):84-103.

[40] Schmidt L. and Wild C. Assessing the public and philanthropic financial contribution to the development of new drugs: a bibliographic analysis. Science, Technology & Public Policy. 2020;4(1):8-14.

[41] Spinal Muscular Atrophy Foundation. About Us: Overview. 2025. Available from: https://smafoundation.org/about-us/.

[42] European Medicines Agency (EMA). Orphan designation: Overview. 2024 [cited 17.09]. Available from: https://www.ema.europa.eu/en/human-regulatory-overview/orphan-designation-overview.

[43] European Medicines Agency (EMA). PRIME: priority medicines. 2024 [cited 17.09]. Available from: https://www.ema.europa.eu/en/human-regulatory-overview/research-development/prime-priority-medicines#:~:text=The%20report%20shows%20that%20the,scientific%20committees%20in%20shorter%20timelines.

[44] European Commission (EC). Proposal for a REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing rules governing the European Medicines Agency, amending Regulation (EC) No 1394/2007 and Regulation (EU) No 536/2014 and repealing Regulation (EC) No 726/2004 Regulation (EC) No 141/2000 and Regulation (EC) No 1901/2006. 2023.

[45] EUROSTAT. EU governments increased R&D allocations by 5% in 2022. 2023. Available from: https://ec.europa.eu/eurostat/web/products-eurostat-news/w/ddn-20230804-2#:~:text=In%202022%2C%20the%20total%20government,(%E2%82%AC78%20656%20million).

[46] Louise Schmidt O. S., Ursula Theuretzbacher, Daniel Fabian, Claudia Wild. Piloting a Framework for analyzing the public contributions to R&D: new antibiotics in focus. Forthcoming (resubmitted after revision). 2024.

[47] Grössmann-Waniek N., Wild, C., Malíková, E., Wolf, S., Fabian, D., Sehic, O. und Zechmeister-Koss, I. . Exagamglogene autotemcel (Exa-cel, Casgevy®) zur Behandlung von Beta-Thalassämie und schwerer Sichelzellkrankheit. 2025 [cited 07.10]. Available from: https://eprints.aihta.at/1548/.

[48] innovative health initiative. History: IHI builds on the successes of earlier European public-private partnerships in health research and innovation.: 2025 [cited 07.10]. Available from: https://www.ihi.europa.eu/about-ihi/history.

[49] European Lead Factory. About us. 2025 [cited 09.10]. Available from: https://www.europeanleadfactory.eu/about/about-us.

[50] Oxford University Innovation. Investments: Companies formed. 2023.

[51] UC Berkeley. Why this UC Berkeley gene therapy spinout is targeting a $100 million IPO. 2023.

[52] Lerner J., Bernstein D., Dev A. and Bai J. The government as an (effective) venture capitalist. VoxEU - Centre for Economic Policy Research (CEPR)2021.

[53] Köppl-Turyna M., Köppl S. and Christopulos D. Government-backed venture capital investments and performance of companies: The role of networks. 2022. Available from: https://www.econstor.eu/bitstream/10419/261494/1/1811128297.pdf.

[54] Nayak R. K., Avorn J. and Kesselheim A. S. Public sector financial support for late stage discovery of new drugs in the United States: cohort study. bmj. 2019;367.

[55] Nayak R. K., Lee C. C., Avorn J. and Kesselheim A. S. Public-sector Contributions to Novel Biologic Drugs. JAMA Intern Med. 2021;181(11):1522-1525. DOI: 10.1001/jamainternmed.2021.3720.

[56] Hartmann J., Schüßler-Lenz M., Bondanza A. and Buchholz C. J. Clinical development of CAR T cells—challenges and opportunities in translating innovative treatment concepts. EMBO molecular medicine. 2017;9(9):1183-1197.

[57] Singhroy D. The public sector role in funding CAR T technologies. Knowledge Ecology International (KEI)2017.

[58] European Medicines Agency (EMA). Funding. 2025 [cited 18.09]. Available from: https://www.ema.europa.eu/en/about-us/how-we-work/governance-reporting/funding.

[59] Fabian D., Sehic O. and Wild C. The origins of Novo Nordisk and Novartis products: piloting a framework

to identify the public contributions. J Pharm Policy Pract. 2025;18(1):2534919. Epub 20250805. DOI: 10.1080/20523211.2025.2534919.

[60] Wild C., Sehic O., Schmidt L. and Fabian D. Public Contributions to R&D of Medical Innovations: a Framework for Analysis. Health policy. 2024:105235. DOI: https://doi.org/10.1016/j.healthpol.2024.105235.

[61] Moon S., Vieira M. and Kimmitt R. Do costs, timeframes and attrition rates differ between non-commercial and commercial biomedical R&D. A study of neglected diseases R&D and the P2I model Geneva: Global Health Centre at the Graduate Institute. 2020.

[62] Junod Moser D., Boulet P., Childs M., Shieh M. and Pécoul B. Striking fair deals for equitable access to medicines. Journal of Intellectual Property Law & Practice. 2023;18(4):323-335. DOI: 10.1093/jiplp/jpad025.

[63] Wild C. and Probst J. Fair pricing for new drugs: Does unbundling help? Soziale Sicherheit. 2018;9.

[64] Devalière A. and Beck A. Pharmaceutical transparency: from resolution to reality: Snapshot of the implementation of WHA resolution 72.8 on transparency of pharmaceutical markets with country examples and recommendations. WEMOS and Health Action International Health Action International (HAI), 2025. Available from: https://haiweb.org/storage/2025/05/Report-pharmaceutical-transparency-Wemos-HAI-2025-1.pdf.

[65] Austrian Institute for Health Technology Assessment (AIHTA). Decision Support Documents for the Austrian Appraisal Board: Chap 7. 2025. Available from: https://aihta.at/page/htas-fuer-bewertungsboard/en.

[66] Organisation for Economic Co-operation and Development (OECD). Frascati Manual 20152015.

[67] Drugs for Neglected Diseases Initiative (DNDi). Transparency of R&D Costs: to promote accountability and fair pricing of medicines. 2025. Available from: https://dndi.org/advocacy/transparency-rd-costs/.

[68] Espín J., Rejon-Parrilla J., Garcia-Diaz M., Spacirova Z., Epstein D., Mestre-Ferrandiz J., et al. Set of Recommendations for Using the Public Investment in the Negotiation/HTA process and Pilot Examples how Price can be Different if Public Investment is considered 2025.

[69] International Association of Mutual Benefit Societies (AIM). AIM offers a tool to calculate fair and transparent European prices for accessible pharmaceutical innovations. Journal. 2021. Epub Epub Date. Original Publication.

[70] International Association of Mutual Benefit Societies (AIM). AIM proposes to establish a European drug pricing model for fair and transparent prices for accessible pharmaceutical innovations. Journal. 2019. Epub Epub Date. Original Publication.

[71] Expert Panel on effective ways of investing in Health (EXPH). Defining Value in "Value-Based Healthcare". 2019. Available from: https://health.ec.europa.eu/document/download/634e0a0c-4bff-4050-ad5f-b80381f36f33_en.

[72] Scientific Foresight Unit (STOA). European pharmaceutical research and development: Could public infrastructure overcome market failures? European Parliament, 2021. Available from: https://www.europarl.europa.eu/RegData/etudes/STUD/2021/697197/EPRS_STU(2021)697197_EN.pdf.

[73] European Health Forum Gastein (EHFG). Rethinking solidarity in health Healing Europe´s fractured social contract. 2025.

[74] So A. D., Ruiz-Esparza Q., Gupta N. and Cars O. 3Rs for innovating novel antibiotics: sharing resources, risks, and rewards. BMJ. 2012;344:e1782. Epub 20120403. DOI: 10.1136/bmj.e1782.

[75] University College London. UCL spinout Autolus gains UK licence for cancer therapy. 2025 [cited 13.08]. Available from: https://www.ucl.ac.uk/news/2025/apr/ucl-spinout-autolus-gains-uk-licence-cancer-therapy.

[76] RePorter. Improving Cord Blood Transplantation. 2025 [cited 14.08]. Available from: https://reporter.nih.gov/search/4Z9Y9mQunEOfZSHtDmB9nA/project-details/9134065.

[77] Carroll J. The CAR-T brain war: Scientific trailblazer inspires a $45M biotech startup. Journal. 2015. Epub Epub Date. Original Publication.

[78] Reynolds J. Autolus Limited secures £40 million funding – Woodford Investment Management and Perceptive Bioscience complete Series B financing. Journal. 2016. Epub Epub Date. Original Publication.

[79] Wilson J. AUTOLUS LIMITED: Autolus Secures US$80 million Series C Funding. Journal. 2017. Epub Epub Date. Original Publication.

[80] Taylor P. IPO bonanza continues with $150M listing for CAR-T player Autolus. Journal. 2018. Epub Epub Date. Original Publication.

[81] Bonanos P. Autolus follows up CAR T data with $101M raise. Journal. 2019. Epub Epub Date. Original Publication.

[82] Autolus Therapeutics plc. Form 10-K: ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934. 2024.

[83] Comanor W. S. and Scherer F. M. Mergers and innovation in the pharmaceutical industry. Journal of health economics. 2013;32(1):106-113.

[84] Jansen S. A. Mergers & Acquisitions: Unternehmensakquisitionen und-kooperationen Eine strategische, organisatorische und kapitalmarkttheoretische Einführung: Springer; 2008.

[85] Galkina Cleary E., Beierlein J. M., Khanuja N. S., McNamee L. M. and Ledley F. D. Contribution of NIH funding to new drug approvals 2010–2016. Proceedings of the National Academy of Sciences. 2018;115(10):2329-2334.

[86] Vogler S., Panteli D., Zimmermann N. and Busse R. Überblick über Maßnahmen zur Förderung des Einsatzes von Biosimilars in europäischen Ländern. Arzneiverordnungs-Report 2022: Springer; 2023. p. 57-81.

[87] Gilead. Gilead Sciences to Acquire Kite Pharma for $11.9 Billion. Gilead; 2017.

[88] Parrish M. A glimpse inside Bristol Myers Squibb's integration with Celgene. Journal. 2022;2024(05.08.2024). Epub Epub Date. Original Publication.

[89] AbbVie. AbbVie Completes Transformative Acquisition of Allergan. 2020 [cited 05.08.2024]. Available from: https://news.abbvie.com/2020-05-08-AbbVie-Completes-Transformative-Acquisition-of-Allergan.

[90] Gagnon M.-A. and Volesky K. D. Merger mania: mergers and acquisitions in the generic drug sector from 1995 to 2016. Globalization and health. 2017;13(1):1-7.
[91] Dunleavy K. The top 20 pharma companies by 2023 revenue. 2024 [cited 07.06.2024]. Available from: https://www.fiercepharma.com/pharma/top-20-pharma-companies-2023-revenue.
[92] Jung E. H., Engelberg A. and Kesselheim A. S. Do large pharma companies provide drug development innovation? Our analysis says no. STAT News; 2019.
[93] Schmidt L., Sehic O. and Wild C. EU FP7 research funding for an orphan drug (Orfadin®) and vaccine (Hep C) development: a success and a failure? Journal of pharmaceutical policy and practice. 2021;14(1):37.
[94] Schmidt L., Sehic O. and Wild C. Counting the cost of public and philanthropic R&D funding: the case of olaparib. Journal of pharmaceutical policy and practice. 2022;15(1):47.
[95] Wild C. S. O., Schmidt L. and Fabian D. Public Contributions to R&D of Medical Innovations: a Framework for Analysis. 2024; Forthcoming (re-submitted after revision).
[96] Herper M. Analysis of pharmaceutical R&D ranks Novo Nordisk and Johnson & Johnson above their peers. 2024 [cited 12.06.2024]. Available from: https://www.statnews.com/2024/05/16/pharma-research-development-rankings/.
[97] Pharma I. Novo Nordisk top 2024 Innovation Index. 2024 [cited 07.06.2024]. Available from: https://www.ideapharma.com/insights/novo-nordisk-top-2024-innovation-index/.
[98] Fouad Y. A. and Aanei C. Revisiting the hallmarks of cancer. American journal of cancer research. 2017;7(5):1016.
[99] Hanahan D. and Weinberg R. A. Hallmarks of cancer: the next generation. cell. 2011;144(5):646-674.
[100] Karamanou M., Protogerou A., Tsoucalas G., Androutsos G. and Poulakou-Rebelakou E. Milestones in the history of diabetes mellitus: The main contributors. World journal of diabetes. 2016;7(1):1.
[101] Sampat B. N. and Lichtenberg F. R. What are the respective roles of the public and private sectors in pharmaceutical innovation? Health Affairs. 2011;30(2):332-339.
[102] Ledley F. D. and Cleary E. G. NIH funding for patents that contribute to market exclusivity of drugs approved 2010–2019 and the public interest protections of Bayh-Dole. PloS one. 2023;18(7):e0288447.
[103] Statista. Total global spending on pharmaceutical research and development from 2014 to 2028. 2024 [cited 02.02]. Available from: https://www.statista.com/statistics/309466/global-r-and-d-expenditure-for-pharmaceuticals/.
[104] Dierks R. M. L., Bruyère O. and Reginster J.-Y. Critical analysis of valuation and strategical orientation of merger and acquisition deals in the pharmaceutical industry. Expert review of pharmacoeconomics & outcomes research. 2018;18(2):147-160.
[105] Gautam A. and Pan X. The changing model of big pharma: impact of key trends. Drug discovery today. 2016;21(3):379-384.
[106] Demirbag M., Ng C. K. and Tatoglu E. Performance of mergers and acquisitions in the pharmaceutical industry: a comparative perspective. Multinational Business Review. 2007;15(2):41-62.
[107] Richman B., Mitchell W., Vidal E. and Schulman K. Pharmaceutical M&A activity: Effects on prices, innovation, and competition. Loy U Chi LJ. 2016;48:787.
[108] Higgins M. J. and Rodriguez D. The outsourcing of R&D through acquisitions in the pharmaceutical industry. Journal of financial economics. 2006;80(2):351-383.
[109] Chan T., Nickerson J. A. and Owan H. Strategic management of R&D pipelines with cospecialized investments and technology markets. Management science. 2007;53(4):667-682.
[110] Danzon P. M., Epstein A. and Nicholson S. Mergers and acquisitions in the pharmaceutical and biotech industries. Managerial and decision economics. 2007;28(4-5):307-328.
[111] Krieger J. L., Li X. and Thakor R. T. Find and replace: R&D investment following the erosion of existing products. Management science. 2022;68(9):6552-6571.
[112] Van der Zwan N. Making sense of financialisation. Socio-economic review. 2014;12(1):99-129.
[113] Greenwood R. and Scharfstein D. The growth of finance. Journal of Economic perspectives. 2013;27(2):3-28.
[114] McGeeney J. D., Sertkaya A., Ross L., Ledley F. and Hyman C. Mergers and Acquisitions (M&As) in Pharmaceutical Markets: Associations with Market Concentration, Prices, Drug Quantity Sold, and Shortages. 2025.
[115] Shibayama S., Tanikawa K., Fujimoto R. and Kimura H. Effect of mergers and acquisitions on drug discovery: perspective from a case study of a Japanese pharmaceutical company. Drug discovery today. 2008;13(1-2):86-93.
[116] Prabhu J. C., Chandy R. K. and Ellis M. E. The impact of acquisitions on innovation: poison pill, placebo, or tonic? Journal of Marketing. 2005;69(1):114-130.
[117] Cloodt M., Hagedoorn J. and Van Kranenburg H. Mergers and acquisitions: Their effect on the innovative performance of companies in high-tech industries. Research policy. 2006;35(5):642-654.
[118] Forster S. P., Stegmaier J., Spycher R. and Seeger S. Virtual pharmaceutical companies: collaborating flexibly in pharmaceutical development. Drug discovery today. 2014;19(3):348-355.
[119] Koenig M. E. and Mezick E. M. Impact of mergers & acquisitions on research productivity within the pharmaceutical industry. Scientometrics. 2004;59:157-169.
[120] Seo M.-G. and Hill N. S. Understanding the human side of merger and acquisition: An integrative framework. The Journal of Applied Behavioral Science. 2005;41(4):422-443.
[121] Paruchuri S., Nerkar A. and Hambrick D. C. Acquisition integration and productivity losses in the technical core: Disruption of inventors in acquired companies. Organisation science. 2006;17(5):545-562.
[122] Monari G.-L. Leap toward innovation: new management, the acquisition of Serono, and focused diversification are driving an era of change at Merck KGaA. Med Ad News. 2007;26(9):138-141.
[123] Cassiman B. and Veugelers R. In search of complementarity in innovation strategy: Internal R&D

and external knowledge acquisition. Management science. 2006;52(1):68-82.
[124] Festel G. Technology transfer models between industrial biotechnology companies and academic spin-offs. Industrial Biotechnology. 2013;9(5):252-257.
[125] Dvulit Z., Mykytiuk O. and Onysenko T. Features of mergers and acquisitions in the pharmaceutical industry. Теоретичні та прикладні питання економіки Збірник наукових праць–2020-Випуск. 2020;1(2):40.
[126] Voss P. S. Innovation Performance in Healthcare M&A: An Empirical Analysis. Junior Management Science. 2022;7(4):1164-1192.
[127] Xue H., Zeng S. and Sun D. Radical or Incremental? Impacts of Mergers and Acquisitions on Firms' Innovation. IEEE Transactions on Engineering Management. 2022.
[128] Ornaghi C. Mergers and innovation in big pharma. International journal of industrial Organisation. 2009;27(1):70-79.
[129] Blanpain R. Corporate ReOrganisations and the Protection of Employees in the European Union: TILBURG UNIVERSITY; 2010.
[130] Smaglik P. Drug industry mergers means career reconsiderations for scientists. Nature. 2007;445(7128):677-677.
[131] Ernst H. and Vitt J. The influence of corporate acquisitions on the behaviour of key inventors. R&D Management. 2000;30(2):105-120.
[132] Schweizer L. Organisational integration of acquired biotechnology companies into pharmaceutical companies: The need for a hybrid approach. Academy of management journal. 2005;48(6):1051-1074.
[133] Keelara R., Wenzl M., Waagstein L., Moens M. and Lopert R. Developing a set of indicators to monitor the performance of the pharmaceutical industry. 2023. DOI: https://doi.org/10.1787/3b5ca61c-en.
[134] Nieto-Gómez P., Castaño-Amores C., Rodríguez-Delgado A. and Álvarez-Sánchez R. Analysis of oncological drugs authorised in Spain in the last decade: association between clinical benefit and reimbursement. The European Journal of Health Economics. 2023. DOI: 10.1007/s10198-023-01584-9.

8. Appendix 1

In Appendix 1 the application of the framework and methodology are applied to five products that were assessed as part of a new Austrian HTA for highly specialized and expensive hospital drugs. We have summarised our findings in the following abstract with the individual assessment of the five products in subsequent subchapters.

Background

In 2024 the Austrian Appraisal Board for highly specialized and expensive hospital drugs was formed by the Ministry of Health to ensure rapid patient access to specialized medicines, standardize nationwide use of high-cost drugs, support healthcare providers with new technologies, and promote efficient resource allocation for long-term healthcare sustainability. Besides the standard domains of HTA, for the first time public contributions are also analysed and reported. After the assessment of the first five products, we can identify trends.

Method

The Austrian Institute for Health Technology Assessment (AIHTA) has developed a methodology and a framework for a Horizon Europe project (HI-PRIX) to capture public contributions to pharmaceutical research and development and have piloted them on drug categories, portfolios of pharmaceutical companies, and specific pharmaceuticals to ensure reliability and granularity. This published and peer reviewed methodology and framework are the tools used to identify public contributions.

Results

Out of the five analysed products (Casgevy®, Beqvez®, Tepezza®, Amtagvi®, Aucatzyl®), two have an ATMP destination by the EMA, one has both ATMP and orphan designation and the remaining two have neither ATMP, nor orphan and all but one have a PRIME: priority medicine designation. For the development of these products direct and indirect public contributions per product ranged from roughly 10 million USD to 115 million USD.

Conclusion

Every single drug that was selected by the Appraisal Board had its origin in academic settings and/ or has received public contributions. These highly specialized and expensive therapies all stem from research conducted in academic settings with substantial public funding involved at all stages of development. Our findings suggest that the role of the public in pharmaceutical innovation is a much bigger one than previously assumed, contrary to the narrative that the pharmaceutical industry is the sole driver of innovation.

Exagamglogene autotemcel (exa-cel)/ CASGEVY®

Own development costs

The market authorization holder (Vertex) delivered no data on development costs.

Public contributions to drug development, acquisition and licensing information

Table 9 provides an overview of the development history and ownership changes of CRISPR/Cas9 gene-edited therapy.

Table 9: CASGEVY® overview

Originator	Developer	Information on acquisitions	Public contribution	Type of public funding
Casgevy®- *Active substance:* Exagamglogene autotemcel (exa-cel)				
CRISPR Therapeutics	CRISPR Therapeutics; Vertex Pharmaceuticals	**Patent deal 2014, 2016:** The Broad Institute, Harvard, and Editas Medicine have signed a global license agreement granting Editas access to specific genome-editing IP for CRISPR/Cas9 (see Table 9) **Patent deal in 2023:** Nonexclusive licensing deal for Editas Medicines' Cas9 gene editing technology for ex vivo gene editing. Editas will in turn pay the Broad Institute and Harvard a "mid-double digit of payments received from Vertex"	Basic research conducted in public research institutes None in late-stage development found	Basic and translational research funding

Basic Research and Development of CRISPR Technology

The development of CRISPR technology emerged from mostly public but also private research institutions, as shown in Table 14. The initial identification of the CRISPR locus came from public research at Osaka University in 1987.

Subsequent foundational discoveries were made primarily at public institutions, including Universidad de Alicante, Utrecht University, and other academic centres through the 1990s and early 2000s (see Table 14 in Appendix 2). A pivotal shift occurred in 2012 when Jennifer Doudna (University of California) and Emmanuelle Charpentier (then at Umeå University) demonstrated CRISPR-Cas9's potential for gene editing. Figure 5 shows the development milestones that ultimately led to the development of Casgevy based on the literature.

The discovery of Doudna and Charpentier bridged basic research and therapeutic applications, leading to increased industry interest and involvement. As detailed in Table 14, the clinical development of CRISPR-based therapies has been dominated by industry players, particularly Vertex Pharmaceuticals and CRISPR Therapeutics for sickle cell disease and ß-thalassemia. Vertex Pharmaceuticals has been particularly active in clinical trials, with several key studies: NCT03655678: Phase 1/2/3 study for β-Thalassemia; NCT03745287: Study evaluating CTX001 in severe Sickle Cell Disease; NCT04208529: Long-term follow-up study for participants who received CTX001. For none of the clinical trials, total clinical trial costs or per-patient costs were publicly disclosed.

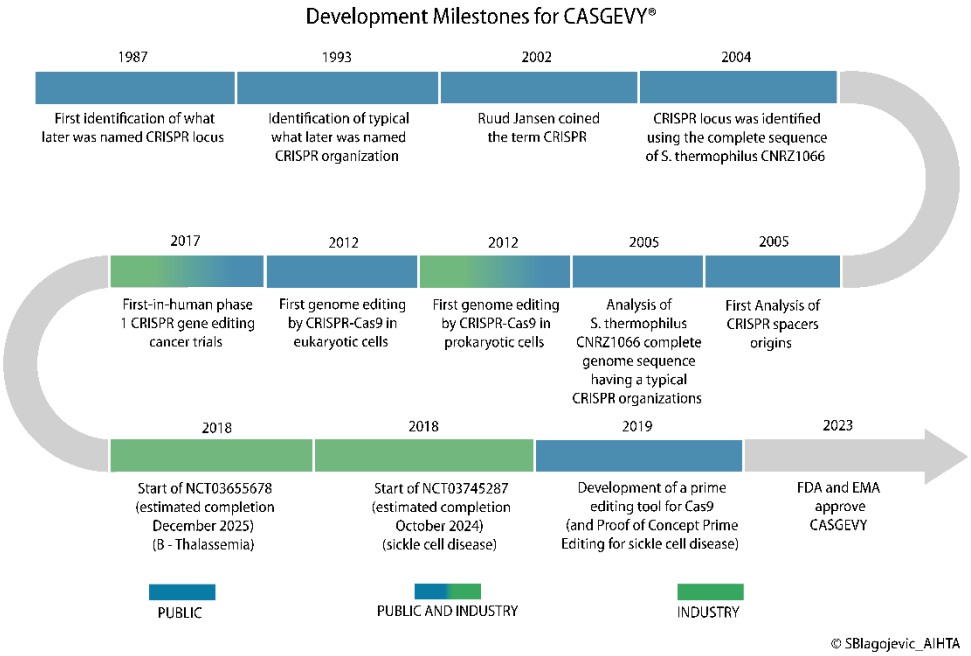

Figure 5: Development milestone for CASGEVY®

Editas Medicine (founded by researchers from the Broad Institute, the University of California, Berkley and Harvard University) has also conducted trials. However, the firm's focus has been broader, as evidenced by its extensive patent portfolio showing a total of 97 granted patents related to CRISPR/Cas9 technology. This led to Vertex acquiring a nonexclusive patent 2023 from Editas Medicines for a 50 million USD upfront payment, up to an additional 50 million USD contingent payment. The annual license fee ranges from 10 million to 40 million USD, with sales-based increases continuing through 2034 (see Table 14 in Appendix 2)

Company Structure and Financials

Vertex Pharmaceuticals' financial information reveals that the company has demonstrated financial growth, with operating revenue increasing from $101,9 million in 2009 to $9,87 billion in 2023. The company has maintained consistent profitability since 2020, achieving a profit before tax of $4,38 billion in 2023. The company has shown significant growth in employee numbers, from 1.432 in 2009 to 5.400 in 2023, indicating substantial Organisational expansion alongside its financial growth.

The ownership structure reveals that venture capital is the most important financier of Vertex Pharmaceuticals. Capital World Investors holds the largest stake with 10,00% direct ownership, operating as an investment management Organisation. The Vanguard Group follows with 8,35%, State Street Corporation maintains 4,65% total ownership, and BlackRock Fund Advisors holds 3,36%. This means the "Big Three" index funds are with Capital World Investors, the most important shareholders.

Research Funding and Collaborations

Table 14 in Appendix 2 shows significant public funding support for CRISPR/Cas9 research, particularly from the NIH. Key recipients include Stuart H. Orkin at Dana-Farber Cancer Institute Jennifer A. Doudna at the University of California Berkeley (who received, alongside Emmanuelle Charpentier, the Nobel Prize in Chemistry). Over the years, these researchers have received over 7,4 million USD from the NIH, and the Broad Institute has received over 73,3 million USD for their research on CRISPR/Cas9 or the application it from the NIH. Even though public funding has been essential for basic research in CRISPR technology development, the total amount of public funding for basic research is not available.

The development of exa-cel represents a collaboration between industry (Vertex Pharmaceuticals, CRISPR Therapeutics, Editas Medicines) and academic institutions (especially the Broad Institute at Harvard but also the University of California, Harvard University and the Massachusetts Institue of Technology (MIT)), leveraging both public and private funding sources. The product received marketing authorization in February 2024, marking a significant milestone in commercializing CRISPR technology. This development pathway demonstrates the evolution from basic academic research to commercial therapeutic applications, with increasing industry involvement and investment as the technology matured. The successful development required substantial financial resources, which we only know partly from the public side. Vertex Therapeutics has not disclosed the total development costs for Casgevy.

The full HTA report with all detailed information on funding amounts can be found here: https://eprints.aihta.at/1548/

Fidanacogene Elaparvovec/ BEQVEZ®

Own development costs, acquisitions and licences

Pfizer has not published the development costs of fidanacogene elaparvovec. Table 10 provides an overview fidanacogene elaparvovec.

Table 10: BEQVEZ® overview

Originator	Developer	Information on acquisitions	Public contribution	Type of public funding
BEQVEZ® - *Active substance:* Fidanacogene Elaparvovec				
Spark Therapeutics, Children's Hospital of Philadelphia	Pfizer	**Patent deal in 2014:** Pfizer licensed BEQVEZ® from Spark Therapeutics for $20 million with up to $260 million in milestone payments **Acquisition 2019:** Roche acquires Spark Therapeutics for $4.3 billion	Basic research is mostly publicly funded Early clinical development in cooperation with publicly funded research institutes and hospitals	Basic, applied and translational research support

Basic Research and clinical development

The development of factor IX (FIX) gene therapy for the treatment of haemophilia B emerged primarily from public research institutions, as shown in Table 15 in Appendix 2 and visualised in Figure 6. The basic research began at public institutions in the early 2000s, with key studies at Children's Hospital of Philadelphia (CHOP) and other academic centres pioneering adeno-associated virus (AAV)-based gene therapy approaches (St. Jude Children's Research Hospital and Perelman School of Medicine).

Several researchers made significant contributions to the development: Katherine A. High at CHOP (and later Spark Therapeutics as co-founder) led many pivotal studies, including early AAV-based gene therapy trials. Valder R. Arruda at CHOP contributed extensively to understanding AAV vectors for haemophilia treatment. In 2006, Catherine S. Manno and colleagues published crucial findings on AAV-FIX transduction in haemophilia patients, noting challenges with immune responses. Adam Cuker at the University of Pennsylvania later led key clinical studies demonstrating fidanacogene elaparvovec's efficacy in reducing bleeding in haemophilia B patients.

A pivotal advancement came in 2015 when Amit C. Nathwani and colleagues at University College London (UCL) Cancer Institute, Royal Free NHS Trust, and St. Jude Children's Research Hospital demonstrated the long-term safety and efficacy of factor IX gene therapy in haemophilia B patients. Their work showing sustained factor IX expression over a median 3.2-year period helped bridge basic research to therapeutic applications, leading to increased industry involvement.

The initial clinical trial in 2012 was conducted by Spark Therapeutics (NCT01620801) in partnership with mostly publicly funded institutions, including Children's Hospital of Philadelphia, University of Pittsburgh, Royal Prince Alfred Hospital in Sydney, and St. James's Hospital in Ireland. Subsequently, Pfizer proceeded with the later-stage clinical trials (NCT02484092 in 2015, NCT03307980 in 2017, NCT03861273 in 2019, NCT05568719 in 2022), expanding the research network to include multiple international centres. The research sites included both public and private institutions, with a significant presence of academic medical centres and public hospitals across Europe, Asia, and North America.

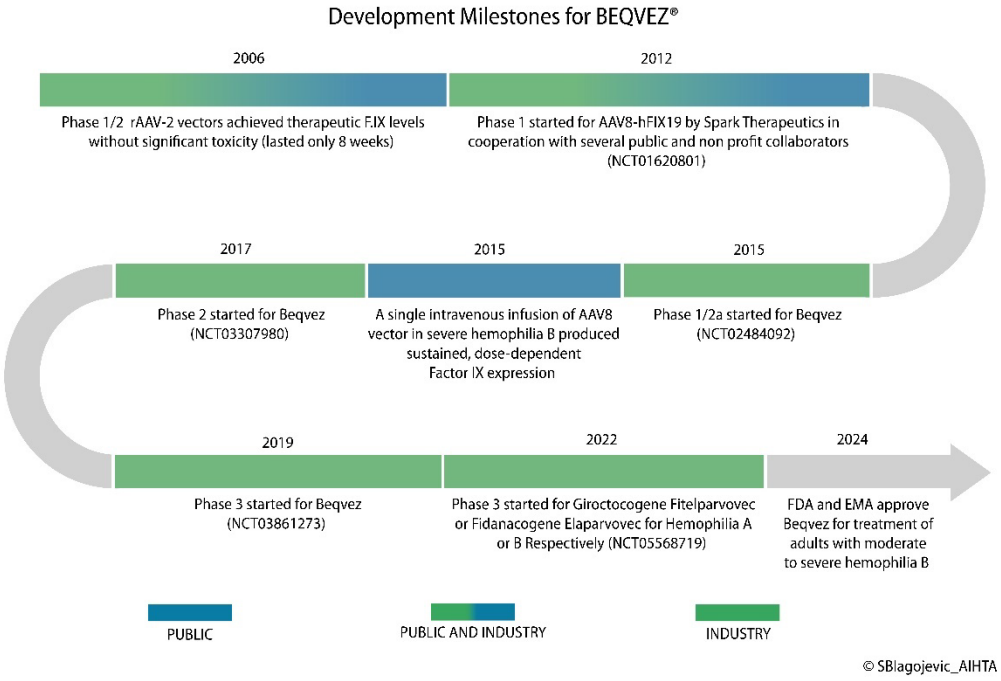

Figure 6: Development milestone for BEQVEZ®

Public contributions on drug development

Table 15 in Appendix 2 demonstrates substantial public funding support for haemophilia B gene therapy research, particularly from the US-state-funded National Heart, Lung and Blood Institute (NHLBI). The CHOP received numerous grants between 1994-2022, with funding directed toward projects ranging from basic biochemistry of FIX to clinical applications of gene therapy. Adding up all National Institutes of Health (NIH) grants to

CHOP related to haemophilia B gene therapy research the total public funding amounted to approximately $38.5 million over this period. This public funding played a crucial role in advancing the basic science that would eventually lead to fidanacogene elaparvovec's development.

While a lesser involvement in the development of fidanacogene elaparvovec, St. Jude Children's Research Hospital received roughly $8.1 million from 2005-2015 in public funding from the US-funded NHLBI for their Haemophilia B and FIX research, which helped researchers worldwide to better understand AAV-based gene therapies.

Industry interest spiked in 2014 when Spark exclusively licensed fidanacogene elaparvovec to Pfizer for $20 million upfront payment with the potential for $260 million in milestone payments. The agreement included a provision where Spark Therapeutics conducts Phase 1 and 2 trials, and Pfizer then proceeded with the development.

Financial information

Pfizer's Organisational structure reveals that Pfizer´s revenues dwindled over time from roughly $49,6 billion in 2014 to $41,2 billion in 2019. However, the company has shown significant growth in employee numbers, from 78,300 in 2014 to 88,300 in 2019, indicating organisational expansion.

Spark Therapeutics has consistently operated at a revenue loss from 2014 to its acquisition by Roche in 2019. However, its employee numbers show that the company has experienced significant growth at the same time from 50 in 2014 to 368 in 2018.

The ownership structure of Pfizer reveals that venture capital is the most important financier. The Vanguard Group holds the largest stake with 9.1%. BlackRock follows with 5.8 %, State Street Corporation maintains 5.1 % total ownership and Wellington Trust holds 2.9%. Meaning the “Big Three” index fund are with Wellington Trust the most important shareholders.

The full HTA report with all detailed information on funding amounts can be found here: https://eprints.aihta.at/1558/

Lifileucel/ AMTAGVI®

Own development costs, acquisitions and licences

Table 11 provides a summary of key information on lifileucel. Iovance Biotherapeutics has not published the total amount of research and development expenses attributed to lifileucel.

Table 11: AMTAGVI® overview

Originator	Developer	Information on acquisitions	Public contribution	Type of public funding
Amtagvi® - Active substance: Lifileucel				
Genesis Biopharma	Iovance Biotherapeutics	Patent deal 2011: Genesis Biopharma licensed patents from the NCI for the development of Lifileucel Acquisition in 2013: Iovance Therapeutics acquired Genesis Biopharma	Basic and preclinical research primarily funded by the National Cancer Institute from 1999 to 2024	Basic, preclinical and clinical research

Abbreviation: NCI … National Cancer Institute

Basic research and clinical development

The development of lifileucel for nonresectable melanoma emerged primarily from public research institutions, as shown in Table 17 in Appendix 2. Basic research on tumour-infiltrating lymphocyte (TIL) for the treatment of melanoma began in public institutions in the late 1990s at the United States (US)-funded National Cancer Institute (NCI). Several researchers and research institutes made significant contributions to the development: Steven Rosenberg (NCI) developed a process where TILs are extracted from the patient’s tumour tissue, expanded to considerable quantities in the laboratory, and then reinfused into the patient to target and eliminate cancer cells. Michael Nishimura (Loyola University Chicago) built on the findings from Rosenberg and continued developing the process of extracting cells from the tumour for subsequent isolation and expansion of immune cells. The University of Pittsburgh has focused on skin cancer relevant to TIL from 2008 onwards and has played a significant part in the research. Several researchers at H. Lee Moffitt Cancer Center & Research Institute further deepened the understanding of mechanisms of action (MOA) such as understanding the function of cluster

differentiation 4 (CD4), cluster differentiation 8 (CD8), programmed cell death 1 (PD-1) or cytotoxic T-lymphocyte antigen 4 (CTLA-4).

Parallel to researchers in the US, several research institutes in Europe, especially in the Netherlands, conducted studies on TILs. Building on Rosenberg and colleagues' findings, in the Dutch equivalent to the NCI, the Netherlands Cancer Institute (NKI), John Haanen conducted basic, as well as late-stage clinical development of TILs, namely the M14TIL clinical trial (conducted by NKI, the Copenhagen University Hospital at Herlev, and the University of Manchester). Additionally, Leiden University conducted phase I/II studies on TILs.

The initial clinical trial for lifileucel was conducted (and sponsored) by Iovance Biotherapeutics in 2015 (NCT02360579) at publicly funded and non-governmental Organisations including the H. Lee Moffitt Cancer Center and Research Institute, Providence Cancer Center Oncology and the University of Pittsburgh. The research sites included both public and private institutions, with a significant presence of academic medical centres and public hospitals across North America and Europe. Currently, there are six ongoing clinical trials using TILs conducted by Iovance Biotherapeutics (NCT03645928, NCT05361174, NCT05727904, NCT06566092, NCT06940739, NCT05398640). Six further clinical trials where Iovance Biotherapeutics is the collaborator and not the primary sponsor are currently either completed or ongoing (NCT03449108, NCT06190249, NCT05607095, NCT05640193, NCT05176470, NCT04111510). We visualised the development milestones in Figure 7.

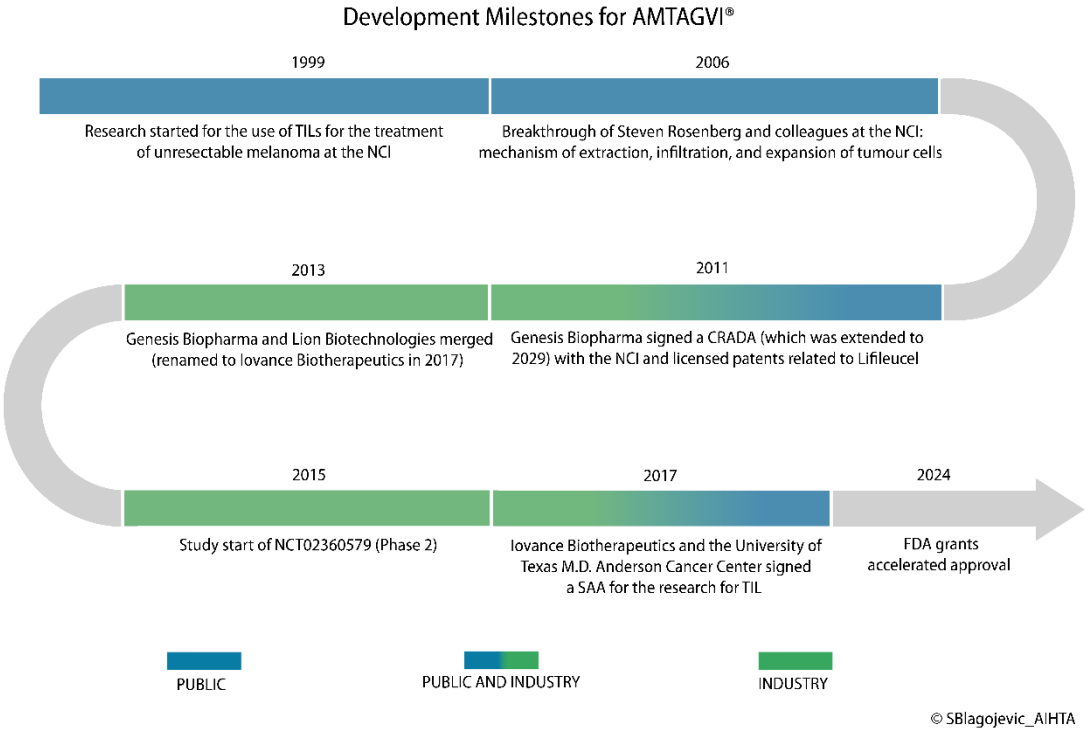

Figure 7: Development milestones for AMTAGVI®

Public contributions to drug development

Table 16 in Appendix 2 demonstrates substantial direct and indirect public research funding for the research on TILs. We found a total of $115.2 million (€100.2 million) in direct and indirect public funding for TIL at all stages of development. All the funding that we found came from the NCI. Research directly at the NCI amounted to roughly $57 million (€49.6 million; $24.9 million/€21.6 million for the University of Pittsburgh, $15.9 million/€13.8 million for Loyola University Chicago and $6.2 million/€5.4 million to the H. Lee Moffitt Cancer Center & Research Institute). The remaining $11 million (€9.6 million) in public funding was for the University of Texas M.D. Anderson Cancer Center, Yale University, University of Southern California, Fred Hutchinson Cancer Research Center, University of Chicago and Trampoline Pharma. The only project-specific Dutch expenses for the research for TILs are from the Innovationsfonden of DKK (Danish krone) 4.3 million (€576.500).

The NCI conducted pivotal basic research on TIL as early as 1999. The research on the topic has only gone more in-depth over the years with involvement in preclinical and clinical development. Industry interest

spiked after the breakthrough of Steven Rosenberg on the mechanism of extraction, infiltration and expansion of tumour cells. In August 2011, Genesis Biopharma (which later merged with Iovance Biotherapeutics) signed a five-year Cooperative Research and Development Agreement (CRADA) with the NCI, which has been continuously extended to 2029. Iovance Biotherapeutics has acquired rights and patents related to lifileucel from the NCI: Patent license agreements, which require quarterly payments to the National Institutes of Health (NIH), royalty payments based on a percentage of net sales (estimated to be less than one percent to low single digit percentage), as well as milestone payments. In 2017, Iovance Biotherapeutics formed a Strategic Alliance Agreement (SAA) with the University of Texas M.D. Anderson Cancer Center. It entails funding for clinical and preclinical research of $14.2 million from Iovance Biotherapeutics (€12.3 million) with all related intellectual property rights (IPR) from the studies directly going to Iovance Therapeutics. Iovance Biotechnologies has additional partnerships with the H. Lee Moffitt Cancer Center & Research Institute, Yale University and Cellectis.

Company structure and financials

The company was founded as "Freight Management Corp." in 2007, focusing on the shipping/freight industry. The company merged with Genesis Biopharma, Inc. in 2010 and then merged with Lion Biotechnologies in 2013. In 2017 Lion Biotechnologies changed its name to Iovance Biotherapeutics. A strategic patent acquisition of Iovance Biotherapeutics was undertaken in 2023: rights to Proleukin® (interleukin-2) were acquired for £166.7 million (€195 million) with additional milestone payments from Clinigen Limited (which acquired rights to Proleukin® itself in 2019).

From Freight Management Corp. to Iovance Biotherapeutics, Venture Capital (VC) played a pivotal role in financing the company. Iovance Biotherapeutics owns over 250 patents pertaining to lifileucel or other TIL-related technology, which leads the company to assume exclusivity until 2042.

This history of lifileucel shows progression from publicly funded basic research to industry cooperation in early-stage clinical development and continuous cooperation between industry and public research institutes until market authorisation. We can conclude that lifileucel is the result of publicly funded research that led to industry cooperation.

The full HTA report with all detailed information on funding amounts can be found here: https://eprints.aihta.at/1570/

Teprotumumab/ TEPEZZA®

Own development costs, acquisitions and licences

Table 12 provides a short overview of teprotumumab. We were unable to find any information regarding the total development cost of teprotumumab.

Table 12: TEPEZZA® overview

Originator	Developer	Information on acquisitions	Public contribution	Type of public funding
TEPEZZA® – Active substance: teprotumumab				
Roche, Genmab, River Vision Development Corporation	Amgen; Horizon Therapeutics	2006: Developed by Genmab in cooperation with Roche but did not lead to a product n.a. but likely between 2010-2012: Licensing deal with River Vision Development Corporation 2017: River Vision Development Corporation acquired by Horizon Therapeutics 2023: Horizon Therapeutics acquired by Amgen	Basic research is publicly funded Early clinical development in cooperation with publicly funded research institutes and hospitals	Basic, applied and translational research support Early-stage research in SME and Biotech start-ups

Basic research and clinical development

Teprotumumab was repurposed for the treatment of thyroid eye disease (TED) after its initial development as a cancer treatment proved unsuccessful. Originally investigated by Genmab and Roche for cancer therapy, it was later studied for both Ewing's sarcoma and diabetic macular oedema, as documented in Table 21. Lundquist Institute for Biomedical Innovation at Harbor-UCLA Medical Center (henceforth: Lundquist Institute) started its research on TED in 1999 and continued it until 2010, when it licensed its patent to River Division Development

Corporation. In 2013, the first clinical trial for teprotumumab for TED was conducted by River Division Development Corporation (NCT01868997), followed by Horizon Therapeutics in 2017 (NCT03298867 "OPTIC", NCT03461211 "OPTIC-X", NCT04583735, NCT05002998 (post-marketing, ongoing).

Academic basic and pre-clinical research for the effect of teprotumumab on TED was mainly conducted at the University of Michigan Medical School, the University of Pisa, but also at Hospitals such as the Cedars-Sinai Medical Center (see Table 21). A better understanding of IGF-IR, PTX-3 and TED can be attributed to academic research. Several researchers made significant contributions to the development: Terry Smith (Ludquist Institute, University of Michigan Medical School), Raymond S. Douglas (Ludquist Institute, University of Michigan Medical School, Cedars-Sinai Medical Center) and Alon Kahana (University of Michigan Medical School) led many pivotal studies.

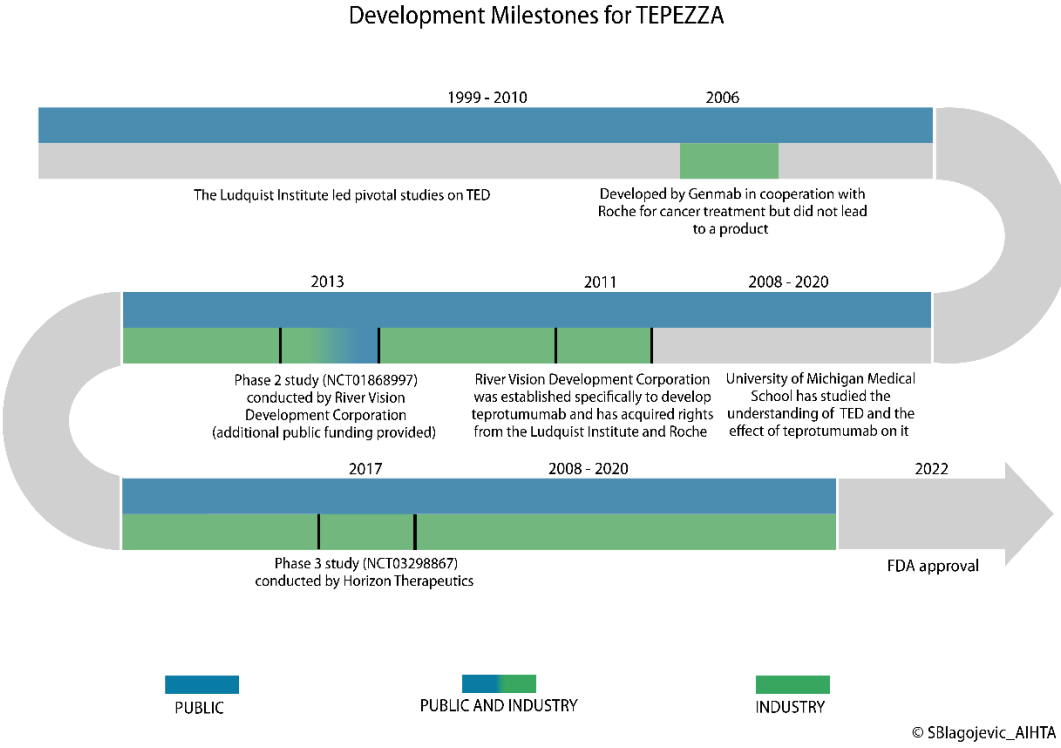

Figure 8: Development Milestones for TEPEZZA

The research sites included both public and private institutions, with a significant presence of academic medical centres and public hospitals mainly in North America (e.g. Cedars-Sinai Medical Center, Kellogg Eye Center at the University of Michigan) and Western Europe (e.g. University of Pisa, Johannes Gutenberg University Medical Center).

Public contributions to drug development

Table 17 in Appendix 2 demonstrates substantial public funding supporting TED-specific research, particularly from the US-state-funded National Eye Institute (NEI) and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). The University of Michigan Medical School has received numerous grants between 2008 and 2020, with funding directed toward projects for understanding the disease and the effect of teprotumumab, accumulating a total funding of roughly $9.4 million. The Ludquist Institute has received roughly $8.6 million in grants from 1999 to 2010 for their research in TED. Additionally, the FDA has awarded River Vision Development Corporation grants of $1.2 million from 2014 to 2016 for a phase 2 study for teprotumumab. In total, we have found roughly $19.3 million of public support, the largest portion of which can be attributed to basic research (roughly $18.1 million).

The University of Pisa made a significant contribution through their understanding of thyroid eye disease pathophysiology and teprotumumab's mechanism of action despite having less direct involvement in teprotumumab development. However, we could not quantify specific public funding allocated to their research efforts.

The Ludquist Institute licensed its patents to River Vision Development Corporation between 2010 and 2012. Two venture capital investors, Lundbeckfonden and S.R. One, each initially held 35.66% rights to future

teprotumumab payments. However, agreements reached in April 2020 reduced these rights significantly, decreasing the Company's (Horizon Therapeutics, now Amgen) payment obligations by 70.25%. Consequently, the two venture capital firms now collectively receive 29.75% of teprotumumab revenues, down from their original 71.32% share.

Under their licensing agreement, River Vision Development Corporation is obligated to pay Roche milestone payments totalling up to CHF103.0 million for teprotumumab development, regulatory approvals, and sales targets. Of this amount, CHF2.0 million was paid in 2017, CHF3.0 million in 2019, and CHF5.0 million in Q1 2020. Additionally, Roche receives tiered royalties ranging from 9% to 12% on annual worldwide net sales.

Company Structure and Financials

River Vision Development Corporation was established in 2011 specifically to develop teprotumumab. The startup secured $17 million in Series A financing in 2012 with support from Narrow River (an investment management company and limited partner) and venture capital firms, including Vivo Capital, Lundbeckfonden BioCapital, and SR One Capital Management. Following promising results from clinical trial NCT01868997, Horizon Therapeutics acquired River Vision Development Corporation in 2017 for $145 million upfront. Subsequently, in 2023, pharmaceutical giant Amgen acquired Horizon Therapeutics for $27.8 billion, ranking as the second-largest pharmaceutical acquisition that year.

The full HTA report with all detailed information on funding amounts can be found here: https://eprints.aihta.at/1560/

Obecabtagene autoleucel (obe-cel)/ AUCATZYL®

Own development costs, acquisitions and licences

Autolus Therapeutics (Autolus, see sub chapter "Company structure and financials") has not published the total amount of research and development (R&D) expenses attributed to obecabtagene autoleucel (obe-cel). Table 13 provides a short overview of obe-cel.

Table 13: AUCATZYL® overview

Originator	Developer	Information on acquisitions	Public contribution	Type of public funding
AUCATZYL® - Active substance Obecabtagene autoleucel (obe-cel)				
University College London	Autolus Therapeutics (formerly Autolus Limited)	Spin-out in 2014: From University College London and Martin Pule as scientific founder License agreement 2014: Exclusive license agreement for T-cell programming modules developed by Martin Pule's team License agreement 2024: Updated licensing agreement between Autolus Limited and UCL	Over €71 million direct and indirect public and philanthropic contributions.	Basic, preclinical and clinical research

Abbreviations: UCL … University College London

Basic research and clinical development

The development of AUCATZYL® (obe-cel) for the treatment of relapsed/refractory B-cell acute lymphoblastic leukaemia (r/r B-ALL) emerged from research at the University College London (UCL), as shown in Table 23. The fundamental chimeric antigen receptor (CAR) T cell research began at the UCL Cancer Institute under the leadership of Martin Pule in the early 2010s, who developed innovative T-cell programming modules and CAR T technologies that would form the basis of Autolus's therapeutic platform [75].

Parallel to UCL, researchers at the University of Texas MD Anderson Cancer Center, primarily Catherine Bollard, studied cord blood transplantation which is highly relevant for obe-cel. Furthermore, a research project "Next Generation T-cell therapies for childhood cancers" (NexTGen) aims at contributing to the broader CAR T field. The Children's Research Institute, University of Texas MD Anderson Cancer Center and the UCL are involved in NexTGen [76].

Public contributions to drug development

Table 18 in Appendix 2 demonstrates extensive public research funding for CAR T development at UCL and collaborating institutions. We identified over €71 million in direct and indirect public (together €55 million) and philanthropic (€16.2 million) funding specifically for CAR T research that contributed to Autolus's technology platform. The largest funding amount of €40 million can be attributed to UCL, followed by €28.3 million for the University of Texas MD Anderson Cancer Center and €2.9 million for the Children's Research Institute (for the individual sources see Table 18).

Martin Pule's research at the UCL received public contributions from national and supranational public institutions: the European Commission (EC) provided substantial support through both the Seventh Framework Programme (€5.9 million for the Advanced T-cell Engineered for Cancer Therapy/ATECT project, 2013–2018) and Horizon Europe (€6 million for CARs for Advanced Therapies/CARAT, 2015–2019). United Kingdom (UK) funding bodies made significant contributions: the National Institute for Health and Care Research (NIHR) Invention for Innovation (i4i) programme provided €3.3 million for phase I/II CAR19 studies, the Welcome Trust invested €2.3 million in CAR T-cell therapy for central nervous system (CNS) lymphoma, and the Medical Research Council (MRC) contributed over €2.7 million through various grants including a major Developmental Pathway Funding Scheme (DPFS) grant of €2.1 million for allogeneic CAR T-cell therapy development. Additionally, a philanthropic organisation also contributed: The Mark Foundation for Cancer Research and Cancer Grand Challenges supported the development of novel immunotherapies for childhood tumours, contributing €13.9 million to advance this research area.

Catherine Bollard at the University of Texas MD Anderson Cancer Center received substantial funding of €28.3 million from the National Cancer Institute (NCI) between 2011 and 2022. The NexTGen project, involving UCL and the Children's Research Institute, received combined funding of over €7 million from the NCI between 2022 and 2024 [76].

The translation from academic research to commercial development occurred through UCL Business (UCLB), UCL's technology transfer company. In 2014, Autolus was spun out from UCL with an exclusive license agreement for T cell programming modules developed by Martin Pule's team. This initial agreement involved 1.5 million ordinary shares, management fees of £120,000, and structured milestone payments totalling up to £104.5 million. The agreement was subsequently amended, with the updated 2024 terms including up to £106.68 million in milestone payments, of which £10 million has been paid following obe-cel's U.S. Food and Drug Administration (FDA) approval. UCLB retains low to mid-single digit royalties on product sales and revenue sharing on sublicenses (not further disclosed).

Strategic partnerships with pharmaceutical companies have been crucial to Autolus's development. In 2024, BioNTech entered a $250 million upfront collaboration, gaining exclusive licenses to certain target binders and options for additional technologies. Blackstone Life Sciences provided $250 million in 2021 to support obe-cel through pivotal trials. Moderna licensed Autolus's targeting technology in 2021 with up to $60 million in milestone payments. We visualised the most relevant development milestones for the development of obe-cel in Figure 9.

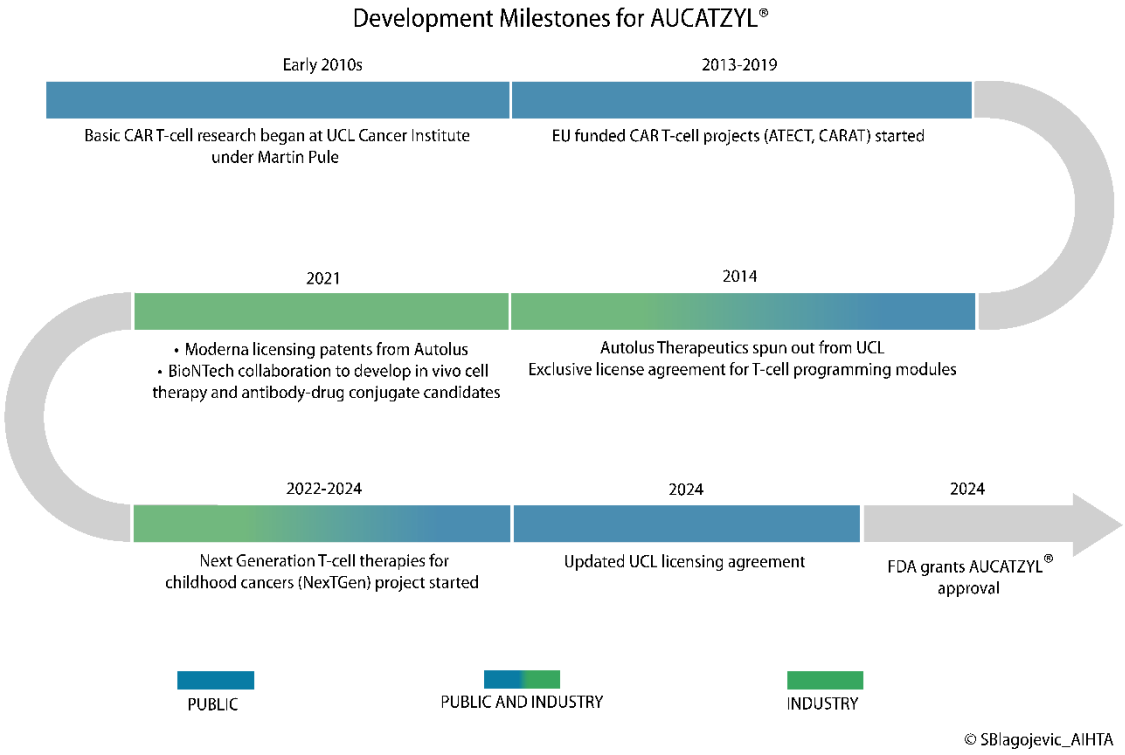

Figure 9: Development milestone for AUCATZYL®

Company structure and financials

Autolus was founded as a spin-out from UCL in 2014, with Martin Pule as the scientific founder and UCLB providing commercialisation support. Since its inception, the company has raised over $1 billion in investment, with most invested in the UK, including the development of a manufacturing facility (The Nucleus in Stevenage) [75].

The company's further financing reflects investor confidence in its CAR T platform. Initial funding came from Syncona with a $45 million Series A financing in 2015 [77], followed by a £40 million Series B from Woodford Investment Management and Perceptive Bioscience in 2016 [78], and a $80 million Series C in 2017 led by Syncona with participation from Nextech Invest, Arix Bioscience, and Woodford [79]. The company went public in 2018 with a $150 million initial public offering (IPO) [80], followed by a $100.8 million follow-on offering in 2019 [81]. Venture capital was the most important type of investor for Autolus.

Patents

The UCL research group, led by original patent holder Martin Pule, developed crucial innovations in receptor design that have become the foundation of Autolus's technology portfolio. These innovations include new suicide genes, novel receptor types, strategies to target T-cell lymphomas, and methods for CAR targeting of multiple antigens simultaneously, all which UCL patented and ultimately licensed to Autolus. As of December 31, 2024, Autolus has built a patent portfolio comprising 83 patent families, with 17 of these originating directly from UCL, reflecting the strong publicly financed academic foundation underlying the company's leading technology [82].

The full HTA report with all detailed information on funding amounts can be found here: https://eprints.aihta.at/1589/

9. Appendix 2

Exagamglogene Autotemcel) (CASGEVY®)

Table 14: Development history, Licensing, Acquisitions and public contributions to Casgevy®

Type of information	Details on collaboration, financing, public funding	Year	Amount (in USD)	Funders/ Investors/ Acquiror	Source
Vertex Pharmaceuticals *Founded:* 1989 *Company type*: Publicly traded *Headquarters:* Boston, Massachusetts, U.S. *Number of employees:* approximately 5,400 employees (as of December 2023) *Operating revenue:* 9.87 billion USD (as of 2023)					
Collaboration with Orum Therapeutics	pre-treatment for gene meds	n.a.	$15 million - up to $945 million	Vertex Pharmaceuticals	https://pharmaphorum.com/news/vertex-orum-partner-safer-pre-treatment-gene-meds
Acqusition	Acquisition of ViaCyte	2022	$320 million	Vertex Pharmaceuticals	https://www.fiercebiotech.com/biotech/vertex-absorbs-viacyte-320m-clearing-out-competition-stem-cell-based-diabetes-treatments
Collaboration that led to Casgevy	Collaboration with CRISPR Therapeutics	2021	$900 million	Vertex Pharmaceuticals	https://www.fiercebiotech.com/biotech/vertex-ups-arbor-ante-potential-1-2b-biobucks-for-crispr-cell-therapies
Collaboration	Collaboration with Arbor Biotechnologies	2021	$1.2 billion	Vertex Pharmaceuticals	https://pharmaphorum.com/news/vertex-builds-in-gene-editing-yet-again-with-1-2bn-arbor-deal https://news.vrtx.com/news-releases/news-release-details/vertex-and-arbor-biotechnologies-establish-collaboration
Collaboration	Collaboration with Obsidian Therapeutics	2021	$75 million	Vertex Pharmaceuticals	https://pharmaphorum.com/news/vertex-eyes-controllable-genetic-drugs-with-1-3bn-obsidian-alliance
Editas Medicines *Founded:* 2013 *Company type*: Publicly traded *Headquarters:* Cambridge, Massachusetts, U.S. *Number of employees:* 265 (as of February 1, 2024) *Operating revenue:* 78.1 million USD (as of 2023)					
Project specific funding	Vector-delivered CRISPR/Cas as a cure for HSV-1-induced keratitis	2015	225.000	National Institute of Allergy and Infectious Diseases	https://reporter.nih.gov/search/7fMvTHuUV06xW3G0sXghHg/project-details/8978393
Licensing	Licensing agreenement for Cas9 gene editing tool	2024	$57 million	DRI Healthcare	https://www.fiercebiotech.com/biotech/editas-cashes-portion-vertex-cas9-licensing-agreement-57m
Licensing	Non-exclusive licensing deal for Editas Medicines' Cas9 gene editing technology for ex vivo gene editing	2023	$100 million + annual payments between $10 million and $40 million until 2034	Vertex Pharmaceuticals	https://www.statnews.com/2023/12/13/editas-vertex-agreement-crispr-cas9/

Type of information	Details on collaboration, financing, public funding	Year	Amount (in USD)	Funders/ Investors/ Acquiror	Source
Research agreement	Developing CRISPR/Cas9-based medicines for cystic fibrosis	2016	$5 million	Cystic Fibrosis Foundation	https://www.biopharmadive.com/news/editas-forges-5-million-crispr-research-deal-with-cystic-fibrosis-foundati/419322/
Research agreement	Research for the use of CRISPR/Cas9 for various types of cancer with guarantees of royalties if products are the result of the research	2015	$47 million	Corporate: Juno Therapeutics	https://www.biospace.com/editas-medicine-juno-therapeutics-hammer-out-727-million-car-t-r-and-d-deal
Financing round	Series B financing	2015	$120 million	Institutional: Casdin Capital, Deerfield, Google Ventures, Khosla Ventures, Viking Global Investors, Polaris Partners, Third Rock Ventures, Flagship Pioneering, Omega Funds Corporate: EcoR1, Fidelity Investments, Jennison Associates, T. Rowe Price, Partners Health Care Innovation Angel: Boris Nikoli	https://www.bioworld.com/articles/326878-editas-lands-120m-to-advance-crispr-cas9-platform-in-oversubscribed-series-b?v=preview
Financing round	Series A financing	2013	$43 million	Institutional: Polaris Partners, Third Rock Ventures, Flagship Pioneering Corporate: Partners Health Care Innovation	https://www.bioworld.com/articles/437460
Broad Institute *Founded:* 2004 *Company type*: Nonprofit research Organisation *Headquarters:* Cambridge, Massachusetts, United States *Number of employees:* n.a. (The Broad Institute's faculty members are all faculty members of MIT, Harvard or one of the Harvard-affiliated hospitals.) *Operating revenue:* n.a.					
Research funding	Research funding with information and first refusal on the developed interventions	2018	up to $125 million	Editas Medicine	https://www.fiercebiotech.com/biotech/editas-commits-125m-to-broad-secure-source-genome-editing-inventions
Licensing	Licensing deal for CRISPR/Cas9	2016	$6.25 million (split between Broad, Harvard University, MIT, Wageningen University, the University of Iowa and the University of Tokyo)	Editas Medicine	https://www.biopharmadive.com/news/editas-locks-down-rights-to-add-on-crispr-tech/432662/
Project specific funding (all research projects	Function of reactive astrocytes in aging and neurodegenerative disease	2024	93.197	NIA	https://reporter.nih.gov/project-details/11080548

Type of information	Details on collaboration, financing, public funding	Year	Amount (in USD)	Funders/ Investors/ Acquiror	Source
that use CRISPR/Cas9 and that have received public contribution).*	Identifying genetic vulnerabilities in KIAA1549-BRAF mutant paediatric low-grade gliomas	2024	78.892	NCI	https://reporter.nih.gov/project-details/10951512
	Development of platforms for sorting, production, editing of beta cells	2024	623.544	NIDDK	https://reporter.nih.gov/project-details/10920460
	Advanced development of the Cancer Dependency Map portal (DepMap.org)	2024	735.340	NCI	https://reporter.nih.gov/project-details/10904866
	Development of methods for highly multiplexed quantification of cancer proteomes using large-scale nanobody libraries	2024	210.516	NCI	https://reporter.nih.gov/project-details/10903802
	Development of p300/CBP histone acetyltransferase inhibitors for oncogene-driven cancers	2024	624.299	NCI	https://reporter.nih.gov/project-details/10843227
	Directed Clonal Evolution of Drug Resistant BRAF Mutant Melanoma for Cross-Sensitization to MAPK Hyperactivation	2024	74.284	NCI	https://reporter.nih.gov/project-details/10826684
	Mechanism of Action of Prion Protein-Lowering Small Molecules	2024	407.400	NINDS	https://reporter.nih.gov/project-details/10815872
	A visible machine learning system to discover targeted treatment solutions in cancer	2024	95.948	NCI	https://reporter.nih.gov/project-details/10806195
	A Chemoproteomic Approach to Identify Molecular Glues for Targeted Cancer Therapy	2024	171.180	NCI	https://reporter.nih.gov/project-details/10797075
	Stitch-seq for genome-wide pooled genomic screening with RNA-seq readout	2024	164.661	NCI	https://reporter.nih.gov/project-details/10792615
	A visible machine learning system to discover targeted treatment solutions in cancer	2023	92.988	NCI	https://reporter.nih.gov/project-details/10784808
	Chemical approaches for precision genome editing	2024	362.632	NIGMS	https://reporter.nih.gov/project-details/10783716
	Identifying genetic vulnerabilities in KIAA1549-BRAF mutant paediatric low-grade gliomas	2023	71.792	NCI	https://reporter.nih.gov/project-details/10752212
	Development of methods for highly multiplexed quantification of cancer proteomes using large-scale nanobody libraries	2023	221.595	NCI	https://reporter.nih.gov/project-details/10714023
	Establishing foundational tools and datasets for investigation of NSD1 gene function in neural development	2023	158.000	OD	https://reporter.nih.gov/project-details/10711291
	Development of platforms for sorting, production, editing of beta cells	2023	691.470	NIDDK	https://reporter.nih.gov/project-details/10682155
	Factors regulating strength and duration of STING signaling	2023	423.643	NIAID	https://reporter.nih.gov/project-details/10677771
	Advanced development of the Cancer Dependency Map portal (DepMap.org)	2023	731.592	NCI	https://reporter.nih.gov/project-details/10666538

Type of information	Details on collaboration, financing, public funding	Year	Amount (in USD)	Funders/ Investors/ Acquiror	Source
	Expanding pharmacological modalities for targeted cancer therapy	2023	101.247	NCI	https://reporter.nih.gov/project-details/10656339
	Investigating epigenetic mechanisms in Down syndrome using human cellular models	2023	2.034.753	OD	https://reporter.nih.gov/project-details/10655152
	Mechanism of Action of Prion Protein-Lowering Small Molecules	2023	395.000	NINDS	https://reporter.nih.gov/project-details/10637745
	Development of p300/CBP histone acetyltransferase inhibitors for oncogene-driven cancers	2023	651.215	NCI	https://reporter.nih.gov/project-details/10627744
	Stitch-seq for genome-wide pooled genomic screening with RNA-seq readout	2023	167.252	NCI	https://reporter.nih.gov/project-details/10620301
	Characterization of structure-function relationships in distinct thalamic reticular nucleus networks	2023	390.000	NIMH	https://reporter.nih.gov/project-details/10615809
	Delineating a role for histone modifications in Down syndrome using human cellular models	2022	285.042	OD	https://reporter.nih.gov/project-details/10595812
	Chemical approaches for precision genome editing	2023	362.632	NIGMS	https://reporter.nih.gov/project-details/10557117
	Factors regulating strength and duration of STING signaling	2022	423.643	NIAID	https://reporter.nih.gov/project-details/10490901
	Advanced development of the Cancer Dependency Map portal (DepMap.org)	2022	774.119	NCI	https://reporter.nih.gov/project-details/10478033
	Advanced tools for HCMI model genetic perturbation and metastasis characterization	2022	787.646	NCI	https://reporter.nih.gov/project-details/10465033
	Expanding the Scope of Base Editing	2022	421.357	OD	https://reporter.nih.gov/project-details/10459380
	Characterization of structure-function relationships in distinct thalamic reticular nucleus networks	2022	390.000	NIMH	https://reporter.nih.gov/project-details/10455621
	Expanding pharmacological modalities for targeted cancer therapy	2022	96.632	NCI	https://reporter.nih.gov/project-details/10416087
	Stitch-seq for genome-wide pooled genomic screening with RNA-seq readout	2022	207.784	NCI	https://reporter.nih.gov/project-details/10413630
	Chemical approaches for precision genome editing	2021	74.047	NIGMS	https://reporter.nih.gov/project-details/10389932
	Chemical approaches for precision genome editing	2022	352.551	NIGMS	https://reporter.nih.gov/project-details/10378157
	Factors regulating strength and duration of STING signaling	2021	423.643	NIAID	https://reporter.nih.gov/project-details/10367563
	Development of p300/CBP histone acetyltransferase inhibitors for oncogene-driven cancers	2022	682.670	NCI	https://reporter.nih.gov/project-details/10344246
	Characterization of structure-function relationships in distinct thalamic reticular nucleus networks	2021	373.200	NIMH	https://reporter.nih.gov/project-details/10279075

Type of information	Details on collaboration, financing, public funding	Year	Amount (in USD)	Funders/ Investors/ Acquiror	Source
	Advanced development of the Cancer Dependency Map portal (DepMap.org)	2021	791.314	NCI	https://reporter.nih.gov/project-details/10252924
	Characterizing TP53 and PPM1D mutations as resistance drivers to radiation therapy in Diffuse Intrinsic Pontine Gliomas	2021	523.271	NCI	https://reporter.nih.gov/project-details/10245071
	Comprehensive functional characterization and dissection of noncoding regulatory elements and human genetic variation	2021	1.496.338	NHGRI	https://reporter.nih.gov/project-details/10241056
	Advanced tools for HCMI model genetic perturbation and metastasis characterization	2021	789.862	NCI	https://reporter.nih.gov/project-details/10229465
	Expanding the Scope of Base Editing	2021	421.536	OD	https://reporter.nih.gov/project-details/10227955
	Chemical approaches for precision genome editing	2021	347.463	NIGMS	https://reporter.nih.gov/project-details/10211408
	High-content optical pooled genome-wide screens of SARS-CoV-2 infection	2020	357.840	NHGRI	https://reporter.nih.gov/project-details/10166221
	CRISPR screens for SARS-CoV-2 Host Factors	2020	440.000	NIAID	https://reporter.nih.gov/project-details/10163544
	Rapid ex vivo biosensor cultures to assess dependencies in gastroesophageal cancer	2021	566.213	NCI	https://reporter.nih.gov/project-details/10115675
	Advanced development of the Cancer Dependency Map portal (DepMap.org)	2020	791.050	NCI	https://reporter.nih.gov/project-details/10058960
	Advanced tools for HCMI model genetic perturbation and metastasis characterization	2020	789.862	NCI	https://reporter.nih.gov/project-details/10005595
	Comprehensive Characterization of Adaptive Regulatory Variation Linked to Human Disease	2020	125.378	NHGRI	https://reporter.nih.gov/project-details/10005404
	Characterizing TP53 and PPM1D mutations as resistance drivers to radiation therapy in Diffuse Intrinsic Pontine Gliomas	2020	517.874	NCI	https://reporter.nih.gov/project-details/9996517
	Expanding the Scope of Base Editing	2020	421.760	OD	https://reporter.nih.gov/project-details/9982216
	Integrating Chemistry and Evolution to Illuminate Biology and Enable Novel Therapeutics	2020	692.073	NIGMS	https://reporter.nih.gov/project-details/9963284
	Arrayed single-cell readout of pooled genetic perturbation libraries	2020	1.112.161	NHGRI	https://reporter.nih.gov/project-details/9960539
	Systematic identification of oncogenic KRAS synthetic lethal interactions	2019	499.996	NCI	https://reporter.nih.gov/project-details/9952702
	Comprehensive functional characterization and dissection of noncoding regulatory elements and human genetic variation	2020	1.496.387	NHGRI	https://reporter.nih.gov/project-details/9952404
	Center for Cell Circuits	2020	2.800.000	NHGRI	https://reporter.nih.gov/project-details/9952395
	Programmable RNA-targeting tools	2020	1.124.060	NHGRI	https://reporter.nih.gov/project-details/9951080

Type of information	Details on collaboration, financing, public funding	Year	Amount (in USD)	Funders/ Investors/ Acquiror	Source
	Rapid ex vivo biosensor cultures to assess dependencies in gastroesophageal cancer	2020	566.213	NCI	https://reporter.nih.gov/project-details/9946259
	Discovery of compounds and genes that regulate cancer's epigenome, using combinatorial screening in a nanodrop-microwell platform	2020	29.860	NCI	https://reporter.nih.gov/project-details/9852879
	Comprehensive Characterization of Adaptive Regulatory Variation Linked to Human Disease	2019	124.916	NHGRI	https://reporter.nih.gov/project-details/9805238
	Characterizing TP53 and PPM1D mutations as resistance drivers to radiation therapy in Diffuse Intrinsic Pontine Gliomas	2019	497.259	NCI	https://reporter.nih.gov/project-details/9781662
	Expanding the Scope of Base Editing	2019	422.147	OD	https://reporter.nih.gov/project-details/9768957
	Comprehensive functional characterization and dissection of noncoding regulatory elements and human genetic variation	2019	1.497.668	NHGRI	https://reporter.nih.gov/project-details/9766882
	Massively-parallel functional interrogation of psychiatric genetics	2019	1.093.342	NIMH	https://reporter.nih.gov/project-details/9749919
	Arrayed single-cell readout of pooled genetic perturbation libraries	2019	1.120.845	NHGRI	https://reporter.nih.gov/project-details/9736763
	Programmable RNA-targeting tools	2019	1.140.080	NHGRI	https://reporter.nih.gov/project-details/9719879
	Comprehensive functional characterization and dissection of noncoding regulatory elements and human genetic variation	2018	933.353	NHGRI	https://reporter.nih.gov/project-details/9696513
	Center for Cell Circuits	2019	2.800.000	NHGRI	https://reporter.nih.gov/project-details/9692736
	Integrating Chemistry and Evolution to Illuminate Biology and Enable Novel Therapeutics	2019	692.434	NIGMS	https://reporter.nih.gov/project-details/9689014
	Discovery of compounds and genes that regulate cancer's epigenome, using combinatorial screening in a nanodrop-microwell platform	2019	61.610	NCI	https://reporter.nih.gov/project-details/9683440
	Expanding the Scope of Base Editing	2018	422.361	OD	https://reporter.nih.gov/project-details/9675825
	Systematic Mapping of the Functional Common Noncoding Variants in the TNFAIP3 Locus	2019	65.606	NIAID	https://reporter.nih.gov/project-details/9628643
	Continuous Evolution of Proteins with Novel Therapeutic Potential	2019	451.488	NIBIB	https://reporter.nih.gov/project-details/9620618
	Comprehensive functional characterization and dissection of noncoding regulatory elements and human genetic variation	2018	500.000	NHGRI	https://reporter.nih.gov/project-details/9564177
	Arrayed single-cell readout of pooled genetic perturbation libraries	2018	1.073.196	NHGRI	https://reporter.nih.gov/project-details/9553855
	Programmable RNA-targeting tools	2018	1.139.738	NHGRI	https://reporter.nih.gov/project-details/9546834

Type of information	Details on collaboration, financing, public funding	Year	Amount (in USD)	Funders/ Investors/ Acquiror	Source
	Systematic identification of oncogenic KRAS synthetic lethal interactions	2018	807.776	NCI	https://reporter.nih.gov/project-details/9538605
	Characterizing TP53 and PPM1D mutations as resistance drivers to radiation therapy in Diffuse Intrinsic Pontine Gliomas	2018	507.552	NCI	https://reporter.nih.gov/project-details/9512814
	Massively-parallel functional interrogation of psychiatric genetics	2018	1.092.930	NIMH	https://reporter.nih.gov/project-details/9509556
	Center for Cell Circuits	2018	2.800.000	NHGRI	https://reporter.nih.gov/project-details/9493509
	Integrating Chemistry and Evolution to Illuminate Biology and Enable Novel Therapeutics	2017	618.244	NIGMS	https://reporter.nih.gov/project-details/9492988
	Continuous Evolution of Proteins with Novel Therapeutic Potential	2017	304.001	NIBIB	https://reporter.nih.gov/project-details/9484392
	Integrating Chemistry and Evolution to Illuminate Biology and Enable Novel Therapeutics	2018	692.783	NIGMS	https://reporter.nih.gov/project-details/9469527
	Systematic Mapping of the Functional Common Noncoding Variants in the TNFAIP3 Locus	2018	61.174	NIAID	https://reporter.nih.gov/project-details/9451927
	Epigenomic, transcriptional and cellular dissection of Alzheimer's variants	2017	1.527.396	NIA	https://reporter.nih.gov/project-details/9440479
	Continuous Evolution of Proteins with Novel Therapeutic Potential	2018	451.488	NIBIB	https://reporter.nih.gov/project-details/9419171
	Programmable RNA-targeting tools	2017	1.095.702	NHGRI	https://reporter.nih.gov/project-details/9379750
	Arrayed single-cell readout of pooled genetic perturbation libraries	2017	1.128.407	NHGRI	https://reporter.nih.gov/project-details/9379592
	Characterizing TP53 and PPM1D mutations as resistance drivers to radiation therapy in Diffuse Intrinsic Pontine Gliomas	2017	502.615	NCI	https://reporter.nih.gov/project-details/9368268
	Systematic identification of oncogenic KRAS synthetic lethal interactions	2017	807.776	NCI	https://reporter.nih.gov/project-details/9330127
	Massively-parallel functional interrogation of psychiatric genetics	2017	1.097.505	NIMH	https://reporter.nih.gov/project-details/9310141
	Center for Cell Circuits	2017	2.800.000	NHGRI	https://reporter.nih.gov/project-details/9278246
	Network-based prediction and validation of causal schizophrenia genes and variants	2017	475.347	NIMH	https://reporter.nih.gov/project-details/9264586
	Systematic Mapping of the Functional Common Noncoding Variants in the TNFAIP3 Locus	2017	57.066	NIAID	https://reporter.nih.gov/project-details/9258074
	Non-coding genetic variants that impact immune phenotypes and diseases	2017	870.349	NHGRI	https://reporter.nih.gov/project-details/9249624
	Comprehensive functional characterization and dissection of noncoding regulatory elements and human genetic variation	2017	654.000	NHGRI	https://reporter.nih.gov/project-details/9247640

Type of information	Details on collaboration, financing, public funding	Year	Amount (in USD)	Funders/ Investors/ Acquiror	Source
	Systematic identification of oncogenic KRAS synthetic lethal interactions	2016	807.776	NCI	https://reporter.nih.gov/project-details/9150537
	Massively-parallel functional interrogation of psychiatric genetics	2016	1.061.900	NIMH	https://reporter.nih.gov/project-details/9147643
	Massively-parallel functional interrogation of psychiatric genetics	2016	1.061.900	OD	https://reporter.nih.gov/project-details/9147643
	Network-based prediction and validation of causal schizophrenia genes and variants	2016	424.175	NIMH	https://reporter.nih.gov/project-details/9108677
	Center for Cell Circuits	2016	3.700.000	NHGRI	https://reporter.nih.gov/project-details/9070877
	Non-coding genetic variants that impact immune phenotypes and diseases	2016	871.466	NHGRI	https://reporter.nih.gov/project-details/9052201
	Genome engineering tools for functional screening of non-coding elements	2016	25.020	NHGRI	https://reporter.nih.gov/project-details/8974432
	Systematic identification of oncogenic KRAS synthetic lethal interactions	2015	817.805	NCI	https://reporter.nih.gov/project-details/8966918
	Genome engineering tools for functional screening of non-coding elements	2015	99.937	NHGRI	https://reporter.nih.gov/project-details/8804084
CRISPR Therapeutics *Founded:* 2013 *Company type*: Public *Headquarters:* Boston, Massachusetts, U.S. *Number of employees:* 407 (as of December 31, 2023) *Operating revenue:* 443 million USD (as of 2023)					
Licensing	Development partnership	2021	$900 million	Vertex Pharmaceuticals	https://www.fiercebiotech.com/biotech/vertex-takes-lead-crispr-therapeutics-partnership-900m-upfront
Financing round	Series B	2016	$38 million	Institutional: New Leaf Venture Partners, Leaps by Bayer Corporate: Vertex Pharmaceuticals, Franklin Templeton Investments, Wellington Facilitator: Guggenheim Partners, VISCHER, Goodwin	https://www.fiercebiotech.com/biotech/crispr-therapeutics-adds-38m-to-series-b-pot-but-lags-behind-parker
Financing round	Series A and Series B	2014	$64 million	Institutional: SR One, New Enterprise Associates, Abingworth, Versant Ventures Institutional: Abingworth, Versant Ventures, New Enterprise Associates Corporate: Celgene	https://www.biospace.com/despite-patent-battle-worth-billions-crispr-raises-64-million-in-series-a-and-b-rounds

Type of information	Details on collaboration, financing, public funding	Year	Amount (in USD)	Funders/ Investors/ Acquiror	Source
Financing round	Series A	2014	$25 million	Institutional: Versant Ventures	https://www.fiercebiotech.com/r-d/an-international-biotech-tackles-crispr-gene-editing-tech-25m-bankroll

Legend:

HHS = United States Department of Health and Human Services

NIA = National Institute on Aging

NCI = National Cancer Institute

NHGRI = National Human Genome Research Institute

NIMH = National Institute of Mental Health

OD = NIH Office of the Director

NIDDKD = National Institute of Diabetes and Digestive and Kidney Diseases

NINDS = National Institute of Neurological Disorders and Stroke

NIGMS = National Institute of General Medical Sciences

NIBIB = National Institute Of Biomedical Imaging And Bioengineering

NIAID = National Institute of Allergy and Infectious Diseases

*= Basic research that used CRISPR/Cas9 but not specifically for sickle cell disease or ß-thalassemia. However, findings may have contributed to the understanding needed for Exa-cel

Public contributions to Fidanacogene Elaparvovec (BEQVEZ®)

Table 15: Development history, Licensing, Acquisitions and public contributions to Beqvez®

Type of financing	Details on collaboration, financing, public funding	Year	Amount (in USD)	Funders/ Investors/ Acquiror	Source
Spark Therapeutics					
Licensing	Spark Therapeutics and CombiGene AB ('Combi-Gene') announced the signing of an exclusive collaboration and licensing agreement for CombiGene's CG01 project, an investigational gene therapy which aims to treat drug resistant focal epilepsy.	2021	n.a.	n.a.	https://www.biospace.com/spark-therapeutics-and-combigene-enter-into-exclusive-global-licensing-agreement-for-gene-therapy-candidate-cg01
Acquisition	Roche bought Spark for $4.3 billion, triggering its move into the gene therapy arena.	2019	$4.3 bn	Roche	https://www.fiercepharma.com/pharma/pfizer-scores-fda-nod-hemophilia-b-gene-therapy-will-charge-35m-dose
Licensing	Spark sells regulatory fast pass to Jazz for $110M Spark Therapeutics has sold a priority review voucher (PRV) to Jazz Pharmaceuticals for $110 million, according to a Monday disclosure	2018	$110 mio	Spark Therapeutics/ Jazz	https://www.biopharmadive.com/news/spark-sells-regulatory-fast-pass-to-jazz-for-110m/522475/
Public offering	Spark Therapeutics Announces Pricing of $350 Million Public Offering	2017	$350 mio	Funding by private investors/ Organisations	https://www.biospace.com/spark-therapeutics-announces-pricing-of-350-0-million-public-offering
Acquisition	Trinity's Gene Medicine Spin Off Genable Technologies Sold to Spark Therapeutics Shareholders in Genable Technologies received $6 million following the sale, along with 265,000 shares of Spark common stock. Additional financial terms were not disclosed.	2016	$6 mio	Spark Therapeutics	https://www.tcd.ie/news_events/articles/trinitys-gene-medicine-spin-off-genable-technologies-sold-to-spark-therapeutics/ https://www.fiercebiotech.com/biotech/spark-therapeutics-announces-acquisition-of-genable-technologies
Initial Public Offering (IPO)	Spark Therapeutics ($ONCE), at work on one-time treatments for rare diseases, pulled off a $161 million IPO, pricing above its range and keeping biotech's Wall Street hot streak rolling.	2015	$161 mio	Investment	https://www.fiercebiotech.com/r-d/spark-nails-a-161m-ipo-to-fund-its-breakthrough-gene-therapy
Licensing	In 2014, Pfizer kicked off its gene therapy program, paying $20 million upfront and $260 million in potential milestones to Spark for the product, with an agreement that the Philadelphia gene therapy specialist would handle phase 1 and 2 development and Pfizer would take it from there.	2014	$20 mio + $260 mio	Spark Therapeutics/ Pfizer	https://www.fiercepharma.com/pharma/pfizer-scores-fda-nod-hemophilia-b-gene-therapy-will-charge-35m-dose
Series A financing	Spark Therapeutics Launched with $50 Million in Financing to Advance Late- and Mid-Stage Gene Therapy Programs with Clinical Proof of Concept	2013	$50 mio	The Children's Hospital of Philadelphia (CHOP)	https://www.prnewswire.com/news-releases/spark-therapeutics-launched-with-50-million-in-financing-to-advance-late--and-mid-stage-gene-therapy-programs-with-clinical-proof-of-concept-228752221.html

					https://www.fiercebiotech.com/venture-capital/gene-therapy-upstart-launches-50m-and-long-term-commercial-goals
Series B financing	Spark Therapeutics Raises $72.8 Million in Oversubscribed Financing	2014	$72.8 mio	Sofinnova Ventures	https://www.prnewswire.com/news-releases/spark-therapeutics-raises-728-million-in-oversubscribed-financing-260806381.html
Children's Hospital of Philadelphia					
Project specific funding (all research projects that are for the treatment of Hemophilia B using gene therapies)	Biochemistry of Intrinsic Xase	2022	732.776	NHLBI	https://reporter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/10439608
	Biochemistry of Intrinsic Xase	2021	732.776	NHLBI	https://reporter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/10175003
	Rational Development of Bioengineered Factor IX Variants for Hemophilia B Therapy	2021	159.408	NHLBI	https://reporter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/10083221
	Biochemistry of Intrinsic Xase	2020	495.230	NHLBI	https://reporter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/9846245
	Rational Development of Bioengineered Factor IX Variants for Hemophilia B Therapy	2020	159.408	NHLBI	https://reporter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/9846245
	Novel factor VIII variants for improved efficacy in gene therapy for hemophilia A	2020	420.000	NHLBI	https://reporter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/9844491
	Biochemistry of Intrinsic Xase	2019	426.871	NHLBI	https://reporter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/9769860
	Rational Development of Bioengineered Factor IX Variants for Hemophilia B Therapy	2019	159.408	NHLBI	https://reporter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/9846245
	Novel factor VIII variants for improved efficacy in gene therapy for hemophilia A	2019	420.000	NHLBI	https://reporter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/9618256
	Rational Development of Bioengineered Factor IX Variants for Hemophilia B Therapy	2018	159.408	NHLBI	https://reporter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/9637419
	Biochemistry of Intrinsic Xase	2018	430.000	NHLBI	https://reporter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/9416300
	Novel factor VIII variants for improved efficacy in gene therapy for hemophilia A	2018	420.000	NHLBI	https://reporter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/9391192
	Novel factor VIII variants for improved efficacy in gene therapy for hemophilia A	2017	420.000	NHLBI	https://reporter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/9198569
	Novel factor VIII variants for improved efficacy in gene therapy for hemophilia A	2016	420.000	NHLBI	https://reporter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/9027334
	Gene Therapy for Hemophilia Using Muscle-Expressed FVIIa	2015	450.208	NHLBI	https://reporter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/8876764
	Novel Therapy for Hemophilia B Using AAV-FIX Variants	2015	511.160	NHLBI	https://reporter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/8876763
	Gene Therapy for Hemophilia	2015	2.046.831	NHLBI	https://reporter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/8876762
	Gene Therapy for Hemophilia Using Muscle-Expressed FVIIa	2014	446.131	NHLBI	https://reporter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/8691968
	Novel Therapy for Hemophilia B Using AAV-FIX Variants	2014	507.191	NHLBI	https://reporter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/8691967
	Gene Therapy for Hemophilia	2014	2.026.513	NHLBI	https://reporter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/8691966
	Gene Therapy for Hemophilia Using Muscle-Expressed FVIIa	2013	430.683	NHLBI	https://reporter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/8502301
	Novel Therapy for Hemophilia B Using AAV-FIX Variants	2013	493.617	NHLBI	https://reporter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/8502298
	Gene Therapy for Hemophilia	2013	1.963.829	NHLBI	https://reporter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/8502297
	Gene Therapy for Hemophilia Using Muscle-Expressed FVIIa	2012	450.426	NHLBI	https://reporter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/8379637
	Novel Therapy for Hemophilia B Using AAV-FIX Variants	2012	532.996	NHLBI	https://reporter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/8379634
	Gene Therapy for Hemophilia	2012	2.069.413	NHLBI	https://reporter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/8313853
	Animal Core for Gene Therapy of Hemophilia	2011	346.339	NHLBI	https://reporter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/8185350
	Gene Therapy for Hemophilia Using Muscle-Expressed FVIIa	2011	371.508	NHLBI	https://reporter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/8185314

	Novel Therapy for Hemophilia B Using AAV-FIX Variants	2011	384.370	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/8185311
	Gene Therapy for Hemophilia	2011	1.951.418	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/8153509
	CORE--Canine	2009	179.397	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/7817146
	Safety & Efficacy of Intravas. Del. of AAV-F.IX to Skeletal Muscle	2009	367.300	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/7817144
	Intravascular Delivery of AAV to Skeletal Muscle	2009	558.266	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/7817143
	CORE--Canine	2008	173.966	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/7617705
	Safety & Efficacy of Intravas. Del. of AAV-F.IX to Skeletal Muscle	2008	349.395	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/7617703
	Molecular engineering of factor VIII gene for rAAV delivery	2009	74.025	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/7546648
	AAV2-F.IX Hepatic Gene Transfer under Immunomodulation	2008	371.214	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/7435223
	CORE--Canine	2007	217.398	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/7417868
	Safety & Efficacy of Intravas. Del. of AAV-F.IX to Skeletal Muscle	2007	345.664	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/7417866
	Molecular engineering of factor VIII gene for rAAV delivery	2008	364.302	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/7371308
	CORE--Canine	2006	212.652	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/7312516
	AAV2-F.IX Hepatic Gene Transfer under Immunomodulation	2007	362.364	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/7246535
	AAV2-F.IX Hepatic Gene Transfer under Immunomodulation	2006	380.350	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/7078208
	Study in Hem B using vector to deliver gene for human factor IX into liver	2004	6.029	NCRR	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/7041815
	CORE--Canine	2005	225.281	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/6959252
	Immunology of Factor IX Gene Transfer to Liver	2005	82.809	NIAID	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/6861051
	AAV mediated muscle directed gene therapy for Hemophilia B	2004	482.240	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/6832799
	Immunology of Factor IX Gene Transfer to Liver	2004	297.500	NIAID	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/6704238
	Gene therapy for Hemophilia	2004	1.464.576	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/6700770
	Gene therapy for Hemophilia	2003	1.522.334	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/6640706
	Immunology of Factor IX Gene Transfer to Liver	2003	297.500	NIAID	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/6622916
	Gene therapy for Hemophilia	2002	1.579.875	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/6556362
	Gene therapy for Hemophilia	2001	82.212	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/6497029
	Immunology of Factor IX Gene Transfer to Liver	2002	291.200	NIAID	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/6459176
	Immune Tolerance to Factor IX in Hemophilia B	2002	44.212	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/6446532
	Human application of AAV mediated muscle directed factor IX gene transfer	2001	380.508	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/6410597
	AAV mediated muscle directed gene therapy for Hemophilia B	2001	380.508	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/6410594
	Inhibitor formation in gene therapy for Hemophilia	2001	295.413	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/6390210
	Gene therapy for Hemophilia	2001	1.863.373	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/6330198

	Human application of AAV mediated muscle directed factor IX gene transfer	2000	253.126	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/6313241
	AAV mediated muscle directed gene therapy for Hemophilia B	2000	25.981	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/6313238
	Inhibitor formation in gene therapy for Hemophilia	2000	295.413	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/6184564
	Gene therapy for Hemophilia	2000	1.959.275	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/6041488
	Inhibitor formation in gene therapy for Hemophilia	1999	303.325	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/6056585
	Novel strategies for gene therapy of Hemophilia B	1998	427.583	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/2771392
	Inhibitor formation in gene therapy for Hemophilia	1998	306.250	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/2762478
	Novel strategies for gene therapy of Hemophilia B	1997	411.139	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/2519457
	Novel strategies for gene therapy of Hemophilia B	1995	380.857	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/2231711
	Novel strategies for gene therapy of Hemophilia B	1994	336.492	NHLBI	https://re-porter.nih.gov/search/Ho2n35ZqUU2GUSY9g4bTRQ/project-details/2231710
St. Jude Children's Research Hospital					
Project specific funding (all research projects that are for the treatment of Hemophilia B using gene therapies)	AAV-Mediated Gene Therapy for Hemophilia	2015	533.454	NHLBI	https://reporter.nih.gov/search/rJSt-lJUSoUOm5kGOIH_KNA/project-details/8882512
	AAV-Mediated Gene Therapy for Hemophilia	2014	522.961	NHLBI	https://reporter.nih.gov/search/rJSt-lJUSoUOm5kGOIH_KNA/project-details/8677943
	AAV-Mediated Gene Therapy for Hemophilia	2013	508.019	NHLBI	https://reporter.nih.gov/search/rJSt-lJUSoUOm5kGOIH_KNA/project-details/8501629
	Clinical trial of self complementary AAV8-mediated gene transfer for hemophilia B	2013	607.042	NHLBI	https://reporter.nih.gov/search/rJSt-lJUSoUOm5kGOIH_KNA/project-details/8389602
	AAV-Mediated Gene Therapy for Hemophilia	2012	545.594	NHLBI	https://reporter.nih.gov/search/rJSt-lJUSoUOm5kGOIH_KNA/project-details/8287104
	Clinical trial of self complementary AAV8-mediated gene transfer for hemophilia B	2012	652.476	NHLBI	https://reporter.nih.gov/search/rJSt-lJUSoUOm5kGOIH_KNA/project-details/8231434
	AAV-Mediated Gene Therapy for Hemophilia	2011	548.387	NHLBI	https://reporter.nih.gov/search/rJSt-lJUSoUOm5kGOIH_KNA/project-details/8115643
	Clinical trial of self complementary AAV8-mediated gene transfer for hemophilia B	2011	782.602	NHLBI	https://reporter.nih.gov/search/rJSt-lJUSoUOm5kGOIH_KNA/project-details/7995962
	Clinical trial of self complementary AAV8-mediated gene transfer for hemophilia B	2010	780.538	NHLBI	https://reporter.nih.gov/search/rJSt-lJUSoUOm5kGOIH_KNA/project-details/7754692
	rAAV-Mediated Gene Therapy for Hemophillia B	2009	355.568	NHLBI	https://reporter.nih.gov/search/rJSt-lJUSoUOm5kGOIH_KNA/project-details/7616449
	Clinical trial of self complementary AAV8-mediated gene transfer for hemophilia B	2009	827.663	NHLBI	https://reporter.nih.gov/search/rJSt-lJUSoUOm5kGOIH_KNA/project-details/7565700
	rAAV-Mediated Gene Therapy for Hemophillia B	2008	355.568	NHLBI	https://reporter.nih.gov/search/rJSt-lJUSoUOm5kGOIH_KNA/project-details/7413581
	rAAV-Mediated Gene Therapy for Hemophillia B	2007	355.568	NHLBI	https://reporter.nih.gov/search/rJSt-lJUSoUOm5kGOIH_KNA/project-details/7228815
	rAAV-Mediated Gene Therapy for Hemophillia B	2006	366.188	NHLBI	https://reporter.nih.gov/search/rJSt-lJUSoUOm5kGOIH_KNA/project-details/7058847
	rAAV-Mediated Gene Therapy for Hemophillia B	2005	375.000	NHLBI	https://reporter.nih.gov/search/rJSt-lJUSoUOm5kGOIH_KNA/project-details/6869183

NHLBI = National Heart Lung and Blood Institute
NCRR = National Center for Research Resources
NIAID = National Institute of Allergy and Infectious Diseases

Public contributions to Teprotumumab (TEPEZZA®)

Table 16: Development history, Licensing, Acquisitions and public contributions to Tepezza®

Type of financing	Details on collaboration, financing, public funding	Year	Amount (in USD)	Funders/ Investors/ Acquiror	Source
Horizon Therapeutics					
Acquisition	Amgen Completes $27.8B Horizon Acquisition Following FTC Challenge	2023	Acquisition for $27.8B	Amgen	https://www.biospace.com/amgen-completes-27-8b-horizon-therapeutics-acquisition-following-ftc-challenge
Acquisition	Horizon Therapeutics has struck a $3 billion deal to buy AstraZeneca spinout Viela Bio. The takeover will give Horizon a clutch of clinical-phase autoimmune and inflammatory disease drug candidates, R&D capabilities and an approved monoclonal antibody.	2021	$ 3B	AstraZeneca	https://www.fiercebiotech.com/biotech/horizon-inks-3b-deal-to-buy-astrazeneca-spinut-viela-for-autoimmune-drugs

Type of financing	Details on collaboration, financing, public funding	Year	Amount (in USD)	Funders/ Investors/ Acquiror	Source
Acquisition	Horizon is putting up $65 million in cash to acquire a drug product manufacturing plant from OPKO Health's EirGen Pharma, the company said in a release. The 44,000-square-foot facility in Waterford, Ireland, comes equipped with a filling line and lyophilizer—or freeze dryer—that the company is eyeing for production of its commercial rare disease meds Tepezza, Krystexxa and Uplizna, plus its pipeline of biologics. The plant also boasts analytical laboratory capabilities, Horizon said.	2021	$ 65M	OPKO Health's EirGen Pharma	https://www.fiercepharma.com/manufacturing/horizon-lays-out-65m-for-house-manufacturing-plant-as-its-eye-med-tepezza-resets
Licensing	Halozyme has struck a licensing deal worth upward of $190 million with Horizon Therapeutics, granting the drugmaker access to Halozyme's Enhanze drug delivery platform. Horizon will tap Enhanze to develop a subcutaneous formulation of its thyroid eye disease med Tepezza (teprotumumab-trbw), the companies said in a release.	2020	Up to $190M	Access to Halozyme's Enhanze drug delivery platform	https://www.fiercepharma.com/drug-delivery/horizon-pays-halozyme-190m-to-develop-subq-thyroid-eye-disease-med
Acquisition	Horizon Pharma Plc to acquire River Vision Development Corp Horizon Pharma Plc - deal for upfront cash payment of $145 million	2017	$ 145M	Acquisition of River Vision Development Corp	https://www.reuters.com/article/business/horizon-pharma-plc-to-acquire-river-vision-development-corp-idUSASA09NMZ/
Acquisition	Ireland's Horizon Pharma ($HZNP) will pay a 21% premium for California-based Raptor Pharmaceutical as it looks to bolster its rare disease portfolio while also expanding its geographical footprint. But it will also gain a tough pipeline that has been hit by failures over the past year. The deal, which is worth $9 a share--or around $800 million--will see Horizon gain access to Procysbi (cysteamine bitartrate) for the orphan condition nephropathic (kidney) cystinosis, as well as Quinsair, which is licensed in Europe and Canada to help manage chronic pulmonary infections due to Pseudomonas aeruginosa in patients with cystic fibrosis.	2016	$ 800M	Acquisition of Raptor Pharmaceutical	https://www.fiercebiotech.com/biotech/horizon-pharma-800m-raptor-rare-disease-buy-but-pipeline-beset-by-failures
Acquisition	Horizon Pharma Buys Crealta Holdings for $510M	2015	$ 510M	Acquisition of Crealta Holdings	https://www.genengnews.com/topics/drug-discovery/horizon-pharma-buys-crealta-holdings-for-510m/
Acquisition	Horizon Pharma Acquires Hyperion Therapeutics and Its Revenue-Boosting Pipeline for $1.1B	2015	$ 1.1BN	Acquisition of Hyperion Therapeutics	https://www.biospace.com/horizon-pharma-acquires-hyperion-therapeutics-and-its-revenue-boosting-pipeline-for-1-1b
Acquisition	Horizon Pharma to Acquire Vidara Therapeutics International Ltd. and Become Horizon Pharma plc. Vidara Therapeutics International Ltd. (Vidara) today announced they have entered into a definitive agreement under which Horizon Pharma will acquire Vidara through a reverse merger for stock and cash valued at approximately $660 million	2014	$ 660M	Acquisition of Vidara Therapeutics International Ltd.	https://www.fiercepharma.com/pharma/horizon-pharma-to-acquire-vidara-therapeutics-international-ltd-and-become-horizon-pharma
Financing	JMP Securities LLC, Cowen and Company, LLC and Stifel Nicolaus Weisel	2012	$ 50.8M	Private placement joint-lead placement agents were from JMP Securities LLC, Cowen and Company, LLC and Stifel Nicolaus Weisel	https://www.fiercebiotech.com/biotech/horizon-pharma-announces-50-8-million-private-placement
Initial Public Offering	Horizon Pharma, Inc. (NASDAQ: HZNP) today announced the pricing of its initial public offering of 5,500,000 shares of common stock at a price to the public of $9.00 per share. Horizon's common stock is scheduled to begin trading on The NASDAQ Global Market on July 28, 2011 under the symbol "HZNP." Horizon has also granted the underwriters a 30-day option to purchase up to an additional 825,000 shares at the initial public offering price to cover overallotments, if any.	2011	n.a. (share 5.5 M shares á $9)	Stifel Nicolaus Weisel, Cowen and Company and JMP Securities LLC act as join bookrunners for the offering	https://www.biospace.com/horizon-pharma-inc-announces-pricing-of-its-initial-public-offering
Merger	Horizon Therapeutics and Nitec Pharma Complete Merger and Combine Businesses	2010	n.a.	Horizon Therapeutics and Nitec Pharma merger	https://www.prnewswire.com/news-releases/horizon-therapeutics-and-nitec-pharma-complete-merger-and-combine-businesses-89705152.html
Series A – C Financing	Horizon Therapeutics, Inc., a privately held biopharmaceutical company, today announced that it has closed a $30 million Series C financing to advance the development of its lead investigational product candidate HZT-501 and pipeline of other "GI-friendly" prescription non-steroidal anti-inflammatory drugs (NSAID). Essex Woodlands Health Ventures (EWHV) led the round with participation from existing investors Scale Venture Partners, Sutter Hill Ventures and Pequot Ventures. Horizon has previously raised $21 million in equity funding.	2007	$ 51M	Essex Woodlands Health Ventures (EWHV)/ Scale Venture Partners, Sutter Hill Ventures and Pequot Ventures	https://www.biospace.com/horizon-therapeutics-completes-30-million-equity-financing-to-advance-pipeline-of-gi-friendly-nsaids-for-mild-to-moderate-pain
River Vision Development Corporation					
Series A financing	River Vision Announces Completion of $17 million Series A Financing	2012	$ 17M	SR One, Lundbeckfonden	https://www.fiercebiotech.com/biotech/river-vision-announces-completion-of-17-million-series-a-financing
Rights to TEPEZZA revenue	S.R. One and Lundbeckfonden, as two of the former River Vision stockholders, both held rights to receive approximately 35.66% of any future TEPEZZA payments. As a result of the Company's agreements with S.R. One and Lundbeckfonden in April 2020, the Company's remaining net	n.a.	35.66% of any future TEPEZZA payments (each but reduced in 2020)	S.R. One, Lundbeckfonden	https://www.sec.gov/Archives/edgar/data/1492426/000156459021007818/R21.htm

Type of financing	Details on collaboration, financing, public funding	Year	Amount (in USD)	Funders/ Investors/ Acquiror	Source
	obligations to make TEPEZZA payments for sales milestones and royalties to the former stockholders of River Vision was reduced by approximately 70.25%, after including payments to a third party.				
Licensing deal	The Lundquist Institute licensed the treatment of thyroid eye disease to River Vision Development Corporation	n.a.	n.a.	The Lundquist Institute	https://lundquist.org/news/technologies-first-created-lundquist-institute-achieve-3rd-fda-approval-5-years
Licensing agreement	Under the Company's license agreement with Roche, the Company is required to pay Roche up to CHF103.0 million upon the attainment of various development, regulatory and sales milestones for TEPEZZA. During the years ended December 31, 2019 and 2017, CHF3.0 million and CHF2.0 million, respectively, was paid in relation to these milestones. The Company made a milestone payment of CHF5.0 million) during the first quarter of 2020. The agreement with Roche also includes tiered royalties on annual worldwide net sales between 9 and 12 percent	Up to CHF103 M	CHF103.0 M	Roche	https://www.sec.gov/Archives/edgar/data/1492426/000156459021007818/R21.htm
University of Michigan Medical School (Raymond S Douglas, Terry J Smith, Alon Rahene)					
Basic research	**Immune Activation of Fibroblasts**	2008	$71,770	NEI	https://reporter.nih.gov/search/UtBDEmD1YUGC4BP4Lwubfg/project-details/7935001
	The role of CD40+ fibrocytes in thyroid associated ophthalmopathy	2011-2015	$1,899,067	NEI	https://reporter.nih.gov/search/klRL-MIHTDUicDFC6NV2B1g/projects
	Regulation of Retroocular Connective Tissue	2008-2020 (break in 2009-2010 & 2016)	$3,663,799	NEI	https://reporter.nih.gov/search/IrTGrU_8dEeOK-JGkycxtNA/projects
	Functional Diversity of Orbital Fibroblasts	2009-2011	$1,226,098	NEI	https://reporter.nih.gov/search/oKC38798b0G5tT_Biowa8g/projects
	Immunoglobulin Activation of Fibroblasts	2009-2012	$1,504,236	NIDDK	https://reporter.nih.gov/search/Kkoe67cxFkSrwR0aTTJjqQ/projects
	A zebrafish model for studying orbital development and disease	2008-2012	$1,079,481	NEI	https://reporter.nih.gov/search/XhDMG-YUYHUm7pceGZrZ2ew/projects
LUNDQUIST INSTITUTE FOR BIOMEDICAL INNOVATION AT HARBOR-UCLA MEDICAL CENTER (Raymond S Douglas, Terry J Smith)					
Basic research	**Immune Activation of Fibroblasts**	2004-2008	$913,818	NEI	https://reporter.nih.gov/search/4kYpy0uHN0m38GXMGccO0A/projects
	Immunoglobulin Activation of Fibroblasts	2004-2008	$1,660,017	NIDDK	https://reporter.nih.gov/search/Zowz6lG2PUy94gDFq8PUWA/projects
	Regulation of Retroocular Connective Tissue	2000-2008	$2,719,043	NEI	https://reporter.nih.gov/search/iE3VdZCBZE6V8wMUwQlSIg/projects
	Regulation of Retroocular Connective Tissue: Interleukin IL-16 Levels in Pati	2004-2010	$107,084	NCRR	https://reporter.nih.gov/search/iE3VdZCBZE6V8wMUwQlSIg/projects
	Functional Diversity of Orbital Fibroblasts	1999-2008	$3,261,497	NEI	https://reporter.nih.gov/search/_9TsY827mker44XC8RcujA/projects

NEI = National Eye Institute
NCRR = National Center for Research Resources
NIDDK = National Institute of Diabetes and Digestive and Kidney Diseases
FDA = Food and Drug Administration …

Public contributions to Lifileucel (AMTAGVI®)

Table 17: Development history, Licensing, Acquisitions and public contributions to Amtagvi®

Type of financing	Details on collaboration, financing, public funding	Year	Amount (in USD)	Funders/ Investors/ Acquiror	Source
Iovance Biotherapeutics (former Lion Biotechnologies, Inc.)					
Post-IPO Equity	Iovance Biotherapeutics, Inc. announces pricing of $211 million underwritten offering of common stock	2024	$211 million	Common stock	https://www.globenewswire.com/news-release/2024/02/20/2831635/0/en/Iovance-Biotherapeutics-Inc-Announces-Pricing-of-211-Million-Underwritten-Offering-of-Common-Stock.html
Acquisition	Iovance Biotherapeutics Inc (NASDAQ: IOVA) has agreed to acquire worldwide rights to Proleukin (aldesleukin), an interleukin-2 (IL-2) product, from Clinigen Limited	2023	£166,7 million (£41,7 million milestone payment)	Clinigen Limited	https://finance.yahoo.com/news/iovance-biotherapeutics-acquires-clinigens-il-163929354.html https://www.sec.gov/Archives/edgar/data/1425205/000155837025006019/iova-20241231xars.pdf
Post-IPO Equity	Iovance Biotherapeutics Announces Pricing of its Public Offering Of $150 Million of Common Stock	2023	$150 million	Public offering of common stock	https://www.reuters.com/article/business/healthcare-pharmaceuticals/iovance-biotherapeutics-announces-pricing-of-its-public-offering-of-150-million-idUSASB0C2BS/

Type of financing	Details on collaboration, financing, public funding	Year	Amount (in USD)	Funders/ Investors/ Acquiror	Source
Post-IPO Equity	DLA Piper advises Iovance Biotherapeutics in its US$604 million common stock offering	2020	$603,7 million	Public offering of common stock	https://www.biospace.com/dla-piper-advises-iovance-biotherapeutics-in-its-us-604-million-common-stock-offering
Post-IPO Equity	Iovance Biotherapeutics, Inc. announces closing of $252 million common stock public offering	2018	$252,2 million	Public offering of common stock	https://www.sec.gov/Archives/edgar/data/1425205/000114420418054098/tv504904_ex99-1.htm
Post-IPO Equity	Iovance biotherapeutics, Inc. announces closing of $172.5 million common stock public offering	2018	$172,5 million	Public offering of common stock	https://www.globenewswire.com/en/news-release/2018/01/29/1313877/0/en/Iovance-Biotherapeutics-Inc-Announces-Closing-of-172-5-Million-Common-Stock-Public-Offering.html
Strategic Alliance Agreement	Iovance Biotherapeutics, Inc. provides a total funding of $14.2 million for clinical and preclinical research studies and all related IP of inventions go to Iovance Biotherapeutics	2017-2024 (but extended)	$14,2 million	Research funding	https://www.sec.gov/Archives/edgar/data/1425205/000155837025006019/iova-20241231xars.pdf
Post-IPO Equity	Lion Biotechnologies raises approximately $100 million in private placement	2016	$100 million	Private placement	https://www.reuters.com/article/business/healthcare-pharmaceuticals/lion-biotechnologies-raises-about-100-mln-in-private-placement-idUSASC08SLK/
Post-IPO Equity	Lion Biotechnologies, Inc. (Nasdaq:LBIO), a biotechnology company that is developing novel cancer immunotherapies based on tumor infiltrating lymphocytes (TIL), today announced the pricing of an underwritten public offering of 8,000,000 shares of its common stock at a public offering price of $8.00 per share. The gross proceeds from this offering to Lion are expected to be $64.0 million, before deducting underwriting discounts and commissions and offering expenses payable by Lion.	2015	$64,0 million	Public stock offering	https://www.biospace.com/lion-biotechnologies-inc-prices-public-offering-of-common-stock
Private financing	Lion Biotechnologies, Inc. Eyes Approximately $23 Million in Private Financing	2013	$23 million	Venture capital	https://www.biospace.com/lion-biotechnologies-inc-eyes-approximately-23-million-in-private-financing
Genesis Biopharma (formerly Freight Management Corp)					
Merger	Genesis Biopharma, Inc. Announces Completion of Merger with Lion Biotechnologies	2013	n.a.	Lion Biotechnologies (Iovance Biotherapeutics)	https://www.biospace.com/genesis-biopharma-inc-announces-completion-of-merger-with-b-lion-biotechnologies-b
Post-IPO Equity	Genesis Biopharma, Inc. places its equity for funding	2013	$1,35 million	Not disclosed	https://www.sec.gov/Archives/edgar/data/1425205/000151316013000035/xslFormDX01/primary_doc.xml
Post-IPO Debt	Genesis Biopharma, Inc. takes on debt from 5 non-disclosed debtors	2011	$5 million	Not disclosed	https://www.sec.gov/Archives/edgar/data/1425205/000114420411044671/xslFormDX01/primary_doc.xml
Venture - Series Unknown	Genesis Biopharma, Inc. places its equity for funding	2011	$640.000	Venture capital funding	https://www.sec.gov/Archives/edgar/data/1425205/000148380611000003/xslFormDX01/primary_doc.xml
Origins in general	Dr. Steven Rosenberg, Chief of the Surgery Branch at the National Cancer Institute, developed a process whereby TILs are isolated directly from the patient's tumor, multiplied to great numbers, and infused into the patient to destroy the patient's cancer. Contego™ is based on the TIL therapy developed by Dr. Rosenberg for the treatment of patients with Stage IV metastatic melanoma.	2012	n.a.	National Cancer Institute	https://www.fiercepharma.com/pharma/base-technology-for-genesis-biopharma-s-contego-tm-featured-cnn-report-md-anderson-s
Private Financing	Genesis Biopharma Announces $700K Private Financing	2010	$700.000	n.a.	https://www.fiercebiotech.com/biotech/genesis-biopharma-announces-700k-private-financing
VC	Combination of equity and warrants for funding	2010	$ 500.000	Venture capital	http://www.sec.gov/Archives/edgar/data/1425205/000148380610000005/xslFormDX01/primary_doc.xml
Seed	Equity offering	2010	$ 250.000	One non-disclosed investor	http://www.sec.gov/Archives/edgar/data/1425205/000148380610000007/xslFormDX01/primary_doc.xml

Type of financing	Details on collaboration, financing, public funding	Year	Amount (in USD)	Funders/ Investors/ Acquiror	Source
National Cancer Institute					
Basic research	Adoptive Cell Transfer Immunotherapy of Cancer (PI Steven Rosenberg)	2008-2024	$53.785.735	National Cancer Institute	https://reporter.nih.gov/search/W9vFhITe502y9n3FdEATRQ/projects
Early basic research (proof of concept)	The Immunotherapy of Animal and Human Cancer (PI Steven Rosenberg)	1999-2007	$3.172.648 (only data for 2007 is available)	National Cancer Institute	https://reporter.nih.gov/search/eWdeLcwr6U-8QValczkQMQ/projects
University Of Tx Md Anderson Can Ctr					
Basic research	Functional Attributes of a CD8+BTLA+ T cell subset in Adoptive T Cell Therapy (PI Chantale Bernatchez)	2013-2014	$376.536	National Cancer Institute	https://reporter.nih.gov/search/AJFF9ihLnkivZP8I6wcXIQ/project-details/8681400
	Biology Of Human Tumor Infiltrating Lymphocytes	1989-1991	$138.671 $138.002 $139.389	National Cancer Institute	https://reporter.nih.gov/search/4oyR-zdv-kqxiOUq-ZO-Nw/project-details/3191720 https://reporter.nih.gov/search/4oyR-zdv-kqxiOUq-ZO-Nw/project-details/3191718 https://reporter.nih.gov/search/4oyR-zdv-kqxiOUq-ZO-Nw/project-details/3191719

Public contributions to Obecabtagene Autoleucel (obe-cel) (AUCATZYL®)

Table 18: Development history, Licensing, Acquisitions and public contributions to Aucatzyl®

Type of financing	Details on collaboration, financing, public funding	Year	Amount (in USD)	Funders/ Investors/ Acquiror	Source
Autolus Therapeutics (spin-out from University College London in 2014)					
General information	Autolus Therapeutics was founded by Martin Pule, based at UCL Cancer Institute, and with the support of UCL Business (UCLB), UCL's commercialisation company, was spun out in 2014. It has since raised over $1B, with most of this invested in the UK, including the development of a state-of-the-art manufacturing facility, The Nucleus in Stevenage, employing 450 people.	2025	Raised over $1B of investment	n.a.	https://www.ucl.ac.uk/news/2025/apr/ucl-spinout-autolus-gains-uk-licence-cancer-therapy
Licensing information	Continuous cooperation between UCL and Autolus Therapeutics: Company amended licensing agreement of 2014 in 2024 for the T-cell technology from UCLB.	2024	Equity (1.8M+ shares) + £120k management fee + cash for amendments (£2M total) Up to £106.68M in milestone payments (clinical, regulatory, commercial, sales) £10M regulatory milestone already paid for obe-cel FDA approval Low to mid-single digit royalties on product sales Revenue sharing on sublicenses (decreasing over time) UCLB retains academic research rights	UCL (through its commercialization company UCLB)	https://www.sec.gov/Archives/edgar/data/1730463/000173046325000019/autl-20241231.htm
Patent information	As of December 31, 2024, Autolus Therapeutics has a patent portfolio of 83 patent families, of which 17 patent families originated from UCLB	2024	n.a.	UCL/ UCLB	https://www.sec.gov/Archives/edgar/data/1730463/000173046325000019/autl-20241231.htm
General pricing information	Aucatzyl® will go for $525,000, a list price that "reflects the clinical evidence and benefit" of the treatment. Competitors Gilead's Tecartus, meanwhile, is priced lower at around $460,000, while Novartis' Kymriah is priced at around $580,000 per treatment, William Blair analysts pointed out in a note to clients.	2024	Estimated price: $525,000	n.a.	https://www.fiercepharma.com/pharma/autolus-readies-its-aucatzyl-car-t-go-after-heavy-hitter-competition-after-landing-fda

Type of financing	Details on collaboration, financing, public funding	Year	Amount (in USD)	Funders/ Investors/ Acquiror	Source
Collaboration	Now, the German biotech has brought British company Autolus Therapeutics on board in an intriguing $250 million upfront collaboration. In addition, BioNTech gains an exclusive license to use certain target binders identified by U.K.-based Autolus as well as the option to license additional binders or cell programming technologies to support the German biotech's own in vivo cell therapy and antibody-drug conjugate (ADC) candidates. Autolus will be eligible to receive milestone payments from any resulting drugs.	2024	$250 million	BioNTech	https://www.fiercebiotech.com/biotech/biontech-pays-autolus-250m-manufacturing-car-t-expertise-wide-ranging-collab
Collaboration	Autolus Therapeutics has found a deep-pocketed supporter of its CD19 CAR-T therapy. Having seen Autolus' stock halved over the past year, Blackstone Life Sciences has stepped in with a $250 million package to support the British biotech through to a pivotal readout and beyond. The first phase of the deal will see Blackstone pay $50 million upfront and make a $100 million investment in Autolus. Beyond that, Blackstone is on the hook for up to $100 million in payouts tied to obecel development and regulatory milestones.	2021	$250 million	Blackstone Life Sciences	https://www.fiercebiotech.com/biotech/blackstone-bets-autolus-cd19-car-t-250m-deal-clearing-path-to-pivotal-readout-2022
Collaboration/ Licensing	The 2021 deal commits Moderna to up to $60 million in milestones, split evenly between development and sales events, per product, plus royalties in the low to mid-single digits on net sales. While the sums are relatively small, Martin Pule, chief scientific officer at Autolus, framed the deal as a validation of the technology.	2021	$60 million	Moderna	https://www.fiercebiotech.com/biotech/moderna-says-yes-autolus-licensing-targeting-technology-immuno-oncology-project
Follow-on $150 million offering	Days after announcing the first response rates from a Phase I/II trial of CAR T cell therapy AUTO1, Autolus raised $100.8 million in a follow-on offering.	2019	$100.8 million	n.a.	https://www.biocentury.com/article/301764/autolus-follows-up-car-t-data-with-101m-raise
IPO	Biotech IPOs continue to come thick and fast this week, with U.K. T-cell therapy specialist Autolus the latest to list with an impressive $150 million raise.	2018	$150 million	n.a.	https://www.fiercebiotech.com/ipo-bonanza-continues-150m-listing-for-car-t-player-autolus
Series C financing	AUTOLUS LIMITED: Autolus Secures US$80 million Series C Funding	2017	$80 million	Syncona, Nextech Invest, Arix Bioscience, Woodford Investment Management	https://www.globenewswire.com/news-release/2017/09/26/1132588/0/en/AUTOLUS-LIMITED-Autolus-Secures-US-80-million-Series-C-Funding.html
Series B financing	Autolus Limited secures £40 million funding – Woodford Investment Management and Perceptive Bioscience complete Series B financing	2016	£40 million	Woodford Investment Management and Perceptive Bioscience	https://www.fiercebiotech.com/biotech/autolus-limited-secures-£40-million-funding-—-woodford-investment-management-and-perceptive
Series A financing	Autolus is getting started with $45 million in startup cash from Syncona. Christian Itin, the former CEO at Micromet, is taking over as chairman of the newly minted biotech. Micromet was bought out by Amgen ($AMGN) back in 2012 for $1.2 billion, largely so it could get its hands on blinatumomab, a bispecific T cell engager (BiTE).	2015	$45 million	Syncona	https://www.fiercebiotech.com/biotech/car-t-brain-war-scientific-trailblazer-inspires-a-45m-biotech-startup

Type of financing	Details on collaboration, financing, public funding	Year	Amount (in USD)	Funders/ Investors/ Acquiror	Source
Licensing agreement (amended in the following year, for the most up-to-date licensing information check "Licensing agreement 2024"	In September 2014, we entered into an exclusive license agreement with UCLB, the technology-transfer company of UCL, for the development and commercialization rights to certain T cell programming modules.	2014	1,497,643 ordinary shares of Autolus Therapeutics plc company licensed T-cell technology from UCLB with: £120k management fee + equity/cash for amendments (£1.65M+ total) Up to £104.5M in milestone payments (regulatory, commercial, sales) Low to mid-single digit royalties on product sales Revenue sharing on sublicenses (decreasing over time) Option to buy out UCLB's rights after reaching sales threshold	UCL/UCLB	https://www.sec.gov/Archives/edgar/data/1730463/000173046318000005/autolus20fdoc.htm#s738C4D9ABE6D5D178D739BAC938F7C5D
University College London					
Basic research funding	Next Generation T cell therapies for childhood cancers [NexTGen]	2022-2024	$3,627,871	National Cancer Institute	https://reporter.nih.gov/search/HE6ks61mc0ie-yhHwLhHDTw/project-details/10631014
Basic research funding	The Mark Foundation for Cancer Research Awards ~$12 million to Cancer Grand Challenges Team Developing Novel Immunotherapies for Childhood Solid Tumors	2022	$12 million	The Mark Foundation for Cancer Research	https://themarkfoundation.org/2022/06/the-mark-foundation-for-cancer-research-awards-12-million-to-cancer-grand-challenges-team-developing-novel-immunotherapies-for-childhood-solid-tumors/
Basic and applied research funding	ATECT (Advanced T-cell Engineered for Cancer Therapy)	2013-2018	€5,931,151	European Commission (Seventh Framework Programme)	https://cordis.europa.eu/project/id/602239/reporting
Applied research funding	Large-scale production of lentiviral vectors	2015-2018	£1.8M	Innovate UK / BBSRC Consortium	https://www.ucl.ac.uk/medical-sciences/divisions/cancer/our-research/ucl-car-t-programme/martin-pule
Applied research funding	Phase I/II study of CAR19 in relapsed/refractory ALL (Principal investigator Martin Pule)	2015-2018	£3.9M	NIHR i4i	https://www.ucl.ac.uk/medical-sciences/divisions/cancer/our-research/ucl-car-t-programme/martin-pule
Basic and applied research funding	Chimeric Antigen Receptors (CARs) for Advanced Therapies	2015-2019	€5,989,158.75	European Commission (Horizon Europe)	https://cordis.europa.eu/project/id/667980
Basic and applied research funding	CAR T-cell therapy of CNS Lymphoma. Principle Investigator Martin Pule	2016-2020	£2.7M	Wellcome Trust. Health Innovation	https://www.ucl.ac.uk/medical-sciences/divisions/cancer/our-research/ucl-car-t-programme/martin-pule https://www.washingtonpost.com/health/2022/08/05/childrens-cancer-research-gains/ (we were unable to verify the exact number)
Basic and applied research funding	A protein-based method for allogeneic CAR T-cell therapy Principle Investigator Martin Pule	2019-2024	£2,507,997	MRC DPFS grant	https://www.ukri.org/publications/competitive-funding-decisions-data-2015-to-2020/ https://www.ucl.ac.uk/medical-sciences/divisions/cancer/our-research/ucl-car-t-programme/martin-pule
Basic and applied research funding	CD21 CAR T-cell therapy for T-ALL Principle investigator Martin Pule	2019-2022	£680k	MRC Project grant	https://www.ucl.ac.uk/medical-sciences/divisions/cancer/our-research/ucl-car-t-programme/martin-pule (we were unable to verify the numbers)
The University of Texas MD Anderson Cancer Center					
Basic research funding	Improving cord blood transplantation Principle investigator Catherine Bollard	2011-2022	$24,444,013	National Cancer Institute	https://reporter.nih.gov/search/4Z9Y9mQunEOfZSHtDmB9nA/project-details/9134065
Children's Research Institute					
Basic research funding	Next Generation T cell therapies for childhood cancers [NexTGen]	2022-2024	$2,528,270	National Cancer Institute	https://reporter.nih.gov/search/4Z9Y9mQunEOfZSHtDmB9nA/project-details/10627010