Shaping a new market for children and young people with cancer.

November 2026

C–FURTHER

Table of Contents

About this paper 3
Perspectives 4
Executive Summary 5
Introduction 7
Challenges & Perspectives 8
The underlying challenge: finance 13
Fixing markets with incentives 15
The global funding landscape 18
Creative models and why they fall short 22
Towards systemic solutions 25
Blended funds in practice 27
Shaping new markets 29
A call to collective action 33
References 34

About this paper

Reference

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Authors

The lead author of this report is Thomas Edwards, with support from the C-Further team. Patient advocates were consulted on emerging ideas and asked to comment on the full paper. Comments, questions or feedback should be sent to info@c-further.org.

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About C-Further

Launched in September 2024, C-Further is a consortium founded by Cancer Research Horizons, LifeArc and Great Ormond Street Hospital Children's Charity. C-Further is dedicated to addressing a critical gap in oncology: childhood cancer. Leveraging deep drug discovery capabilities and collectively helped bring over 20 drugs to market, C-Further moves beyond repurposing of existing adult cancer therapies, designing therapeutics tailored specifically to the unique biology of childhood tumours.

About Cancer Research UK

Cancer Research UK is the world's leading cancer charity dedicated to saving and improving lives through research. We fund research into the prevention, detection and treatment of more than 200 types of cancer through the work of over 4,000 scientists, doctors and nurses and invest £400m+ annually. In the last 50 years, we've helped double cancer survival in the UK and our research has played a role in around half of the world's essential cancer drugs. Our vision is a world where everybody lives longer, better lives, free from the fear of cancer.

About Cancer Research Horizons

Cancer Research Horizons is the innovation engine of Cancer Research UK. The organisation takes cutting-edge innovations from the lab bench to the bedside, translating them into effective treatments and diagnostics for cancer patients. To date, Cancer Research Horizons has played an instrumental role in forming over 90 spin-out companies. The organisation has helped bring 14 cancer drugs to market, born out of Cancer Research UK's pioneering research. Through these drugs, Cancer Research Horizons has enabled in excess of 6 million courses of treatment for cancer patients across the world.

About LifeArc

LifeArc is a not-for-profit medical research organisation that turns promising scientific research into impact for people living with rare diseases and Global Health infections. We form partnerships and provide scientific expertise and funding to help break down the barriers preventing scientific breakthroughs from becoming life-transforming treatments and cures. We have been doing this for more than 30 years and our work has resulted in five licensed medicines, including cancer drug pembrolizumab and lecanemab for Alzheimer's disease. Our goal is a world where no one with a rare disease or a global infectious disease misses out on life-changing innovation because of complexity, cost or risk.

About Great Ormond Street Hospital Children's Charity

Great Ormond Street Hospital Charity (GOSH Charity) stops at nothing to help give seriously ill children childhoods that are fuller, funner and longer. For the hundreds of children from all over the UK who are treated by Great Ormond Street Hospital (GOSH) every day, for children with rare or complex illnesses everywhere, for this generation and all those to come.

Perspectives

Pamela Kearns OBE, PhD, FRCPCH

Emeritus Professor of Clinical Paediatric Oncology
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This comprehensive paper from C-Further sets out a compelling pathway to translate the strong scientific advances achieved in paediatric oncology into authorised medicines that can reach children and young people with cancer in real-world clinical practice. By clearly identifying the structural market failures that have too often prevented life-changing therapies from progressing to marketing authorisation and patient access, it presents an ambitious yet credible roadmap for change.

Its proposed model of blended financing and cross-sector collaboration has the potential to unlock investment, de-risk innovation development, and accelerate the translational journey from promising science to approved medicines. Most importantly, it offers a realistic financial pathway towards a future in which children and young people with cancer are not denied access to therapeutic advances because of market constraints. This is an important and potentially transformative contribution to address one of the most persistent barriers to innovation in paediatric cancer.





Sam Blackman, MD, PhD

Entrepreneur-in-Residence at Google Ventures;
Founder and Former Head of R&D at
Day One Biopharmaceuticals.

One of the major challenges for industry in developing new medicines specifically for children with cancer is that individual disease populations are very small, while the costs and risks of new drug development are enormous. In addition, current regulatory incentives – both the "carrots" and the "sticks" are insufficient to overcome the significant financial barriers facing biopharmaceutical companies.

This extensive paper examines childhood cancer therapeutic development through an economic and financial lens, which, in addition to current scientific gaps, are key drivers of the lower rate of new therapeutic development for children with cancer.

C-Further's approach of developing a dedicated pipeline of new therapeutics, designed from the outset to address the distinct biology of cancer in children and young people, may help reduce the upfront costs and risks for new drug development, and thus enable investment at later stages of development. This important paper makes the case that philanthropic and public funding, deployed strategically, with expert input from both academia and industry, can help incentivise private investment and close this historic gap.

Executive Summary

Why has the global market economy failed to develop new precision treatments for children and young people with cancer, despite the vast societal unmet need and fifty years of technological progress?

Two million years of healthy life are lost to childhood cancer in high and middle-income countries each year, with most of that loss attributable to young lives cut short. Science is revealing childhood cancers to be biologically distinct from cancer in adults and with nearly half of cases carrying a genetic change that could, in principle, be drugged. At the same time we have more powerful tools than ever before, and society rightly is demanding an end to cancer in children and young people. *So why today are there still so few targeted treatments available to them?*

The answer to this paradox is increasingly economic. Developing a novel targeted medicine to treat childhood cancer costs as much and carries as much risk in development as any other disease, while the market at the end of research is far smaller. As a result, investors rarely see enough financial return to justify the risk, so pharmaceutical and biotech companies build their research pipelines around other diseases where the market is bigger or more established.

Non-commercial efforts have attempted to translate early science to new medicines. However, without the scale of resources or breadth of expertise needed, they most often stall before reaching the children who need them.

This major healthcare challenge hasn't gone unnoticed by society at large. Regulators have increasingly mandated the inclusion of children and young people in trials of novel targeted adult cancer therapies. Non-profit medical research funders have increased, if unevenly, their financial commitments, growing a small but interconnected academic and clinical research ecosystem. Select governments have created national missions, responding to impassioned calls from those affected by childhood cancer, establishing modern infrastructure, financial incentives and shared resources. Together, these have built a small but mature base. However, they collectively operate far below the scale the problem demands and none of them can repeatedly carry new targeted medicines all the way through capital-intensive clinical trials or launch new paediatric medicines to health systems globally.

Key Messages

01: Cancer is the leading cause of death from illness in children and young people.

02: New tailored and well-tolerated treatments are urgently needed.

03: Childhood cancer is a structural market failure, not necessarily a scientific one.

04: Existing incentives are necessary but insufficient.

05: Models to bridge and scale early-stage, child-first drug discovery already exist and need to scale.

06: Fully overcoming the market failure requires matching ambition at the next stage of drug development.

07: What's needed now is a multi-sector stakeholder consultation, to move from concept to coalition.

This paper sets out a two-stage approach that seeks to create an end-to-end pathway for the discovery and development of new precision medicines for children and young people with cancer.

First, a non-profit drug discovery consortium that leverages the knowledge and expertise of the established academic and clinical community, assumes the development gap normally occupied by biotech and pharmaceutical companies. C-Further, already in operation, has been designed from the outset to play this role: increasing the supply of high-quality, child-first therapeutics by pooling philanthropic funding, drug discovery infrastructure and therapeutic concepts globally through a dedicated translational drug discovery vehicle. Now is the time to scale and grow this and support similar leading initiatives.

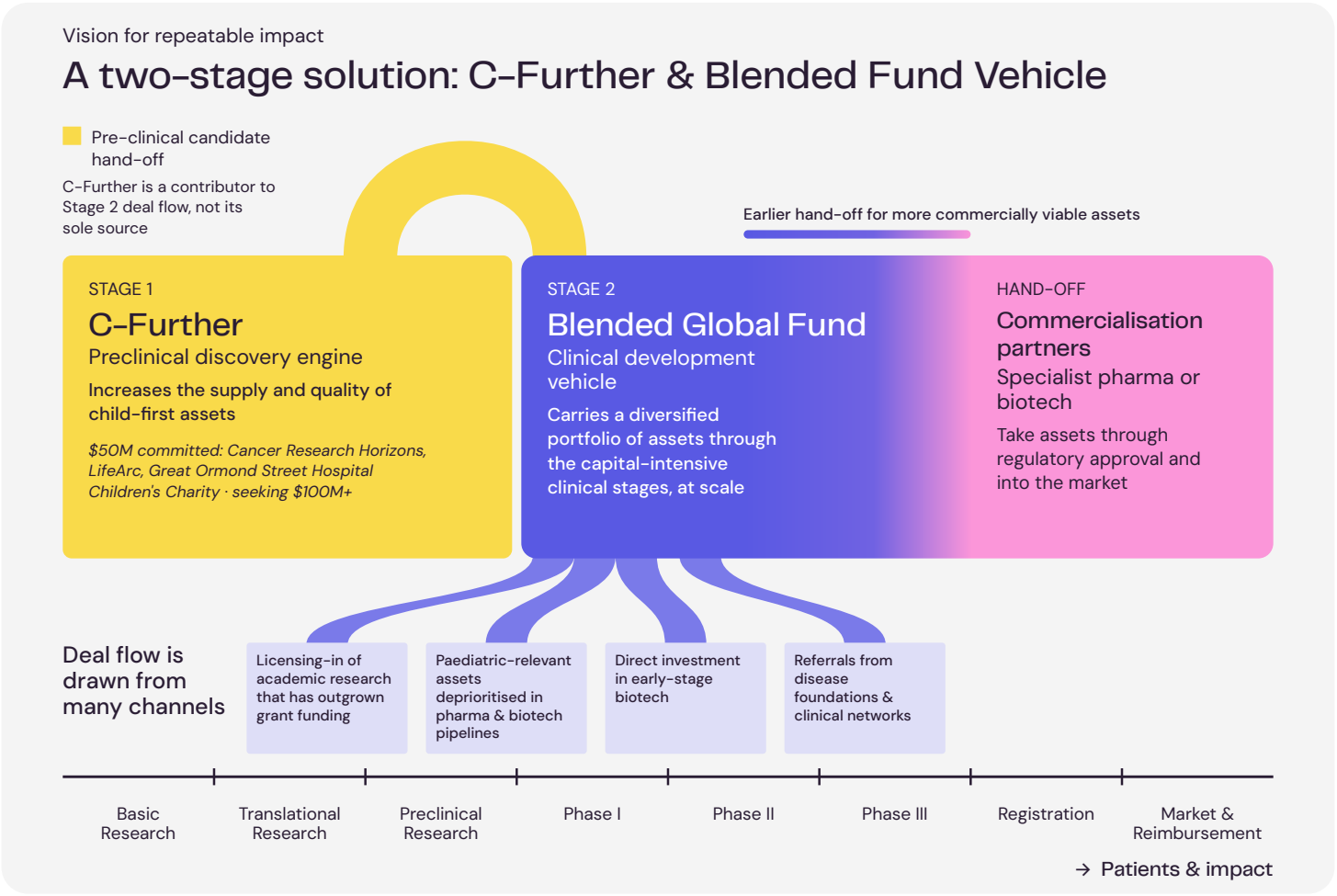
Second, a blended global fund with sufficient scale to finance a diverse portfolio of children's cancer therapeutics into the clinic. In a blended fund, philanthropic, public and private capital are combined and structured so that the more risk-tolerant funders absorb any potential losses, catalysing a larger pool of private investment to participate, collectively enabling many more new medicines to be evaluated in parallel.

New modelling in this paper demonstrates the conditions where a blended fund could support a portfolio of such therapeutics, simultaneously delivering societal impact and modest investor returns. Crucially, we believe this can be aligned to the goals, behaviours and expectations of diverse capital providers. This proposal further benefits from learnings that can be drawn from other fields that have leveraged similar financial mechanisms such as antimicrobial resistance, dementia and neglected tropical diseases which face analogous structural market failures. *Children's cancer has not yet been given the same structural response.*

So how do we move from modelling to proven model? Our analysis supports the case for using structured finance, building upon the strong foundations in the paediatric research ecosystem. The next steps are to identify a coalition prepared to turn this vision into a viable, operational initiative. This paper is a call to all stakeholders across sectors, but in particular to individuals, organisations, investors, institutions and governments with the financial means, vision and willingness to work together and refine the initial proposal set out here.

This paper invites you to begin that conversation, consider the role and conditions that will enable individuals and organisations to participate; playing your part in shaping a new market for children and young people with cancer.

A consultation to assess feasibility is being prepared to launch in 2027.



Introduction

Despite improvements in survival, significant unmet need remains for children with cancer.

Since the 1970s cancer survival in children and young people as defined as individuals from 0 – 24 years old (hereafter referred to as childhood cancer) has more than doubled in the UK [1]. This success is largely attributed to the advent of combination chemotherapy, with or without radiotherapy, as well as the entry of paediatric patients into rationally designed clinical trials [2]. However, childhood cancer remains a major healthcare challenge globally. In 2017, there were two million disability adjusted life years (DALYs) lost due to childhood cancer in high and middle socio-economic countries, with 91% of this due to years of life lost [3]. Stated plainly, cancer is a leading cause of death for children and adolescents.

In particular, overall survival for children with rare, relapsed, metastatic and/or refractory cancers remains low, with significant variance in outcomes remaining across indications and ethnicities [4].

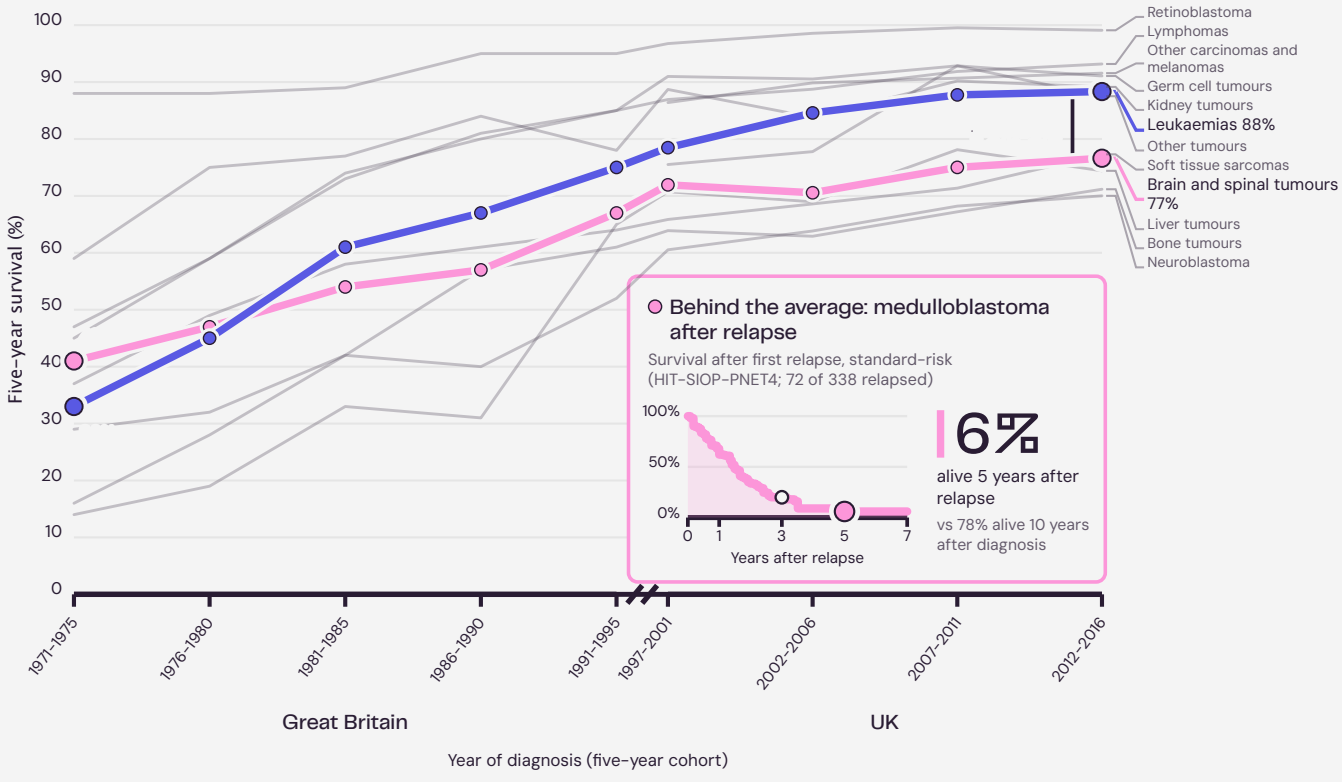
For example, survival rates of medulloblastoma, the most common malignant paediatric brain tumour, are near 80% with use of adjuvant chemoradiation, yet recurrent medulloblastoma has a 3-year survival rate of 20% and only 6% survive 5 years (see *Figure 01*) [5]. Indeed, children diagnosed with diffuse midline gliomas have a dismal prognosis, a median survival of 12 months, and this statistic has not improved appreciably in decades [6].

Yet the increasing population of adult survivors of childhood cancer has also revealed a secondary challenge - survivors are at risk for adverse health and quality of life outcomes. Neurocognitive late effects of CNS radiation and intrathecal therapy, cardiomyopathy from anthracyclines and cardiac radiation, gonadal dysfunction from alkylating agents, and increased risk for secondary malignancies among other chronic toxicities make a case for not only more effective therapies, but kinder and more precise ones [7][8].

01: Survival has transformed since the 1970s - but not equally

Five-year population-based survival (%), children aged 0-14, by diagnostic group

Neuroblastoma, brain and spinal, liver and bone tumours remain well behind leukaemia, lymphoma, germ cell tumours and retinoblastoma.



Source: Cancer Research UK, Children's Cancer Statistics — cruk.org/cancerstats
Inset: Sabel M et al., J Neurooncol 2016;129(3):515-524, doi:10.1007/s11060-016-2202-1, Fig. 1b.

Challenges & Perspectives

Why has the promise of precision medicine not risen to the challenge of childhood cancer?

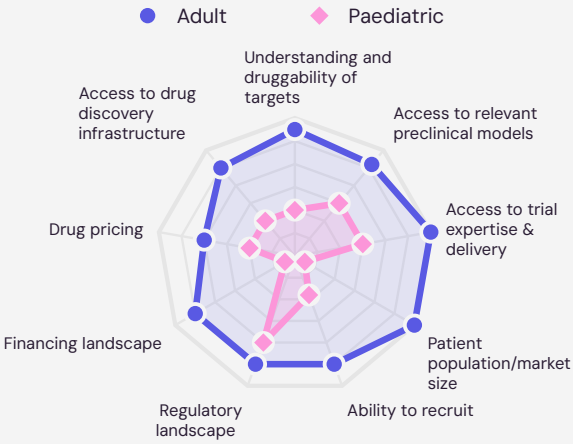
Until the last decade, drug development focused on enhancing untargeted chemotherapies and improving supportive care. However, recent advances in sequencing technologies have enabled the deep molecular characterisation of tumours at the DNA, RNA and epigenetic levels. These analyses have uncovered marked differences in the biology of cancers in children and young people compared to adults. Moreover, nearly 50% of paediatric tumours harbour a potentially druggable event, providing an untapped opportunity for a precision medicine approach [9][10]. The introduction of national initiatives of whole genome sequencing for children such as the Zero Childhood Cancer Program in Australia, the 100,000 Genomes Project and the Stratified Medicine Paediatrics (SMPaeds) in the UK as well as at other specialist centres in the USA and Europe mean that health systems are increasingly eager to use this wealth of information to optimise patient management.

Yet with few exceptions, almost all the targeted therapies available to paediatric oncologists were first commercialised for adult indications and then subsequently made available for specific childhood cancer indications, in the FDA parlance, via 'supplemental' approvals (see *Figure 03*). While such approvals are a real success for parents and children affected by cancer, they mask a long road of failures and ultimately a delayed route to access. Children that relapse from standard of care treatment are often enrolled in early phase trials of repurposed adult cancer drugs which are largely ineffective: a meta-analysis in solid tumours found only a 4% objective response rate and under 4 months of median progression-free survival, substantially worse than the nearly 20% response rate seen in pooled analyses of adult phase 1 trials [11], [12]. The availability of targeted drugs for children with cancer is largely opportunistic; it is not based upon an optimised mechanism of action of the therapeutic in children but instead the arbitrary availability of a complementary adult indication and a willing commercial partner at the right stage of their asset lifecycle. As Moreno et al put it – 'Are we now researching drugs for paediatric targets, or have we just become more efficient at studying drugs [in children] developed for adult cancers?' [13]. This is not only sub-optimal mechanistically but additionally results in a two-tier system; analyses show that the median time between the start of a first-in-human trial (in adults) and the subsequent first-in-child trial was 6.5 years. Children with cancer have to wait unacceptably long for innovation to reach them [14].

There are compelling scientific, operational and regulatory reasons why, to date, there have been few therapies designed, developed and commercialised, from the outset, for children and young people with cancer, so-called 'child-first' therapeutics (see *Figure 02*). Yet the development and successful commercialisation of child-first therapeutics are vital to improve outcomes for children and young people affected by cancer. *So, what's going on?*

02: Systemic challenges: adult v paediatric

Favourability of nine drug-discovery and development conditions

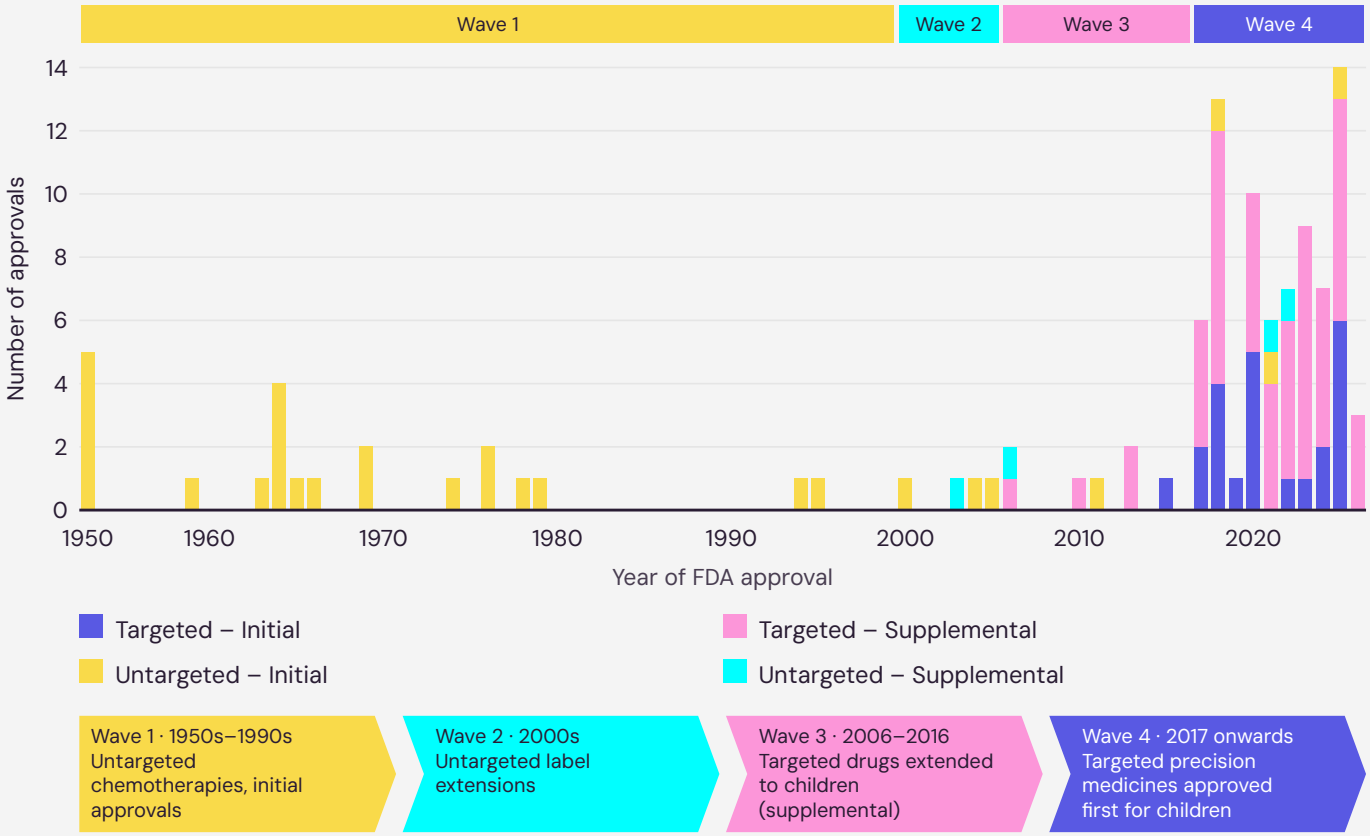


> Are we now researching drugs for paediatric targets, or have we just become more efficient at studying drugs [in children] developed for adult cancers?
>
> Moreno et al. [13]
> Expert Opinion on Drug Discovery, 2020

Source: L. Moreno, S. G. DuBois, L. V. Marshall, E. Fox, F. Carceller, and A. D. Pearson, 'How to address challenges and opportunities in pediatric cancer drug development?', Expert Opin. Drug Discov., vol. 15, no. 8, pp. 869–872, Aug. 2020.

03: FDA paediatric oncology approvals: initial and supplemental

Approvals have shifted progressively from untargeted chemotherapy towards targeted precision medicines approved first for children.



Selected targeted initial approvals, 2016–2026

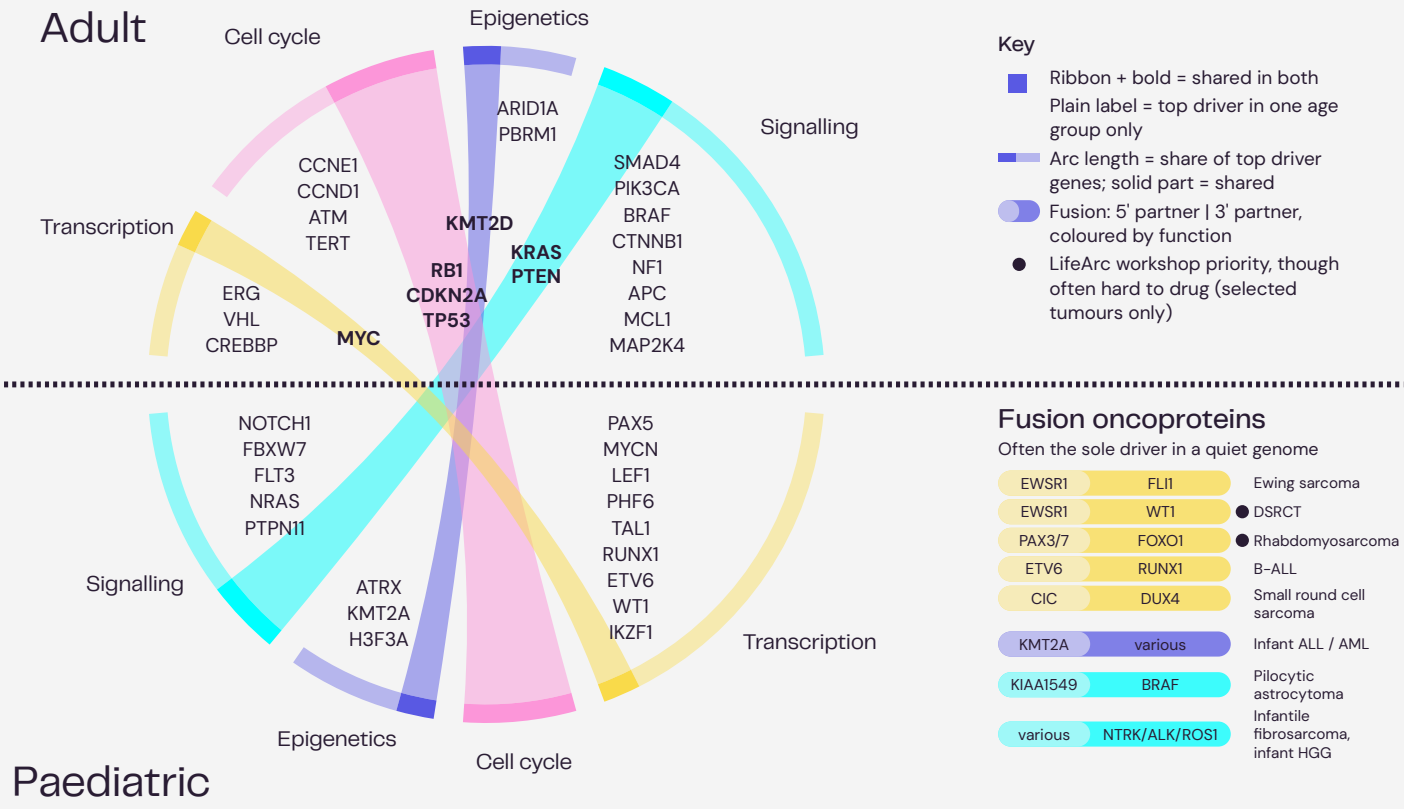
Year	Drug [brand]	Target / modality	Paediatric indication	Age
2017	Tisagenlecleucel [Kymriah]	CD19 CAR T-cell therapy	B-cell precursor ALL, refractory or in second or later relapse	≤25 years
2018	Larotrectinib [Vitrakvi]	NTRK1–3 kinase inhibitor	NTRK fusion-positive solid tumours (tumour-agnostic)	All ages
2020	Tazemetostat [Tazverik]	EZH2 methyltransferase inhibitor	Metastatic or locally advanced epithelioid sarcoma	≥16 years
2020	Selumetinib [Koselugo]	MEK1/2 kinase inhibitor	NF1 with symptomatic, inoperable plexiform neurofibromas	≥2 years
2020	Naxitamab [Danyelza]	GD2-binding antibody	Relapsed or refractory high-risk neuroblastoma in bone or bone marrow	≥1 year
2023	Eflornithine [Iwilfin]	ODC1 inhibitor	High-risk neuroblastoma, to reduce the risk of relapse	All ages
2024	Tovorafenib [Ojemda]	BRAF / CRAF kinase inhibitor	Relapsed or refractory paediatric low-grade glioma with a BRAF alteration	≥6 months
2024	Revumenib [Revuforj]	Menin inhibitor	Relapsed or refractory acute leukaemia with a KMT2A translocation	≥1 year
2025	Mirdametinib [Gomekli]	MEK1/2 kinase inhibitor	NF1 with symptomatic plexiform neurofibromas not amenable to resection	≥2 years
2025	Dordaviprone [Modeyso]	ClpP activator / DRD2 antagonist	Progressive H3 K27M-mutant diffuse midline glioma	≥1 year

10 of the 22 targeted initial approval actions since 2016, selected for tumour types that occur in children. Indications and age ranges abbreviated from the FDA label wording; "All ages" = adult and paediatric label with no lower age limit.

Source: FDA, Oncology Center of Excellence — Pediatric Oncology Drug Approvals

04: Paediatric cancers are driven by distinct genes and developmental programmes

Shown are the top-ranked drivers across age groups identified in the literature. Genes listed for one group can still occur, less often, in the other. Drivers are not necessarily druggable targets; tumour suppressors, transcription factors and fusion proteins are often hard to drug directly.



Source: adapted from Chen X et al., Nat Rev Cancer 24, 382-398 (2024), Fig. 1B. Structural variation: Greenhalgh R et al., The landscape of structural variation in pediatric cancer (2025). Fusions: Zhang J et al., Nat Genet 45, 602-612 (2013); Knezevich SR et al., Nat Genet 18, 184-187 (1998). Fusion priorities: LifeArc Paediatric Therapeutic Development Workshops, Br J Cancer (2026).

Scientific barriers.

There are numerous scientific and technical barriers to developing childhood cancer therapeutics. This paper does not provide a comprehensive overview of these challenges as they have been well documented in the literature (see references [15], [16]). However, some of these nuances have been highlighted below to illustrate why technical challenges remain.

1. The 'Silent' Paediatric Genome

A large proportion of the genetic drivers in paediatric cancer do not overlap with those of adult cancers (see *Figure 04*). Paediatric tumours are diverse and while often characterised by a lower mutational burden some indications are driven by structural variants, including copy-number alterations and translocations [17]. While this can create a more direct relationship between the initiating alteration and the cancer's biology, it does not make the disease inherently simpler to understand or target. For instance, targeting non-kinase fusion oncoproteins has remained elusive, with efforts to date largely focused on effectors downstream of the oncoprotein [18].

2. Preclinical models that recapitulate disease.

Due to the rarity and diversity of childhood cancer as a disease, there are relatively few paediatric tumour samples available, hindering molecular characterisation of the disease. Moreover, the availability and appropriateness of cell lines and preclinical models to assess the efficacy and safety of candidate therapeutics remains challenging although major efforts are being made, for example, by developing juvenile mouse models which better reflect the immune system of children and young people [19][20][21].

3. Clinical Development Expertise.

Delivering first-in-child studies requires a vast breadth of expertise which is usually concentrated at specialist centres. There are significant challenges around assessment of preclinical rationale and translational relevance, formulation development, pharmacokinetics, pharmacodynamics, clinical endpoints and clinical trial design, as well as monitoring late toxicities which differ markedly from adult trials.

Operational barriers.

1. All paediatric disease is rare disease

As focus shifts increasingly to targeted therapy, conduct of studies of targeted agents can be challenging in the paediatric population. Identifying and selecting for subpopulations with specific mutations or biomarkers presents challenges around sample size and the power to detect an effect. Moreover, numerous competing trials of agents in the same class may compromise recruitment of children and young people into trials, delaying or preventing the ability to define efficacy within the target population. There is therefore an increasing need to align all stakeholders; academic scientists, clinicians, industry, regulators, before starting to develop a new medicine ensuring we identify the right target, the right disease population, using the right therapeutic modality [22].

2. Recruitment across borders

To recruit and accrue patients over reasonable timeframes, paediatric oncology studies often need to be spread across multiple sites and sometimes countries, leading to increased logistical challenges and higher infrastructure costs, compared with trials utilising fewer sites. Standard-of-care treatment often varies between countries and centres, and off-label and compassionate use of drugs is common, meaning the backbone on which trials are designed is complicated. Therefore, developing therapeutics for paediatric oncology may require more infrastructure and longer lead times than for adult cancer [14].

Regulatory & Ethical Barriers

1. Regulatory harmonisation.

The pharmaceutical industry is heavily regulated to ensure that the dignity, health and treatment of human participants in medical research are protected. The frameworks and legislation that regulate drug development for children date back several decades across the European Union, the UK and the USA (see *Figure 05*), where historically most of the commercial development of precision cancer medicines occurs. A paediatric cancer drug may by necessity progress through all three regulatory jurisdictions during development and commercialisation, and while there are structural similarities between these jurisdictions, divergences between the European Medicines Agency (EMA), Medicines and Healthcare products Regulatory Agency (MHRA) and the Food and Drug Administration (FDA) produce duplicative or conflicting development paths that impact upon children's access to innovation. Although the intent of such regulations is sound, their success has been somewhat limited, largely because the level of investment required to execute a paediatric development path against the financial reward of doing so is misbalanced, as discussed in detail below [23].

2. Ethical uncertainty and exclusion.

Conducting clinical trials in children is ethically and logistically challenging due to heightened safety concerns, which leads to a reliance on off-label drug use, which itself has ethical concerns as clinicians must balance potential benefits with increased risks of toxicity [24]. Recent revisions to The Declaration of Helsinki, the foundational set of ethical principles which has set the standards for medical research involving human participants, have introduced the principle of responsible inclusion, which will put a greater onus on considering the harms of exclusion of children from clinical trials, particularly where exclusion would perpetuate their disparities. While nuanced, this provides a firmer ethical footing to conduct first-in-child studies in parallel to first-in-man studies for new precision medicines, where previously this may be considered unethical [25].

Taken together, these factors explain in part why discovering and developing well-tolerated therapeutics designed specifically for cancers that affect children and young people is so hard. Each barrier has the same effect: it raises the cost of development, lengthens the timeline, or shrinks the eventual market. Overcoming them takes significant human and financial capital, and the reward at the end is smaller than in almost any other area of oncology. This is why the rest of this paper looks not at the science, but at what financing and market conditions are needed.

> "The harms of exclusion must be considered and weighed against the harms of inclusion. In order to be fairly and responsibly included in research, they [children] should receive specifically considered support and protections.
>
> WMA Declaration of Helsinki [25]
> Ethical Principles for Medical Research Involving Human Participants

Source: World Medical Association. WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Participants (2024 revision).

05: Summary of key legislation and regulation in the EU and USA

EU

The European Regulation on Orphan Medicinal Products for medicines for rare diseases and the Paediatric Medicines Regulation (PMR) were adopted in 2001 and 2007, respectively.

Orphan Regulation (EC 141/2000) (2000/2001)	Provides ten years of market exclusivity for the adult orphan indication; fee reductions for regulatory submissions; and eligibility for EMA protocol assistance. Critically, it does not currently impose any paediatric development obligation on the sponsor.
Paediatric Regulation (EC 1901/2006) (2006/2007)	It created the Paediatric Committee (PDCO) to assess paediatric development plans, introduced the Paediatric Investigation Plan (PIP) as the document through which sponsors agree the paediatric studies required for a medicine, and linked completion of an agreed PIP to regulatory incentives. The regulation was a success in that the number of agreed PIPs and approvals increased yet embedded a disease-based waiver system that allowed many potentially relevant oncology drugs to be excluded from paediatric assessment at the outset.
Pending EU pharmaceutical legislation revision (proposed)	The European Commission has proposed comprehensive revision of EU pharmaceutical legislation, which would bring in a formal mechanism-of-action criterion for paediatric development (structurally parallel to the US RACE Act), introduce a new "breakthrough" orphan medicinal products category with eleven years of market exclusivity and a stepwise PIP process.

USA

In the United States (US), Paediatric Research Equity Act (PREA), the Best Pharmaceuticals for Children Act (BPCA), the Research to Accelerate Cures and Equity Act (RACE), the Creating Hope Act as well as Rare and Orphan Drug Designations aim to encourage those developing drugs to implement paediatric cancer programmes early on in development; however, limited success has been achieved so far.

PREA (Paediatric Research Equity Act) (2003)	Authorises the FDA to require paediatric assessment of any new drug for which a New Drug Application (NDA) or Biologics License Application (BLA) is submitted for any indication that also exists in children. The FDA may waive paediatric study requirements on grounds of study feasibility, likelihood of use, or toxicity concern.
BPCA (Best Pharmaceuticals for Children Act)	Provides six months of additional market exclusivity to manufacturers who voluntarily complete FDA-requested paediatric studies.
RACE Act (Research to Accelerate Cures and Equity for Children Act) (2017/2020)	Resulted in the Relevant Molecular Target List maintained by the FDA Oncology Center of Excellence (well over 100 targets as of early 2026); a requirement that NDA/BLA sponsors directed at those targets include a paediatric study plan; and the elimination of the orphan drug exemption for oncology drugs within RACE's scope.
Give Kids a Chance Act (2025)	Recently, the Give Kids a Chance Act amends the Federal Food, Drug and Cosmetic Act in relation to RACE, giving the option to require a paediatric investigation of the new single novel cancer drug in combination with another active ingredient (generic, approved adult drug or novel agent).
FDA Plausible Mechanism Pathway (2025)	Announced in the New England Journal of Medicine in November 2025 [26], draft guidance has been published that discusses the circumstances in which data generated from highly individualised therapies could be used to support approval under existing regulatory approval pathways, where a randomised trial isn't feasible. This pathway is designed with ultra-rare indications, (often paediatric cancer) in mind and may enable sponsors to build a case to regulators on mechanistic plausibility with a smaller evidence base [27]. This is supported by the Rare Disease Framework Initiative which seeks to build a structure for rare disease drug development and regulatory review where advice and decision-making are consistently tailored to what evidence is reasonably attainable given the nature of the disease, its onset and progression, target population, patient needs, and the characterisations of the product under investigation, and clearly communicated throughout the development and review process. [28]

Source: authored summary based on de Rojas T, Kearns P, Blanc P, et al. Changing incentives to ACCELERATE drug development for paediatric cancer. Cancer Med. 2023;12:8825-8837. doi:10.1002/cam4.5627; and primary EU/US legislative texts (Regulation (EC) No 141/2000; Regulation (EC) No 1901/2006; US PREA (2003); US BPCA; RACE for Children Act, HR.1231, 115th Congress (2017), effective 2020; Give Kids a Chance Act, 2025; FDA Plausible Mechanism Pathway, N Engl J Med, November 2025, and associated FDA draft guidance; FDA Rare Disease Framework Initiative). [26-28]

The underlying challenge: finance

Is capital really a constraint to product innovation in childhood cancer therapeutics?

Developing new precision medicines from early research all the way to market is an extremely capital-intensive process with estimates varying wildly depending on the methodology used. A more recent study looking across a ten-year period estimated $879.3 million, including the cost of failure and the cost of capital [29]. For this reason, access to finance is one of the key factors constraining innovation in all areas of health and life sciences. Investors (defined broadly to include venture capital, angel or other return-seeking, private-market investors) are therefore required not because they necessarily bring insights or expertise not present in an academic or not-for-profit environment, but because these private markets form a targeted and more expansive pool of capital than available purely through philanthropy alone.

An investor's viewpoint

Pharmaceuticals are viewed as a traditionally risky asset class not only because the investor is betting on the market risk – how well will the market uptake the final product, but also a heavily cascaded technical risk – how well do we understand the disease or technology, all in a tightly regulated environment. Yet as a therapeutic progresses through key technical milestones, the probability that it reaches the market increases, therefore attracting different pools of capital. Much early-stage discovery research is funded through public (government) and charity research funding, generating fundamental knowledge and a pipeline of innovation and patentable technologies available for licensing to established companies or incorporation into new companies. Today early-stage funding for companies takes the form of a venture model whereby an experienced team are assembled and invested-at-risk, to drive forward the development of a preclinical asset or technology. Once companies have established proof-of-concept in the clinical setting, the company can often access further capital through public or private markets. Finally, assets are passed along the value chain to those companies that have reached a critical threshold of scaled operations to obtain regulatory approval and deliver the therapy to the market. Historically, this has been a licensing deal arrangement between a biotech and pharma, but in light of the current market conditions, pharma pursuing an acquisition strategy [30].

Investors pay close attention to the risk-adjusted Net Present Value (NPV) of an opportunity – essentially figuring out whether spending money now is worth it, after adjusting for risk of technical failure, given the future value of money you expect to get back later. Investors do not look at NPVs in isolation. Instead, they must consider the opportunity cost - the cost of choosing one opportunity over another. If an investor puts $100 million into a cancer drug that fails, the opportunity cost includes both the original investment that went to zero and the profit that money could have made elsewhere had the alternative been successful.

The cost of one new drug

$879.3 million



Source: Sertkaya et al. [29]

The result is a structural market failure: the risk and cost of development are, if anything, higher than in more commercially attractive disease areas, while the achievable return is lower. This is why promising early-stage paediatric cancer science routinely stalls before it reaches a stage where private capital is willing to engage. **Therefore, unlike the typical adult oncology market, the paediatric oncology market requires financial incentives to encourage investment almost at every step of development.**

Conceptually, incentives can be broadly divided into push and pull incentives. Push incentives focus on subsidising the input: allocating capital to childhood therapeutic discovery and development by reducing costs or risk for onward private investment thereby lowering the barrier to entry for new technologies and therapeutics. Pull incentives, on the other hand, reward the outputs: broadening the pool of investors seeking to participate in the market by making opportunities more profitable or certain to occur than they would otherwise be in the free market.

Within any research ecosystem there are different stakeholders with the capability to influence the development of push and pull incentives. Children and young people affected by cancer and their families are possibly the most effective stakeholder group to advocate for incentives to catalyse progress, given their rich lived experience and interactions with multiple parts of the care system during their cancer journey. In the following section we outline some of the more prominent incentives and policy interventions which, with the support of patient advocates, were designed to encourage private investment into paediatric drug discovery and development.

06: PRISM: from uncertainty to capital decisions

PRISM (Pipeline Risk and Investment Simulation Model) is a purpose-built financial modelling tool for C-Further's paediatric oncology therapeutics portfolio. It runs Monte Carlo simulations – thousands of simulated futures for each individual asset and for the portfolio, translating technical uncertainty (will a drug clear clinical trials?) and economic uncertainty (pricing, timelines) into financial outputs such as portfolio Net Present Value, Internal Rate of Return distributions, capital sufficiency, and pipeline sizing.

Why it matters

C-Further needs an honest, risk-adjusted view of what its paediatric oncology portfolio is worth, not a single optimistic headline number.

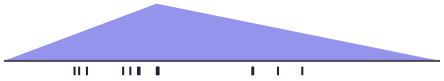
In short, it turns biological and clinical uncertainty into the financial language that investors, funders, and the C-Further team need to make and defend capital decisions.

What goes in

Biological uncertainty
Will a drug clear clinical trials?

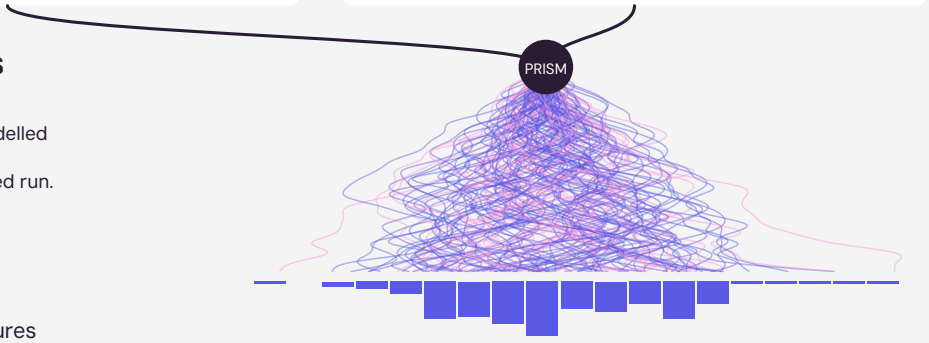


Economic uncertainty
Pricing, timelines



What PRISM does

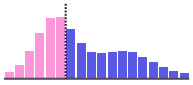
Stage durations, costs, and probabilities of success are modelled as statistical distributions sampled fresh on every simulated run.



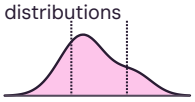
Thousands of simulated futures for each individual asset and for the portfolio

What comes out

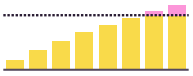
Portfolio Net Present Value



Internal Rate of Return distributions



Capital sufficiency



Blended fund structure



Pipeline sizing



Who it is for

The C-Further team
who run the tool for capital planning and portfolio decisions.
We use PRISM to inform us, ***not*** to select the projects which are solely investable

Investors and funders (philanthropic, PRI/impact, and private equity)
who use the IRR distributions and repayment probabilities to understand their specific risk and return

Technical reviewers and governance
who review the outputs and build upon the assumptions

Source: C-Further PRISM (Pipeline Risk and Investment Simulation Model), version May 2026. Charts are illustrative only and do not show model results

Fixing markets with incentives

How have pull incentives been structured to 'fix' the market?

In the sections that follow we examine the tools built to correct this failure, first the pull incentives designed to restore the reward, then the push funding that sustains the science, then the newer structural models, and we ask of each the same question: does it help to shape a new market, or does it only attempt to temporarily fix it?

Pull incentives work at the finished-product end of development. They restore or protect the reward once a well-designed therapeutic has been approved, creating real value for people affected by cancer. However, they share a set of limitations in that they often act late, once the risky science has been completed, rewarding the endpoint rather than funding the capital-intensive development hurdles where products currently stall. Many incentives are one-off or individually tradable rather than a standing source of development capital. As the recent policy record shows, the same legislative power that grants an incentive can withdraw it. Pull incentives are necessary and powerful, but on their own are structurally fragile.

Orphan Drug Designation

Orphan drug designation is the clearest evidence that a well-designed incentive package can transform a market. In the decade before the US Orphan Drug Act of 1983, only ten drugs for rare diseases had been approved; by 2010 the figure exceeded 350, and orphan products, which barely existed beforehand, now account for around a third of all newly approved drugs and biologics [31]. The reward is a period of market exclusivity that delays competing generics and gives a developer longer to recoup its costs (as well as small push incentives in the form of tax credits and fee waivers), extended further in EU and US jurisdictions when requested paediatric studies are completed (see *Figure 05*).

Orphan designation in oncology clusters at the common end of what counts as rare: almost 70% of rare neoplastic designations cover conditions affecting one to three people per 10,000, far more prevalent than most childhood cancers [32]. Cancer dominates the orphan landscape, but overwhelmingly adult cancer, with seven of the ten most-designated diseases being adult malignancies [33], and in the USA some 40% of oncology orphan designations attach to biomarker-defined subsets of common adult cancers rather than to rare diseases in their own right [34]. For the child-first development this paper is concerned with, orphan designation is necessary but not sufficient.

Priority Review Vouchers

Other types of pull incentives reward the company rather than the product. When a company obtains approval for a therapeutic treating a serious or life-threatening paediatric condition in the USA, it receives a Priority Review Voucher, which shortens FDA review of a future drug from ten months to six. The voucher can be applied to another of the company's own drugs or sold outright, and it is this transferability that gives it value, letting a developer accelerate a later, potentially blockbuster launch or convert the reward into cash. For a small or pre-revenue company in particular, it is a rare liquid asset: one that can be sold for a substantial lump sum (as of publication the sale price ranges from $180M–$220M) without diluting equity or waiting on a sales curve to ramp up, helping to smooth cashflow in an otherwise volatile financing environment. Demand has stayed strong, with some companies stockpiling vouchers for future launches, and resale prices have held up even after the Commissioner's National Priority Voucher introduced an alternative route to faster review for drugs meeting certain "national priorities" (see *Figure 07*).

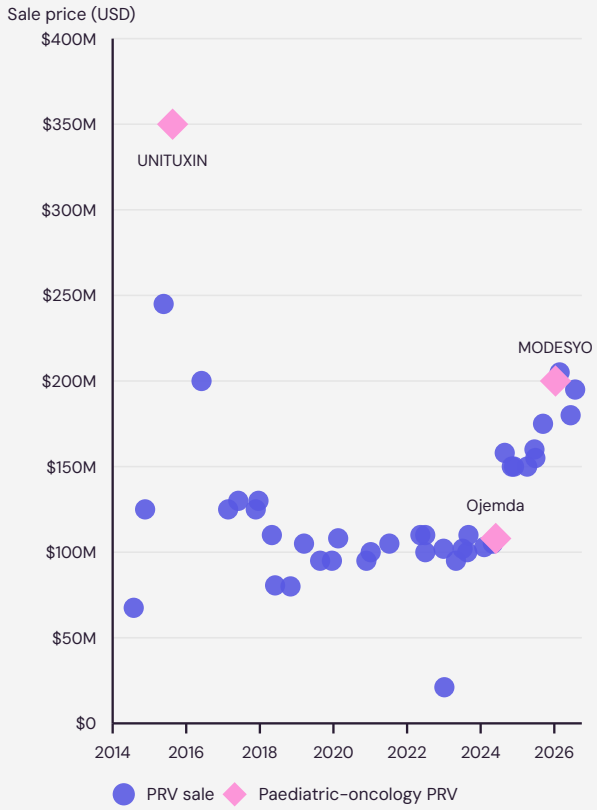
The incentive is also politically contingent. The programme lapsed in December 2024 when Congress did not reauthorise it in time, before being extended to 2029 through the Give Kids a Chance Act, with the FDA recently proposing to make it permanent [35]. The reward can be substantial, but it is a one-off windfall, decoupled from the cost of the development.

Disincentives amongst a dynamic policy environment

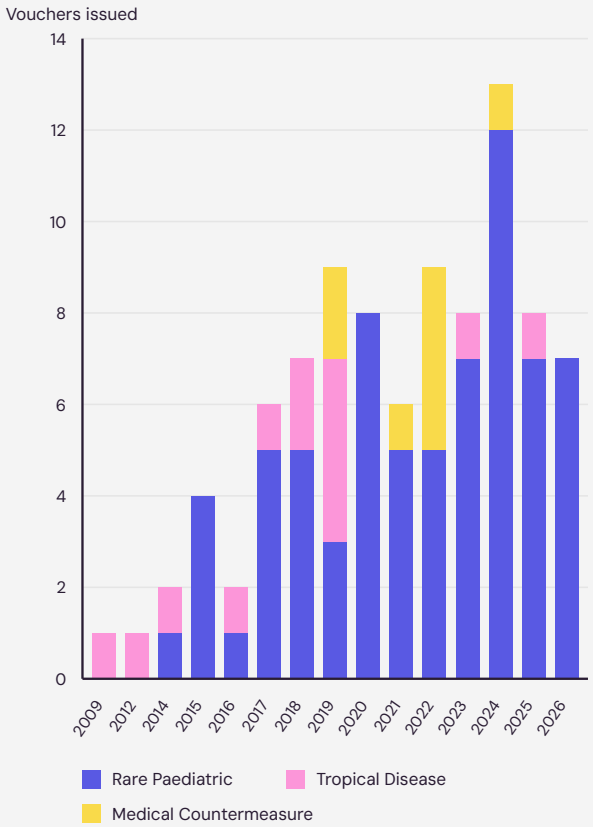
The amount of capital needed for a successful pull incentive is significantly higher than for a push incentive, in part because pull incentives require sustained funding. This can lead to a trade-off between balancing affordability for increasingly strained health systems and encouraging investment and innovation. This tension between cost control and innovation is not hypothetical, and incentives are only as durable as the policy that underpins them. Just as legislation can create a reward, it can withdraw or offset one, sometimes as an unintended consequence of measures aimed at something else entirely. The Inflation Reduction Act (IRA) is the clearest example. Although intended to sustain drug development, it may in practice have disincentivised investment. The IRA allows an exemption from otherwise compulsory price negotiation for therapeutics (after 7 or 11 years of sales for Small Molecules and Biologics respectively) which are only commercialised for a single indication and orphan

07: Trends in Priority Review Voucher sales and types

PRV market price by date sold



Count of PRV issuance by type



Source: C-Further PRV Tracker; FDA / Federal Register PRV issuance notices and disclosed secondary-market transactions. Updated Aug 2026 with post-cutoff disclosed sales (MODESYO, KRESLADI, AVLAYAH) and five 2026 Rare Paediatric issuances.

therapies. As supplemental approvals for paediatric indications have historically followed initial approvals in adult indications (see *Figure 03*), the compulsory negotiation imposed by the IRA for expanding the label of the medicine to the paediatric setting caused companies to question if the revenue penalties are worth the risk of investing in paediatric supplementary approvals [36]. The IRA was cited by Eli Lilly and Alnylam as a factor for terminating their programmes. To address this issue on orphan incentives, the exemption was ultimately expanded to medicines with multiple rare indications with the passage of the One Big Beautiful Bill Act in July 2025. More broadly, as the IRA impacts revenues of pharmaceutical and biotech companies, it will likely impact R&D spending on early innovation [37].

More recently, many major pharmaceutical companies have pledged hundreds of billions of dollars of investment into US pharmaceutical manufacturing in order to avoid tariffs the Administration is planning to place on medicines manufactured outside the US [38]. These striking moves may have unintended consequences beyond their primary aim of reducing America's dependence on foreign generic manufacturing. Tariffs in particular may have a disproportionate negative impact on small and midsize biotech companies where many innovative medicines, platform technologies and tools are being developed which may directly or indirectly lead to new treatments for children with cancer [39].

The vast majority of early-stage paediatric cancer research is funded through public or philanthropic money, primarily via grants, which are awarded without expectation of repayment or return. Grants can be viewed as structured push incentives in that they enable high-risk, early-stage basic research which would otherwise not be funded by bio-pharmaceutical companies. Public and philanthropic money sustains the science base from which everything downstream flows, and in aggregate it does so at real scale. But it carries three limits that matter for what follows. 1) It funds knowledge more than true product development (often generically referred to as translation), with only a minority reaching the development of actual treatments. 2) It is often insufficient to fund the capital-intensive clinical stage. 3) It is delivered through a fragmented landscape of institutions, agencies and foundations, each making important contributions, but none structured to carry an asset all the way to market.

The next section examines the role of childhood cancer funding and different capital providers in creating new treatments for children and young

08: An opportunity for the UK

A rare alignment of legislation, strategy and regulatory reform

Policy timeline

Legislation · Strategy or plan · Regulatory pathway · Open window: still being shaped

Nov 2023
Rare Therapies Launch Pad announced
A pathway for children with rare conditions to access individualised therapies

Mar 2025
Innovative Licensing and Access Pathway relaunched
UK-wide, with the NHS as a core partner

16 Jul 2025
Life Sciences Sector Plan
Commercial trial set-up in under 150 days; up to £600m for a Health Data Research Service

4 Feb 2026
National Cancer Plan for England
First dedicated chapter on children's and young people's cancer

27 Feb 2026
England Rare Diseases Action Plan 2026

5 Mar 2026
Rare Cancers Act signed into law

28 Apr 2026
New UK clinical trials regulations in force
Combined regulatory and ethics review

21 May 2026
MHRA draft rare disease therapies framework
Out for consultation: proposes an Investigational Marketing Authorisation that combines trial and market approval

2026–2029
Secretary of State's review
Of orphan cancer medicine regulation, considering approaches in other countries

2027
National Cancer Plan actions due
National research priorities for children's and young people's cancer; clinical justification required for age limits on trials; better national data

By 5 Mar 2029
Report to Parliament

The UK paediatric and orphan framework today

Paediatric plans are mandatory

A new medicine needs an agreed UK paediatric investigation plan (PIP) or a waiver, on every MHRA route, including the International Recognition Procedure and Project Orbis

Orphan reward

Up to 10 years' market exclusivity, plus 2 more years if results from a completed PIP are in the product information

Waivers

Can be granted where a condition does not occur in children, or where no significant benefit over existing treatments is expected

Questions for the review: learning from other countries

The Act directs the review to consider regulatory approaches taken in other countries. For EU and US detail, see *Figure 05*.

1 Should a drug's molecular target, not its adult indication, trigger a paediatric plan?

In the US, the RACE for Children Act (in effect since August 2020) requires paediatric studies of new targeted cancer drugs whose target is relevant to a childhood cancer, even when the adult indication has orphan designation

2 Is there a role for a transferable reward?

The US rare paediatric disease priority review voucher was reauthorised in February 2026 and runs to September 2029

3 Could rewards be staged?

The ACCELERATE platform proposes paying part of the reward for early paediatric data that inform go/no-go decisions, and the rest when the plan is complete

Sources: T. Kirby, "Rare Cancers Bill to become law in UK", Lancet Oncol. 27(4):411 (2026); "Rare therapies and UK regulatory considerations", GOV.UK; D. J. O'Connor et al., Nat. Med. 31:1379–1380 (2025); Genomics England, Rare Therapies Launch Pad pilot announcement (22 Nov 2023); MHRA, ILAP relaunch statement of policy intent (2024), Procedures for UK paediatric investigation plans and Orphan medicinal products guidance (accessed Oct 2026); HM Government, Life Sciences Sector Plan (16 Jul 2025); DHSC, The National Cancer Plan for England, ch. 6 (4 Feb 2026) and England Rare Diseases Action Plan 2026 (27 Feb 2026); Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025, SI 2025/538; MHRA, consultation on a draft regulatory framework for rare disease therapies (21 May 2026); FDA Reauthorization Act 2017, s.504 (RACE for Children Act); US Consolidated Appropriations Act 2026, P.L. 119-75, s.6604; T. de Rojas et al., Cancer Med. 12(7):8825–8837 (2023), doi:10.1002/cam4.5627. [40-43]

The global funding landscape

Who funds the push incentives and how effective are they at developing new child-first treatments?

people with cancer.

What is the role of early-stage funding in the development of new treatments for childhood cancer?

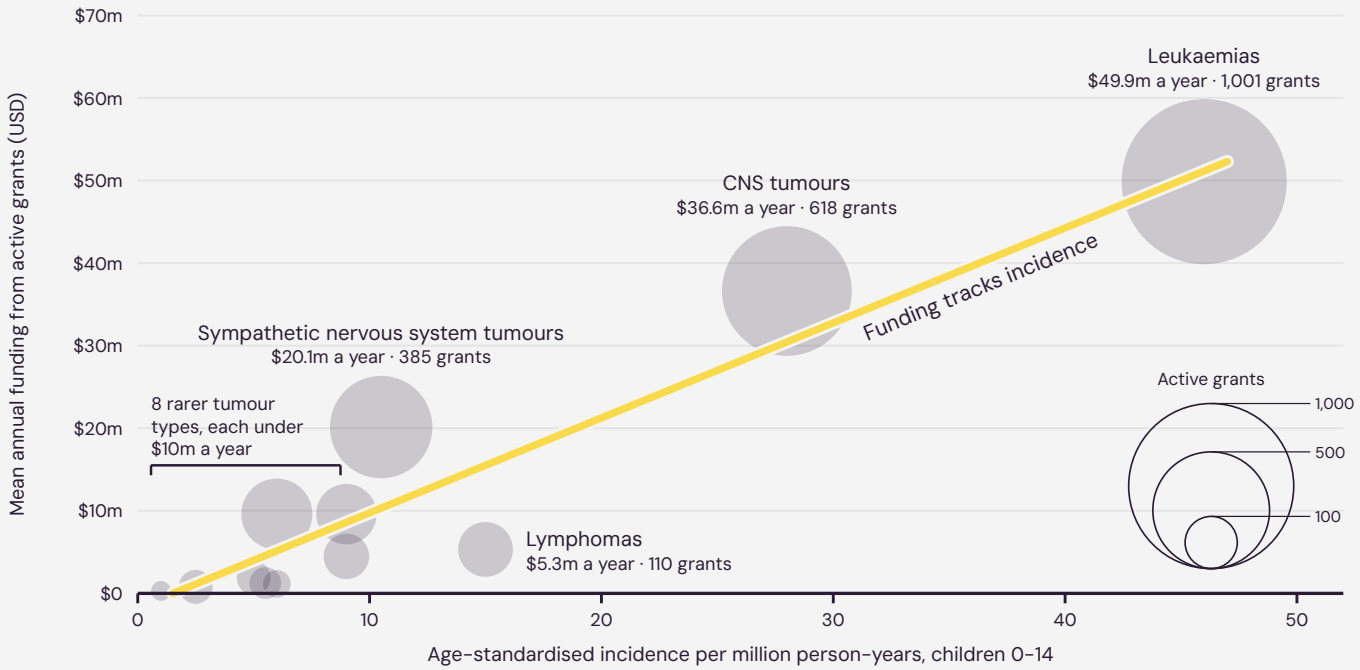
Based on an analysis from Loucaides et al the mean annual grant funding allocated to childhood cancer research worldwide from 2008-16 was $307.1M annually, totalling over $2B for the study period, and largely tracks the incidence of childhood cancer indications (see *Figure 09*) [44]. While $2B is a large number, it is dwarfed even by the NCI annual budget dedicated to cancers in adults. Drilling into the data further reveals that less than 30% of this research funding was categorised as being used to research 'Treatments', and once subdivided between childhood cancer subtypes, this represents sub-critical levels of funding, for what is highly capital-intensive research.

Does childhood cancer remain a national and international priority for the State?

Government agencies, particularly the National Cancer Institute (NCI) have played a major role in underpinning the long-term investment in fundamental biological research, providing the raw materials for scientific and clinical advances, each advance building on past discoveries and in turn spurring new ideas. Beyond basic research, as the largest government funder worldwide, the NCI also underpins major hospital infrastructure spanning transdisciplinary boundaries to research and care for children with cancer - so called comprehensive cancer centres (CCC). These centres leverage this critical capability to raise significant philanthropic donations from family trusts, foundations, high-net worth individuals and the public. Through this critical mass, these CCCs have played an important role in delivering academia-initiated clinical trials through major co-operative groups such as Children's Oncology Group (COG). While these CCCs have strong translational research agendas, they often act independently. As a result focused strategic initiatives have been established to encourage the development of a critical mass of expertise, infrastructure and research at a national level.

09: Global childhood-cancer research funding broadly tracks tumour incidence, 2008-16

Mean annual funding from active grants vs age-standardised incidence, by tumour type. Bubble area = number of active grants. More recent analyses are not currently available.



Excludes general paediatric oncology grants (37.8% of all funding), which are not tumour-type specific. Source: Loucaides et al., Lancet Oncol 2019;20:e672-84 (Fig 3). Incidence from Steliarova-Foucher et al. (IICC-3), Lancet Oncol 2017;18:719-31.

President Biden's role in reigniting the Cancer Moonshot initiative included consortia and initiatives that seek to address paediatric challenges across fusion oncoproteins, immunotherapy in children, and paediatric brain tumours [45]. President Trump's 2019 proposal, included in the State of the Union address, to spend $500 million over 10 years on childhood cancer research, highlights the political alignment across the floor that more needs to be done for children with cancer [46]. Data integration and harmonisation via federated sharing has materialised as a major thrust of an initial $50M commitment via the Childhood Cancer Data Initiative (CCDI) which is currently in design phase in close collaboration with COG [47].

Europe's public funding into childhood cancer research has been more conservative, although many centres of excellence provide high-quality care and carry out ground-breaking clinical and preclinical research (according to Loucaides et al, only 16% of global childhood grant funding was allocated to European centres in the research period) [48]. There has been political will to make changes; Ursula Von Der Leyen, the European Commission President, established childhood cancer as a top priority under the Helping Children with Cancer Initiative, when launching the European Beating Cancer Plan and the Cancer Mission. These efforts in Europe have focused on understanding and management of late effects of treatments, expanding social services for psychosocial support and rehabilitation for children and their families including through a €36 million Horizon Europe Cancer Mission [49].

Australia offers one of the clearer examples of government using dedicated, matched funding to de-risk childhood cancer research and pull in capital that would not otherwise materialise. Australia has maintained a decade-long series of strategic initiatives to prioritise children's cancer research, including investment in paediatric hospitals, clinical-trial research infrastructure and research programmes including major investments such as the Zero Childhood Cancer Program (ZERO). In 2017, the Australian Government established the Australian Brain Cancer Mission, committing AU$50 million through the Medical Research Future Fund (MRFF). It then sought matching contributions from philanthropy, other governments, industry and the private sector, with Cure Brain Cancer Foundation and Minderoo Foundation's Eliminate Cancer Initiative among the philanthropic co-funders. In 2026, Cancer Australia published the Childhood, Adolescent and Young Adult Cancer Roadmap, setting out a strategic framework to guide policy and investment in this area backed by an initial AU$210M as part of a broader funding commitment [50][51].

In contrast, there is currently limited funding of children's cancer research in China, but this also certainly represents missing data. However, international efforts such as St Jude Global China Regional Program has accelerated the impact of governmental interventions with rates of survival from children's cancer making major progress over the last decade. [52]

In the UK, the Rare Cancers Act was signed into law in March 2026. It does not itself change orphan drug law. Instead, it requires the Secretary of State to review the regulation of marketing authorisations for orphan medicines used to diagnose, prevent or treat cancer, and to report to Parliament by 5 March 2029. The review is expressly directed to consider regulatory approaches taken in other countries. This is a significant opportunity to strengthen the link between MHRA orphan drug status and paediatric research, development, and to learn from incentives in other jurisdictions. In 2026 the UK government also published a National Cancer Plan for England which for the first time included dedicated commitments to children's cancer. Although these commitments were made largely without dedicated research funding to support their delivery, other initiatives such as the Rare Therapies Launch Pad and the MHRA's forward looking rare disease framework as well as the England Rare Diseases Action Plan 2026 demonstrate that now is an opportune moment for the UK to become international leaders in developing, regulating, and integrating new therapeutics which address all rare diseases, including paediatric cancer. [40-43](see *Figure 08*).

What role do charities and philanthropy play in supporting the development of new treatments for childhood cancer?

St Jude Children's Hospital is the first and only CCC focused solely on paediatric research and medicine which operates a semi-independent funding model supported by the American Lebanese Syrian Associated Charities (ALSAC), raising nearly 90% of the $1.7B operating costs on an annual basis via mass fundraising [53]. This mixed public-foundation model has also proved successful at the Dana-Farber Cancer Institute with the Jimmy Fund historically underpinning mass fundraising campaigns. Major philanthropic gifts also play a key role such as a recent $150M gift to MD Anderson, enabling the establishment of the Kinder Children's Cancer Center at Texas Children's [54].

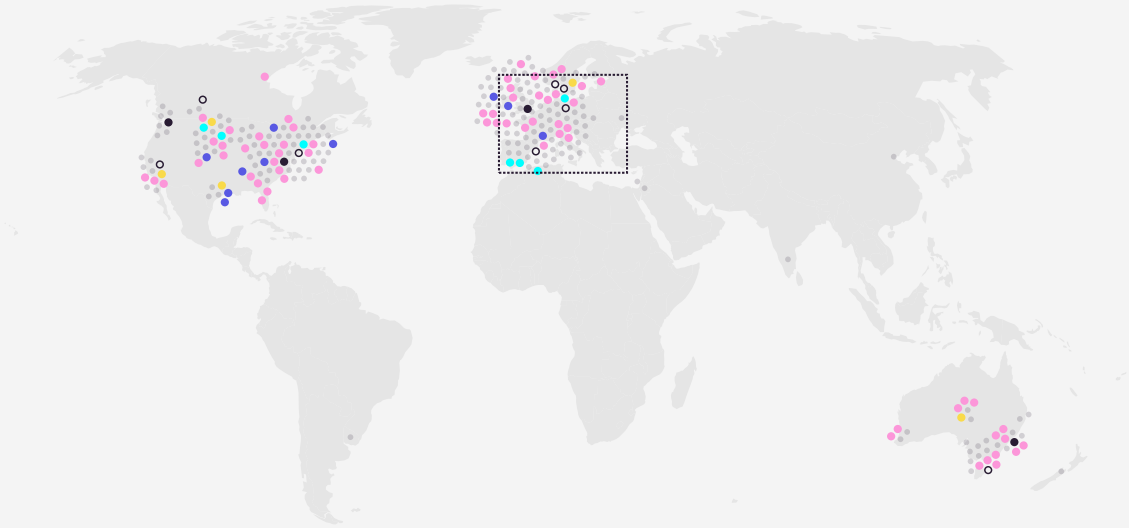
While mass fundraising has proved extremely effective, small but focused philanthropic foundations have also played an important role in underpinning paediatric cancer research at the early stages of therapeutic development. Given the many families affected by childhood cancer, foundations large and small have been established to support research in this area. There is a particular proliferation of non-profits with a focus on supporting a single cancer indication, so for brevity, only a few diverse indication agnostic exemplars focused on

010: Who funds paediatric cancer therapeutic research?

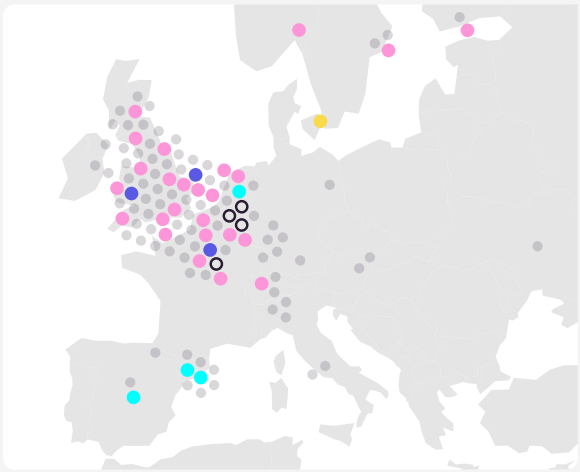
The vast majority of early-stage paediatric cancer research is funded through public or philanthropic money, primarily via grants, which are awarded without expectation of repayment or return. *The following analysis is not exhaustive* but seeks to illustrate the complex global funding landscape.

- Governments with national priorities
- Charities
- Foundations and corporate giving
- Fundraising hospitals and centres
- Impact investors and accelerators
- Networks and consortia
- Other research partners

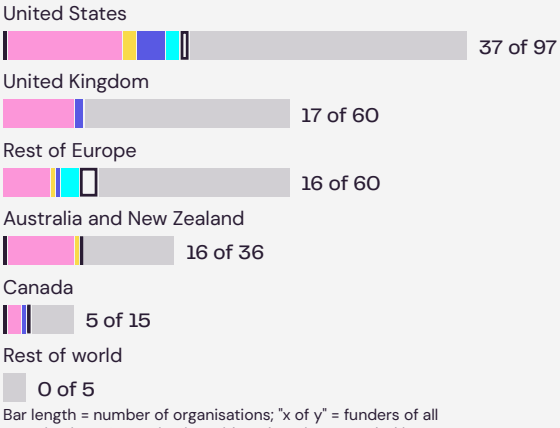
Where the funders are



Europe and the UK, enlarged



Funders and others by region



Bar length = number of organisations; "x of y" = funders of all organisations. 1 organisation with no location recorded is not shown.

United States

Beyond basic research as the largest government funder worldwide, the NCI also underpins major hospital Infrastructure.

Europe

According to Loucaides et al, only 16% of global childhood grant funding is allocated to European centres in the research period [48]"

Australia

In 2017, the Australian Government established the Australian Brain Cancer Mission, committing AU$50 million through the Medical Research Future Fund (MRFF).

China

There is currently limited funding of children's cancer research in China, but this also certainly represents missing data.

Source: C-Further organisation landscape dataset (n = 274 organisations, October 2026). Funders = organisations identified as providing funding for paediatric cancer research (charities, government, foundations, impact investors and fundraising hospitals). Networks and consortia coordinate rather than fund. Other organisations with paediatric relevant research are shown in grey. Financial scale is each organisation's overall size, not its paediatric spend. Quoted text and figures from the report, refs [48]–[59].

therapeutic development are highlighted below:

- *CureSearch*, a not-for-profit set up with the mission to change the drug development landscape by accelerating the development of safe, effective treatments with an explicit goal of funding projects with the potential to reach the clinic or marketplace within three to five years. [55].
- *Alex's Lemonade Stand Foundation* (ALSF), the largest independent childhood cancer charity in the United States, has grown from a child's front-garden lemonade stand into a major research funder, raising more than $300 million and supporting over 1,500 projects at around 150 institutions across North America and Europe [56]. Its grant-making increasingly reaches toward the translational end of research: alongside early-career awards, its Crazy 8 Initiative, launched in 2020, has committed $35 million to collaborative teams tackling the hardest problems in childhood cancer, including the biology that underpins new therapeutics [57]. ALSF shows both the reach and the limit of philanthropy; it can mobilise substantial sums and steer them toward therapeutic discovery, but it does so almost entirely as a grant-maker to academic investigators with limited control of the ultimate translational output.
- *The Children's Cancer Therapy Development Institute* (cc-TDI) takes a more hands-on approach to the same problem. Modelled on the ALS Therapy Development Institute and led by its founder Charles Keller, cc-TDI is a non-profit built specifically to address the "preclinical gap" where paediatric programmes so often stall. Rather than funding work at arm's length, it runs its own laboratory-based drug discovery engine, combining disease biology with computation to move candidates toward the clinic. Recognising that discovery alone does not secure a route to patients, cc-TDI has established Artisan Biopharma, a for-profit public benefit corporation it owns outright, as the vehicle to develop and commercialise the assets it generates and to channel sustainable funding back to the discovery engine behind it [58]. This is a notable attempt to close the loop within a single mission-driven structure, carrying an asset from bench toward market rather than handing it off. It remains early and modest in scale relative to the capital that later-stage development demands, but it is exactly the kind of structural experiment the rest of this paper argues for.
- *M4K pharma*, a wholly owned subsidiary of the non-profit, Agora Open Science Trust, takes a different approach. It advocates for an open-science approach to ease the legal and practical challenges of international collaboration and accelerate independent scientific inquiry by others at the early stages of paediatric drug development. This open-science approach relies on data exclusivity benefits to secure market share instead of the monopoly rights afforded to patent protection [59].

How can networks address coordination and reduce fragmentation?

While philanthropic funding to childhood cancer research delivers tremendous benefits in aggregate, the sheer proliferation of not-for-profits focused specifically on childhood cancer has an unintended consequence: misaligned priorities, fragmentation of capital and duplication of effort.

Clinical networks and paediatric oncology societies have evolved to address this complexity, coordinating efforts and acting as a cohesive voice for the paediatric research community. In Europe, the European Reference Network on Paediatric Cancers (ERN PaedCan) and the European Society for Paediatric Oncology (SIOPE) fulfil this role at a regional level, while national and international clinical trials cooperative groups such as COG in the US, Innovative Therapies for Children with Cancer (ITCC) in Europe, and the Australian and New Zealand Children's Haematology/Oncology Group (ANZCHOG) have driven substantial progress in their respective regions.

Further recognition that the challenges facing paediatric cancer drug development are interdependent and multi-sectoral rather than addressable by any single clinical network or region acting alone led to the establishment of ACCELERATE in 2015. ACCELERATE is a multi-stakeholder platform bringing together clinicians, translational researchers, regulators, patient advocates and industry representatives to ensure new medicines are developed for the maximum benefit of children with cancer. Since then, the group has advocated a mechanism-of-action approach through its Paediatric Strategy Forums, spanning a range of workstreams including the assessment of financial solutions to fund paediatric cancer research [48].

Creative models and why they fall short

How are public-private partnerships, platforms and venture philanthropy are trying to fill the gaps?

The push and pull incentives described so far work at the edges of the problem, trimming costs at one end or improving rewards at the other. Neither structurally resolves the barriers set out earlier in this paper: the difficulty in drugging paediatric targets, the scarcity of predictive preclinical models, the operational burden of small and dispersed trial populations, and the manufacturing and commercial challenge of vanishingly small markets. A set of more creative structures has emerged to overcome these barriers head-on and a subset of which are examined below. However, when examined by where in the development pipeline they act, how much risk they absorb, at what scale, and crucially whether they are *repeatable and sustainable*, they represent only part of the solution.

Venture-Backed Biotech

Capital invested in the earliest stages of therapeutic discovery is unlikely to be recovered since there is little to no visibility into the revenue potential of the product and because such a small fraction of a therapeutic pipeline makes it to the market. In the later stages, however, investors begin to understand the potential business case for a therapy. This is where opportunities to tap into capital markets have been used to date. One way to reduce risk is to repurpose existing but 'stalled' assets which have already been evaluated for safety and efficacy in humans in a different cancer indication. Day One Biopharmaceuticals used this model to successfully acquire a highly selective type 2 pan-RAF inhibitor from Takeda, which was subsequently repositioned for children with paediatric low-grade glioma (pLGG) harbouring an activating BRAF alteration, now commercialised under the brand name Ojemda (Tovorafenib). Data from their phase II trial in pLGG showed an overall response rate of 67% [60] which enabled them to raise substantial investment from private markets ($60M, $130M at Series A and B respectively) and complete an IPO in 2020 ($184M), ahead of significant sales when the asset received FDA approval. Day One's $2.5 billion acquisition by private French pharmaceutical company, Servier, demonstrates that commercial capital deployed on the right assets can accelerate progress, in what is likely a rare combination of patient impact and return on investment for childhood cancer [61]. The nature of the for-profit model, however, does limit its applicability to childhood cancer indications with a minimum market size required for investors to make a sufficient return. Even then, the role of any commercial entity is very often limited to supporting pivotal trials or market commercialisation of an already largely derisked therapeutic [62].

Public–Private Partnership

Although public and charitable programmes have been essential in sustaining early development of therapeutic programmes, private stakeholders have also taken an increasing role due to their necessary interaction with the public sector. These models show real promise for convening actors around targeted time-bound problems.

ITCC-P4: The Innovative Medicines Initiative (IMI) is the world's largest public-private partnership in health with a total budget of €5 billion – half from the European Union and half from the pharmaceutical industry, secured through in-kind contributions from the EFPIA. Innovative Therapies for Children with Cancer Paediatric Preclinical Proof-of-concept Platform (ITCC-P4) was established through funding by the IMI to develop a large repertoire of patient-derived xenograft (PDX) models representing all major high-risk solid paediatric cancer types for in vivo drug testing. The success of the programme has resulted in the German biotech ITCC-P4 gGmbH which is licensing over 400 well characterised patient-derived xenograft (PDX) models, enabling access to pharmaceutical companies who are legislatively compelled to evaluate their programmes for in vivo drug testing in paediatric populations thereby supporting long-term sustainability for the resource [63].

Foundation for National Institutes of Health (FNIH): Established by Congress in 1990, the FNIH is a not-for-profit 501(c)(3) charitable organisation that has a long history of convening public and private partnerships between the NIH, academia, life science companies, and patient advocacy groups. FNIH is currently scoping a bold new public-private partnership dedicated to accelerating the development of innovative ultra-rare cancer treatments - The Ultra-Rare Cancer Treatment Advancement Program 'ULTRA', initially addressing the challenges of manufacturing and access for two ultra-rare cancers driven by EWSR1 gene fusions affecting children and young people [64]

Platform Models

Platform technologies are reshaping drug development by enabling cross-indication adaptability, rapid reuse of data, and faster paths to clinical success. Because grant funding is inherently high-risk, high-reward, new platform technologies often originate in universities and specialist hospitals,

where they are validated before being spun out into new ventures whose assets are then acquired or licensed by pharmaceutical companies.

This later-stage transfer of intellectual property from academia to industry has already proven successful for therapeutics relevant to children's cancer: tisagenlecleucel moved from the University of Pennsylvania to Novartis and axicabtagene ciloleucel moved from the National Cancer Institute to Kite Pharma. Modalities such as cell and gene therapies (CGTs) have platform qualities of their own, in that manufacturing processes, vector systems and regulatory pathways can often be reused across different diseases rather than developed afresh for each product. In principle this should make CGTs well suited to the academia-to-industry pipeline described above. In practice, however, small paediatric market sizes limit the return on investment achievable within the traditional biopharmaceutical model, producing a market failure that has left children with cancer underserved by CGT development to date.

To address this, investigators at Stanford University have proposed the creation of a new non-commercial entity, the Pediatric Advanced Medicines Biotech, to lead late-stage pivotal development of CGTs and commercialising these outside the traditional biopharmaceutical model. Rather than each academic platform seeking its own individual commercial licensing deal, such an entity would pool platform technologies licensed from academia under one roof, partner with the academic ecosystem who have validated these therapeutics in early trials, manufacture products in academic GMP facilities, and work closely with regulators, so that promising paediatric cancer therapies can be carried across the development "valley of death" collectively rather than one at a time. Crucially the model relies on a mixed model of payor reimbursements, sublicensing deals to pharma (where such technologies may be generally applicable) and philanthropic grants. [65][66]. It is a promising idea, but it currently remains a proposal, confined to one modality, and dependent on reimbursement.

Venture Philanthropy

Direct investment into companies by impact investors (also know as venture philanthropists), private investors who seek to generate simultaneously financial and 'social' returns, have attracted intense interest and controversy over the last decade. Recent quantitative research has demonstrated that impact investment funds mostly invest in companies that traditional financiers would have funded anyway, with a lower expectation of return. However, their value is their patient and risk tolerant capital; allowing for longer time horizons and taking on more risk than traditional investors [67]. The Cystic Fibrosis Foundation (CFF) was a forerunner in venture philanthropy, investing $150 million in Vertex Pharmaceuticals over 12 years to develop a new approach to treat cystic fibrosis. Vertex brought ivacaftor (Kalydeco) to market in 2012, and through a later transaction with Royalty Pharma, the CFF received $3.3 billion in exchange for its royalty interests in ivacaftor and related assets – capital it can sustainably reinvest into fundamental research and more venture investments to further their mission. No such non-profit has shared the same success to date in paediatric cancer, although new examples of venture philanthropy are emerging. Seattle Children's spun out and incubated BrainChild Bio in 2023 acting as its sole funder for its first two years [68]. Now, the biotech has gained the support of an unnamed private family fund and foundation, as well as WRF Capital, the investment wing of the Washington Research Foundation to direct its CAR-T cell therapy platform towards pivotal trials in diffuse intrinsic pontine glioma (DIPG) [69].

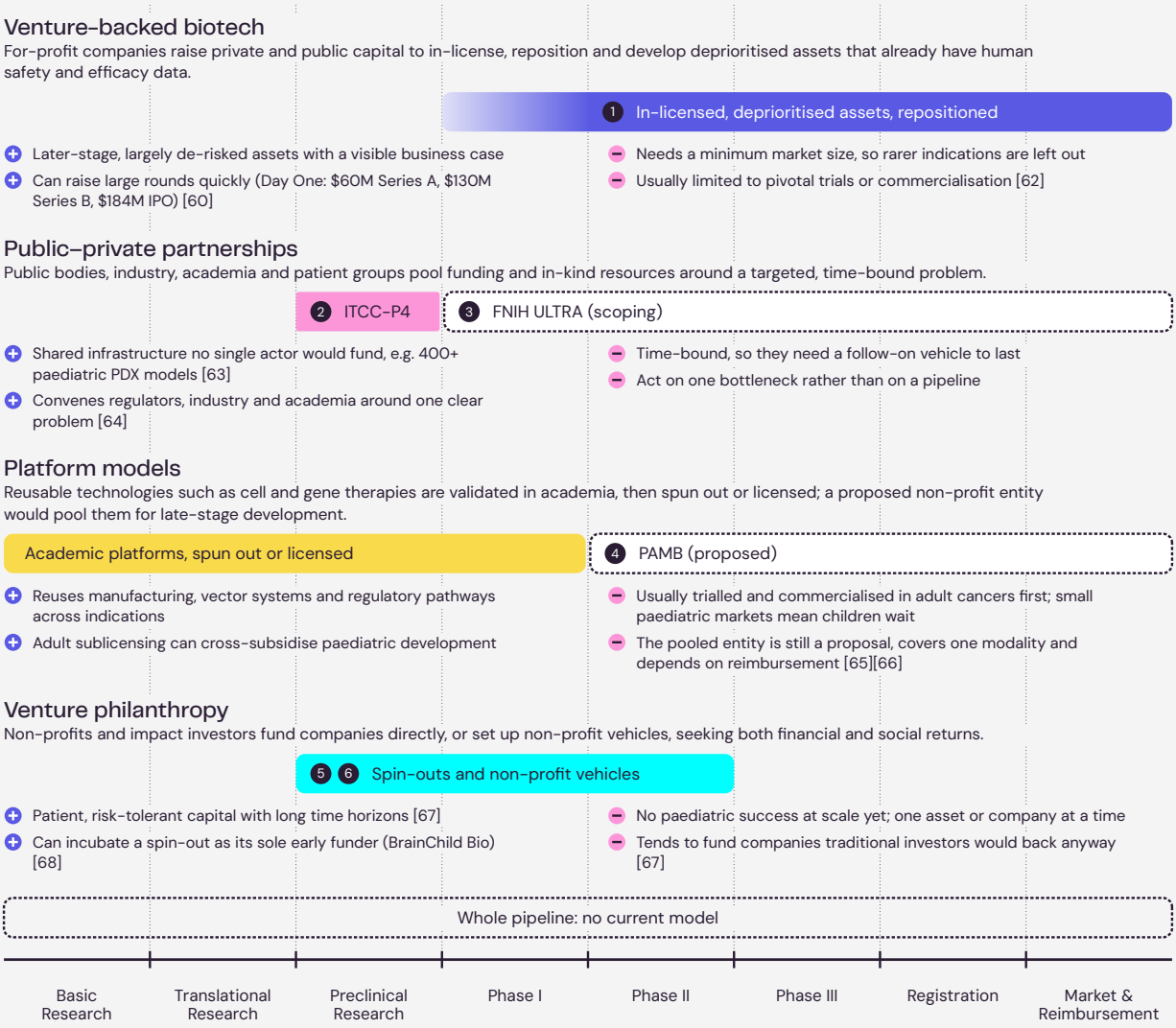
Other major healthcare funds such as Deerfield Management prefer to keep their return seeking investments and impact investments distinct from one another. Rather than making direct impact investments into companies, they have used their extensive resources obtained through the success of their fund to launch various non-profit vehicles, taking a more active role in generating operational capacity. They recently launched the Advancium Health Network and CobiCure, two independent entities which are actively looking to secure the rights to therapeutics with relevance to paediatric cancer and take them through the early stages of clinical development. These newly formed initiatives benefit from synergistic infrastructure, capital and expertise that its parent Deerfield controls [70].

The common thread across all of these approaches is that they act on a single asset, company, or bottleneck. What none of them does is change the structure of the risk itself so that capital can be raised against a whole therapeutic pipeline dedicated to childhood cancer. That is the question the next section takes up.

011: Where new creative models act in the childhood cancer pipeline

Push and pull incentives work at the edges of the problem. A set of more creative structures has emerged to tackle the barriers head-on, but each acts at only part of the development pipeline.

Active today · Partial involvement · Proposed or being scoped · ❶ See key examples



Key examples

❶ **Day One Biopharmaceuticals → Servier**
In-licensed a pan-RAF inhibitor from Takeda and repositioned it for paediatric low-grade glioma (Ojemda); acquired by Servier for $2.5B [60][61].

❷ **ITCC-P4**
IMI-funded platform of patient-derived xenograft models for high-risk paediatric solid tumours; now licenses 400+ models through ITCC-P4 gGmbH [63].

❸ **FNIH ULTRA**
Being scoped by FNIH to tackle manufacturing and access for two ultra-rare EWSR1 fusion-driven cancers in children and young people [64].

❹ **Pediatric Advanced Medicines Biotech**
Proposed by Stanford investigators: a non-commercial entity pooling academic CGT platforms for pivotal development and commercialisation [65][66].

❺ **BrainChild Bio**
Spun out of Seattle Children's in 2023, its sole funder for two years; now taking a CAR-T platform towards pivotal trials in DIPG [68][69].

❻ **Deerfield (Advancium, CobiCure)**
Advancium Health Network and CobiCure: non-profit vehicles launched by Deerfield to secure paediatric-relevant therapeutics and take them through early clinical development [70].

Towards systemic solutions

How do we move beyond opportunistic gap funding to repeatable pathways to impact for children with cancer?

Everything so far has been incremental, working within the existing risk profile rather than changing it. The models in this next section are different in kind. They set out to alter the structure of the financial risk, by pooling many programmes together so that the failure of any individual one matters less, and by layering flexible capital so that different investors can take the parts of the risk they are willing to hold. This is where a repeatable structure begins to appear.

Megafunds

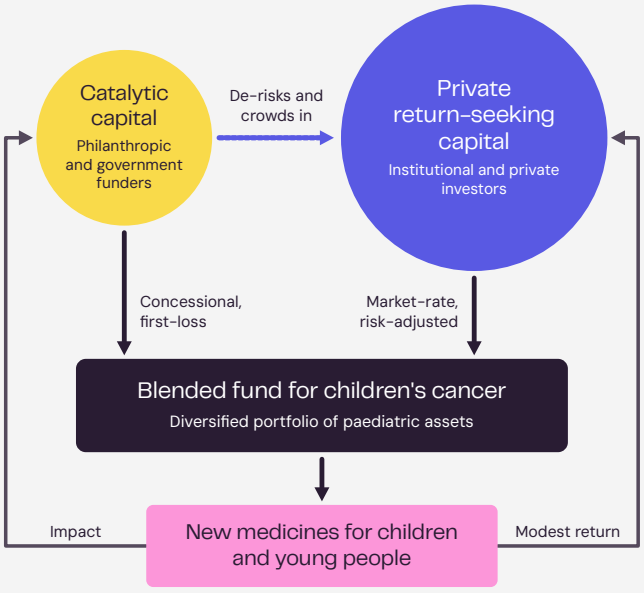
The concept of creating large, diversified portfolios of assets is not new in capital markets. The higher the co-variance between a set of assets, the more an investor will be able to reduce risk for an optimised level of return. Venture capital investors such as Atlas Venture and Flagship Pioneering have already applied these principles in biotech by creating (and having a controlling stake in) companies across various targets, modalities and indications. In this model, a portfolio manager controls a set of companies spanning multiple technologies and disease areas. Instead of focusing on a single technology in the traditional way, the portfolio manager uses a distinctive form of expertise - such as in fundraising, investment, venture creation, R&D, manufacturing, commercial management, leadership, and broad credibility to start a suite of subsidiaries, each dedicated to an individual therapeutic program. However, increasing the number of 'shots' on goal also requires an increasing pool of capital to deploy, all while keeping costs and productivity maintained at a steady level.

This concept can be taken to the extreme via the establishment of a megafund structure - a much larger pool of capital than the typical venture capital fund and potentially using both debt and equity rather than equity alone [71]. Development programmes for drugs and biologic agents are undertaken simultaneously rather than serially (i.e., as a portfolio) and are funded by issuing equity (e.g., stock) and, if feasible, debt (e.g., bonds or loans) and as claims on the portfolio. BridgeBio Pharma and Roivant Sciences have utilised the megafund capital structure to some success [72]. Each has a central management team with a distinctive skill set and a diversified portfolio of programmes covering different therapeutic areas, indications, and technologies. The portfolio managers not only make investment decisions but also play critical roles in managing the portfolio companies, with varying levels of direct control over decision making in them. This model enables access to a greater pool of capital because it attracts investors that seek exposure to early-stage biotech but lack the technical-due-diligence capabilities or risk appetite for individual bets. The megafund structure is often operationalised as a hub-and-spoke type model whereby each company in a portfolio can be dedicated to a single asset or small family of assets. As each 'spoke' has expertise and management optimised to each companies' own area, they can in theory remain focused while maintaining central allocation of shared resources from the 'hub'. Preliminary simulations at the MIT Sloan School of Management suggest that such a structure is possible for childhood cancer therapeutics, albeit not when consisting of purely private capital, as it would necessitate an unrealistically large portfolio of clinic-ready therapeutics [73].

Blended Funds and Catalytic Capital

That last point is key; a pure-private megafund does not work for children's cancer, which is why the risk must be shared intelligently. Blended finance is a strategy that combines capital with different levels of risk to catalyse risk-adjusted, market-rate-seeking financing into impact investments. The providers of the risk-tolerant "catalytic" capital in blended finance structures aim to increase their social impact by accessing larger, more diverse pools of capital

012: How catalytic capital crowds in private investment



Circle area indicates relative size of each capital pool (illustrative).

from commercial investors. In the context of childhood cancer therapeutics, risk is inevitably tied to the stage of the drug asset development in the pipeline. While scientific risk is reduced year over year, the capital requirements continually increase with a significant proportion of the costs due at the clinical phases. Daems et al propose a solution to these challenges: establish a blended impact investment fund that could flexibly raise grantor capital for early-stage research to catalyse linked commercial capital at the clinical phases. With a large, diversified portfolio of projects, the portfolio could be sufficiently de-risked to provide a modest return for investors and create sufficient impact that philanthropists would be motivated to maintain these structures that created this increased value as a repeatable model for creating new childhood cancer therapeutics [74].

While the early stages would continue to receive the majority of funding from academic, public, philanthropic or concessionary capital during the high-risk phases of development, as the asset progresses through key milestones it typically will add different types of capital to the balance sheet, which is often referred to as a “capital stack.” Because each layer appeals to different types of investors, a blended capital fund can be a useful instrument for attracting and capturing a wide pool of potential investors. Private capital could potentially be catalysed in blended finance solution at the clinical development stage where the risks and commercialisation potential of drugs become reasonably clear and the size of the pull incentive reward becomes visible. Public policy is beginning to move in this direction. The European Commission's proposed reform of EU pharmaceutical legislation, through the European Biotech Act and the proposed Critical Medicines Act, pairs regulatory simplification with a set of access-to-finance measures. These include major investment pilots delivered with the European Investment Bank Group, among them a Health Biotechnology Investment Pilot and Strategic Projects intended to bridge the "valley of death" and build shared infrastructure. Although still light on detail, and welcomed on that basis by SIOPE [75], it signals public institutional capital being positioned to catalyse private investment of the kind this paper argues for.

Blended funds in practice

How can we learn from other market failures in health?

Investors in health are familiar with the blended capital structure and some of them have been deployed in other disease areas facing similar market failure.

Antimicrobial Resistance

In antimicrobial drug development, a market failure exists because any new drugs entering the market will be prescribed extremely sparingly as a last resort to prevent antimicrobial resistance (AMR). Recognising the seriousness of the problem, the industry itself has stepped in to co-fund the risk it depends on managing. The AMR Action Fund is an industry-led venture capital vehicle managing approximately $1 billion in committed capital, designed to bridge the funding gap between early-stage scientific research and late-stage commercialisation, backed by 23 pharmaceutical companies alongside the World Health Organization, the European Investment Bank, and the Wellcome Trust. Rather than each company independently absorbing the commercial risk of a category with famously poor returns, competitors have pooled capital into a shared fund that invests directly in clinical-stage biotechs, recognising that the health system as a whole depends on a functioning antibiotic pipeline even though no single company can profitably sustain one alone [76].

Neglected tropical diseases (NTDs)

NTDs illustrate a different, non-equity model better suited to diseases with essentially no viable commercial return: the product development partnership (PDP). Organisations such as the Drugs for Neglected Diseases initiative (DNDi) coordinate collaboration between industry, academia, and public funders to develop and deliver treatments directly, rather than trying to make the underlying market investable. Analysis by Policy Cures Research has estimated that every dollar invested in neglected disease R&D generates $405 of societal and economic return, underlining that the case for intervention in these areas rests on public value rather than financial return, a dynamic that has clear parallels for the smallest and least commercially viable segments of childhood cancer [77].

Global Health

Blended finance has also played an important role. The Global Health Investment Fund (GHIF), for example, reduces the risk to traditional investors by absorbing a portion of initial losses. The $108 million social impact investment fund employs a range of capital options, including various layers of debt investments and equity, with an average investment target of $10 million per project. The Bill & Melinda Gates Foundation provides a first-loss guarantee by absorbing the first 20% of potential downside. If an investment loses more than 20% then the Gates Foundation splits additional losses 50/50 with the other investors. This structure helps to significantly reduce downside risk, therefore enticing other private capital to participate. The GHIF structure has encouraged philanthropic investors (like the Children's Investment Fund Foundation) as well as traditional investors like AXA Investment Managers, JPMorgan Chase & Co, and the International Finance Corporation to address public health challenges [78].

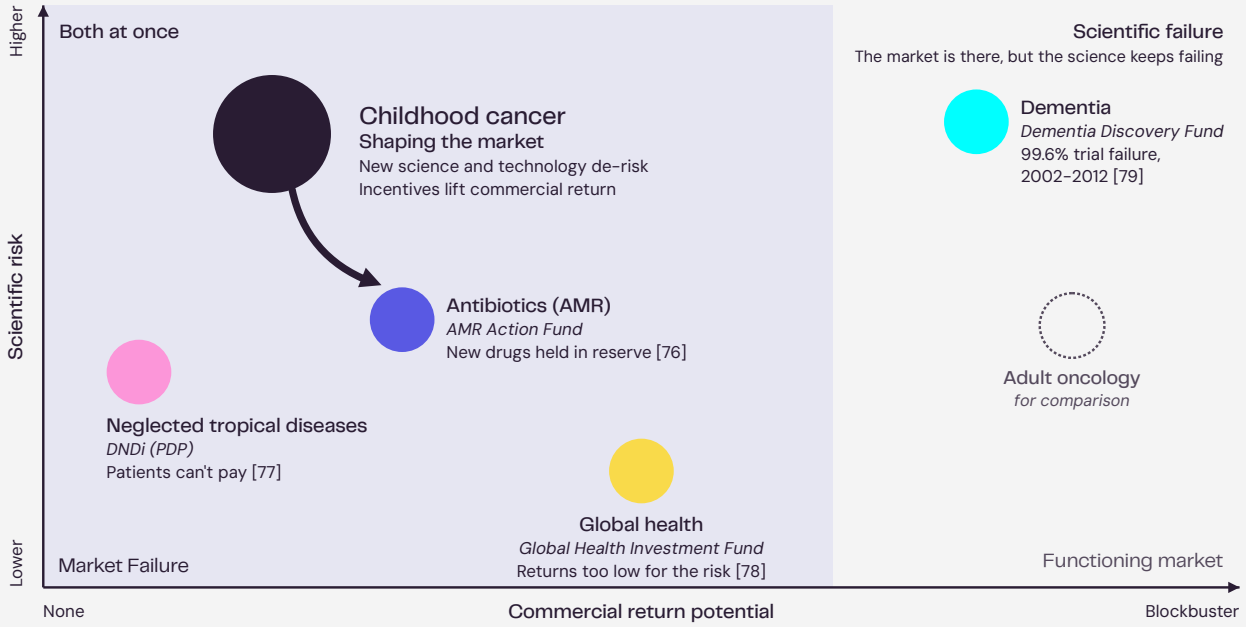
Dementia

Dementia also offers a model to learn from, where between 2002-2012 a 99.6% failure rate in Alzheimer's drug discovery disillusioned the pharmaceutical industry and led to a disinvestment in the area [79]. This led to the government seeding the Dementia Discovery Fund with £15 million from the UK Treasury after the government identified dementia research as a global priority, with officials at the time noting that the optimal approach would blend different types of investors. It has since grown into a family of venture funds managed by SV Health Investors, with more than $475 million raised from limited partners including seven major pharmaceutical companies, philanthropists such as Bill Gates, and organisations including AARP and British Patient Capital. Although dementia doesn't represent an area of true market failure, since dementia drugs hold blockbuster potential, the structure demonstrates how a relatively modest amount of government seed funding, if used to establish credible fund governance and a professional venture management team, can go on to crowd in far larger sums of industry and philanthropic capital.

Children's cancer has not yet been given this same structural response. The four lessons above, that competitors will pool risk, that a public-value case can justify a non-equity partnership, that a first-loss guarantee crowds capital in, and that a modest, well-governed seed can multiply, are the raw materials of the vision we set out next.

013: Childhood cancer is moving towards where blended funds have already been established

New science and technology are lowering scientific risk, and incentives are lifting commercial return, shifting childhood cancer towards the space where the AMR Action Fund operates



Four precedents, and what childhood cancer can borrow

Antimicrobial resistance

AMR Action Fund

~$1B industry-led fund backed by 23 pharma companies, WHO, the EIB and Wellcome [76]

Market failure
Market is deliberately kept small: new antibiotics are held back as a last resort, so sales can't repay R&D

How it worked
Competitors pool capital into a shared VC fund that invests directly in clinical-stage biotechs

Lesson for childhood cancer
Competitors will pool risk when the whole system depends on a pipeline no single company can sustain

Neglected tropical diseases

DNDi (PDP)

$405 per $1 societal and economic return on neglected disease R&D [77]

Market failure
Essentially no commercial return: patients can't pay, so the market can't be made investable

How it worked
Non-equity partnership coordinating industry, academia and public funders to develop and deliver treatments directly

Lesson for childhood cancer
A public-value case can justify a non-equity route for the smallest, least viable indications

Global health

Global Health Investment Fund

20% first loss absorbed by the Gates Foundation; further losses split 50/50 [78]

Market failure
Returns too low and risky to attract traditional investors on their own

How it worked
$108M blended fund using layers of debt and equity, averaging $10M per project

Lesson for childhood cancer
A first-loss guarantee crowds in mainstream capital (AXA IM, JPMorgan, IFC)

Dementia

Dementia Discovery Fund

$475M+ raised from a £15M UK Treasury seed; a family of venture funds managed by SV Health Investors

Market failure
Not a true market failure (blockbuster potential), but extreme scientific risk: 99.6% failure rate (2002–2012) and a need for better biomarkers drove pharma out [79]

How it worked
Capital raised from 7 major pharma companies, philanthropists such as Bill Gates, AARP and British Patient Capital

Lesson for childhood cancer
A modest, well-governed government seed can multiply into far larger industry and philanthropic capital

Shaping new markets

How do we move beyond opportunism to systematically developing new tailored and well-tolerated childhood cancer therapeutics?

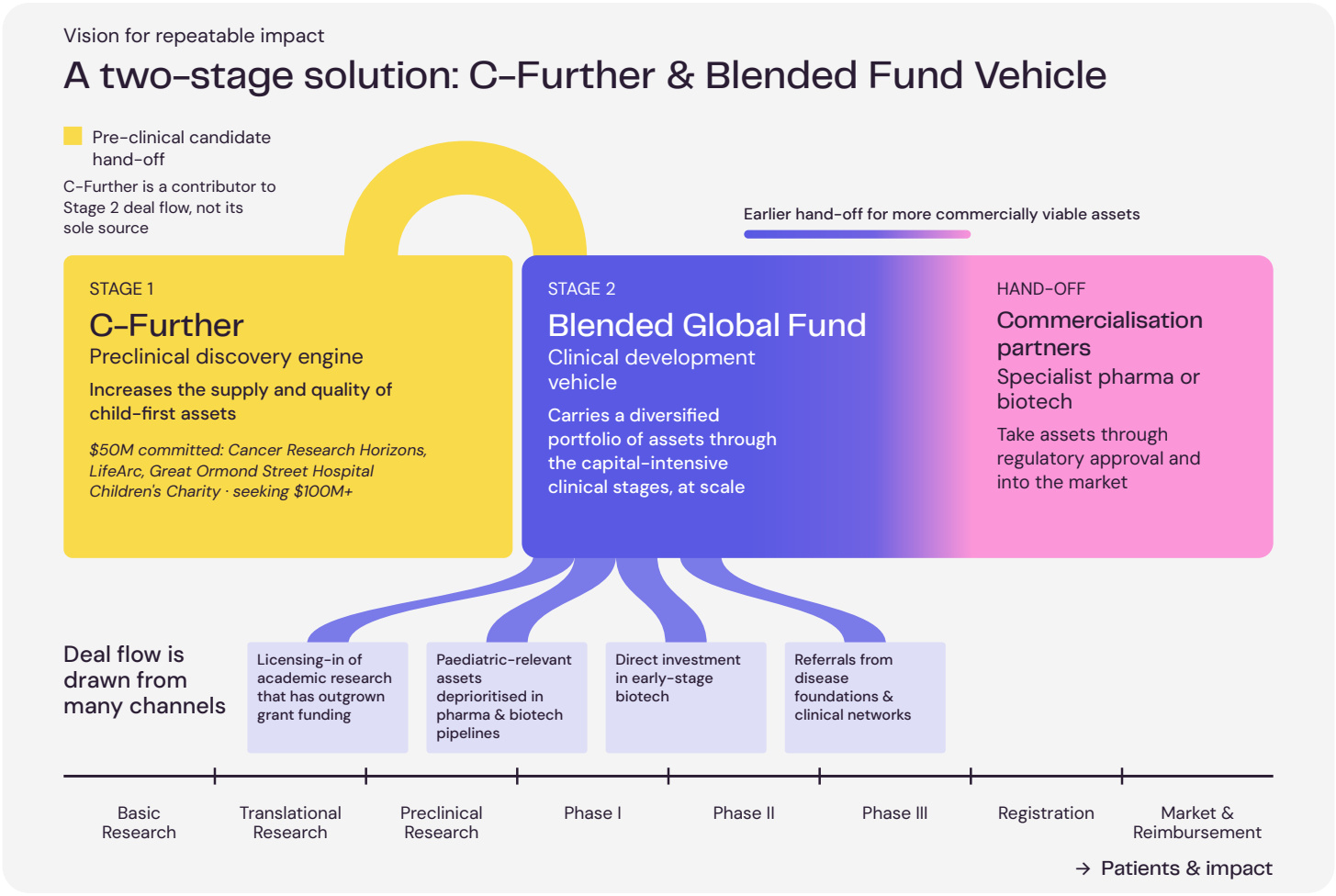
So far, we have described the fragile and largely opportunistic ecosystem by which new precision therapeutics for children's cancer are developed. The investment case of childhood cancer therapeutic discovery and development is challenging but it is not unique: similar market failures affect innovation across other healthcare areas that are also subject to the limitations of free market systems. While it would be easier to sit back and try to patch up the presented challenges with isolated initiatives or new pull incentives, the complexity of the problem and the scale of the unmet need demand something more. Indeed, the ways in which public, private, and philanthropic capital are governed, designed, and delivered matters as much as the quantity of finance. As a briefing for the WHO put it "*[we need to] move to a new paradigm where health is an investment, […] and transforms the relationship between public and private sectors, towards common goals. In other words, increasing financing is not enough: the quality of finance is crucial to delivering Health for All*"[80]. Here, we set out a two-stage vision for scaling the discovery and development of modern precision therapeutics for children and young people with cancer which seeks to meet this ambition.

A vision for scalable impact

First, we need to increase the 'supply' and visibility of high quality and rationally designed childhood therapeutic discovery projects by bringing together the brightest minds in academia and industry, accelerating these through preclinical development via focused but well-resourced, collaborative projects. This means actively originating and advancing early-stage paediatric science using donor capital with particular focus on biology which is unique to childhood cancer, which would otherwise stall in academic or industry labs for lack of market.

Second, build a new blended finance fund capable of financing and executing a portfolio of these assets through the far more capital-intensive stages of clinical development and trials. This requires the coordination of multiple actors, rather than relying on opportunistic, asset-by-asset philanthropic funding that cannot absorb the investment profile of drug development at this stage.

Vision for repeatable impact



Part 1: A design-led solution for child-first therapeutic discovery

C-Further is already in operation to increase the drug discovery pipeline of child-specific therapeutics. It operates as a philanthropically supported virtual biotech that bridges early-stage academic research and formal drug discovery. Rather than funding research passively at arm's length, C-Further identifies, resources, and actively manages a portfolio of paediatric oncology programmes, driving each toward the nomination of a preclinical candidate in collaboration with the academic or industry originators of the therapeutic concept. It industrialises paediatric drug discovery at scale, using substantial internal teams of scientists running programmes through milestone decision gates, allowing dynamic allocation of its capital to the projects that stand the highest chance of delivering impact. By building a diversified pipeline across a wide range of childhood cancer indications, development stages and therapeutic modalities, C-Further hopes to build a unique international platform for the discovery of child-first medicines. With an initial $50M collectively committed by Cancer Research Horizons, LifeArc and Great Ormond Street Hospital Children's Charity, C-Further is actively seeking philanthropic partners who share in this vision to support its ambition of raising at least $100M.

Part 2: Building a global blended fund

We propose a second vehicle: a blended-capital fund built to carry a diversified portfolio of childhood cancer assets through clinical development. The megafund logic set out above, pooling many programmes, tranching risk, and using catalytic first-loss capital and guarantees to crowd in private investment, was first proposed over a decade ago [71] and tailored to paediatric cancer by Daems et al., who applied it to a tranche-pooled structure with target-specific SPVs and advance reimbursement agreements. The approach is untested in childhood cancer but well-precedented in other areas of market failure, as the examples above show. Our contribution is not to restate the theory but to specify what such a fund must do to work in this disease, and to be clear about what has so far stopped it being built.

We have additionally completed some preliminary modelling using PRISM to illustrate that a fund of this type is feasible given the right combination of assets and blended capital (see *Figure 016*).

015: What a blended fund for children's cancer must do

A fund of this kind would need to meet four requirements.



1. Diversify at portfolio scale.

It must hold dozens of programmes across different cancer types, targets and clinical stages, so that portfolio-level risk falls even though most individual assets will fail. A handful of assets will not do; the diversification is the mechanism.



2. Layer the capital stack.

Philanthropic, government or other catalytic capital could take the subordinated, first-loss position, de-risking the senior tranches enough for institutional and private capital to participate at a lower, more predictable return. Where that is not sufficient, a public-sector or philanthropic guarantee should absorb losses beyond an agreed threshold, as it has in the global-health funds described above.



3. Manage actively, and govern for the mission.

The fund cannot be a passive capital pool. It needs a manager built like a venture or private-equity firm, able to select, stage-gate and make go/no-go calls on assets, with governance sitting as a distinct layer that holds investor returns and the child-first mission in tension without letting either dominate.



4. Draw paediatric cancer deal flow from many channels.

No single source will fill the portfolio. It must draw on paediatric-relevant assets deprioritised in pharma and biotech pipelines for commercial rather than scientific reasons, direct investment in early-stage biotech, licensing-in of academic research that has outgrown grant funding, C-Further, and referrals from disease foundations and clinical networks.

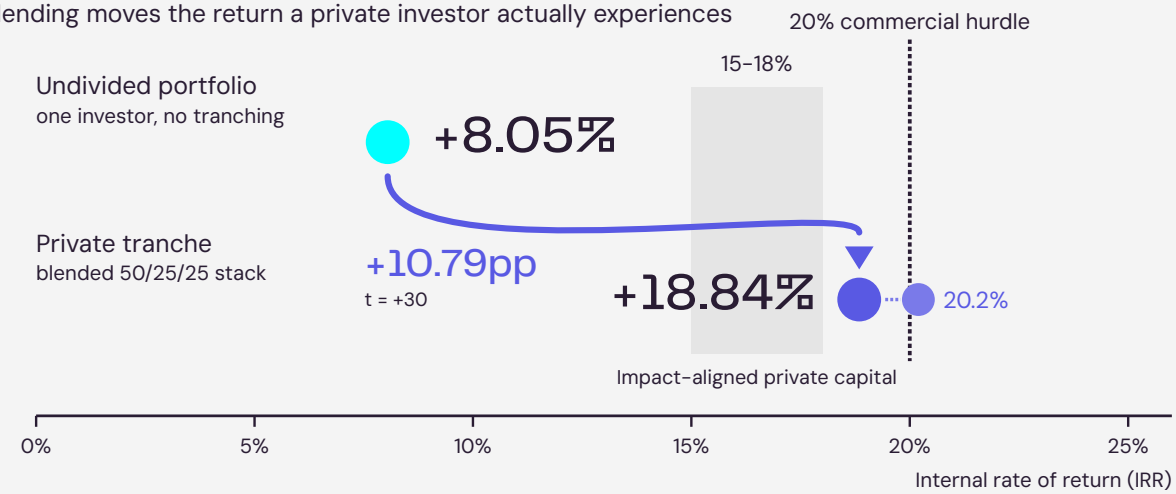
016: A conventional fund cannot finance this portfolio. Perhaps a blended one can?

The same 21 paediatric oncology assets and the same simulated cashflows, financed two ways

21 assets · Phase I entry, licensed at Phase II · All PRV-eligible · 50/25/25 capital stack
10 x 2,000 Monte Carlo runs · 9.1% WACC · 20-year horizon

The shift

Blending moves the return a private investor actually experiences

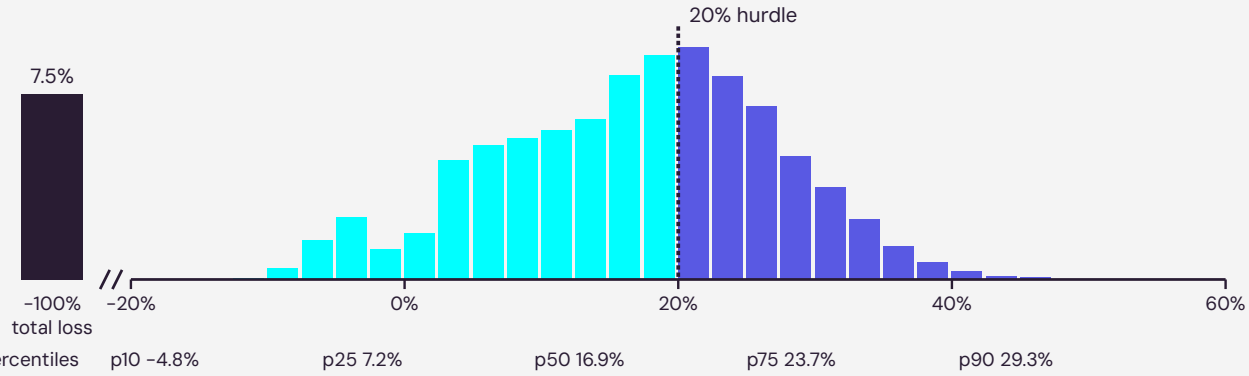


1.16pp below the 20% commercial hurdle

Platform trials would share control arms, sites and protocols, bringing licensing events forward. Modelled at a compressed cadence, the private tranche reaches 20.2%.

1. Why a conventional fund says no

All 20,000 simulated outcomes, undivided portfolio



Percentiles p10 -4.8% p25 7.2% p50 16.9% p75 23.7% p90 29.3%

61.4% of runs land below the 20% commercial hurdle, and 7.5% return nothing at all. A single investor carrying the whole portfolio would not underwrite this.

2. Where the return comes from

£387.8M of capital is called on average, against £602.5M if every asset ran to Phase II exit, because assets that fail stop spending. A £500M facility covers 95% of outcomes. Seniority, not new money, is what turns an 8.0% blended average into an 18.8% private return.



-100% by design
Philanthropic · £193.9M called

-3.2%
Impact · £97.0M called

+18.8%
Private · £97.0M called

Source: C-Further PRISM tool

± 1 se of the mean of 10 draws, smaller than the markers

How do we move from a model to an initiative?

The literature supporting a blended fund has existed for over a decade without a paediatric oncology (or broader rare paediatric disease) vehicle emerging at scale, despite the case being made and working examples from other areas in health. We propose there are several interwoven reasons why this is so:

1. **No convening body with the standing to lead it.** Megafunds require a sponsor credible enough to bring institutional capital, philanthropy, and industry to the same table.
2. **The cornerstone investor problem.** Every blended structure depends on someone willing to take first-loss or subordinated terms to de-risk the senior tranches for others. Identifying which partners are prepared to do that, and under what terms is a requirement to advance the idea.
3. **Deal-flow uncertainty.** A blended fund only works with enough assets to diversify away idiosyncratic risk. Nobody has yet demonstrated, credibly, that paediatric oncology specifically can populate a portfolio of the necessary size and quality. This is a true challenge for paediatric oncology; hence C-Further is step one of this vision.
4. **Governance and mission risk.** Investors accustomed to conventional return profiles and charities protective of a child-first mission have, to date, struggled to agree in advance on how control, insight, and decision rights would be shared.
5. **Clarity of scope:** while we see a global blended fund as one natural progression for assets that C-Further's pipeline generates, it would be established as an independent entity, with its own remit to source clinical-stage programmes globally. That includes paediatric-relevant assets deprioritised or stalled within pharma and biotech pipelines where a change in corporate strategy, not scientific failure, has shelved a programme as well as the ability to invest directly in early-stage companies. C-Further would be a contributor to the fund's deal flow, not its sole source, which is a requirement to address the challenge of deal uncertainty.

The unmet need in children's cancer justifies this ambition.

Children's cancer deserves the same order of attention and financial innovation that has been directed at other areas of market failure discussed here. We consider a global blended fund as the kind of initiative that is ambitious but realistic, genuinely capable of moving the needle and stabilising a currently fragile funding landscape.

> "[we need to] move to a new paradigm where health is an investment, [...] and transforms the relationship between public and private sectors, towards common goals. In other words, increasing financing is not enough: the quality of finance is crucial to delivering Health for All
>
> World Health Organization [80]
> Council Brief No. 2, 2021

Source: WHO, 'Financing Health for All: Increase, transform and redirect.', Council Brief No. 2, Oct. 2021.

We propose the next step is a stakeholder conversation, to co-build the model, and identify the different types of partner needed to bring such a vision to reality. We don't believe potential partners need or want a fully worked structure presented to them. The more productive route is to bring current and potential funders into the conversation early, structured around open questions addressing the challenges we set out.

1. **Mission and remit.** What is the fund's purpose, and how does its structure protect a paediatric, child-first mission as it scales and takes on different classes of capital?
2. **Acceptability of a blended structure.** What do different classes of investor expect, and critically who might be willing to take the terms that underpin the model, particularly as a cornerstone, first-loss investor?
3. **Deal-flow confidence.** Do stakeholders believe there is genuinely enough opportunity, globally, to populate a diversified portfolio at the quality and volume the model needs?

Important to the dialogue is building consensus and alignment within the current ecosystem of children's cancer partners; such an initiative could be transformative but also disruptive. The critical test, though, is additionality. Simply pooling capital that non-profits and philanthropies already earmark for children's cancer would reduce fragmentation, which has some value, but would not represent the transformative step-change needed to improve outcomes for children and young people with cancer. The fund only justifies its existence if it can catalyse capital that has never been directed at children's cancer before by giving it a structure and risk profile it can invest against.

A call to collective action

Help shape a new market for children and young people with cancer.

Creating more effective, targeted medicines for children and young people with cancer is no small feat. Discovery is expensive, technically challenging and fraught with risk. Financial incentives are underwhelming, and expertise diffuse. To succeed we need to bring together multiple actors across disciplines, sectors and borders, always involving children and young people affected by cancer in what we do. Only by stimulating bottom-up innovation, pooling technologies and expertise, attracting capital and channelling it intelligently can we execute this roadmap for delivery.

To funders, government and public research bodies:

Give children's cancer the priority it requires as a leading cause of death for children and adolescents. Where governments announce new strategies and ambitions for children's cancer, these ambitions should be matched with ring-fenced, multi-year capital into R&D rather than intent alone.

To philanthropists and foundations:

Children's and young people's cancers present unique scientific and clinical challenges, requiring a funding model tailored to their specific needs and opportunities. It requires a move beyond one-off, asset-by-asset grant-making toward the kind of venture philanthropy and portfolio-based models that can absorb risk at the scale drug development requires. Consider playing the cornerstone or first-loss role that blended finance vehicles depend on. The single biggest obstacle to structures like a paediatric oncology blended fund is not necessarily a lack of intellectual case, but a lack of capital willing to take subordinated terms first.



To investors: Paediatric oncology need not be evaluated purely against the return profile of adult oncology.

As the precedents in AMR, dementia, and neglected tropical diseases show, well-structured blended vehicles can deliver risk-adjusted, and in some cases market-competitive, returns once first-loss capital and diversified deal flow are in place. We invite investors into the stakeholder conversation now underway on fund structure, mission protection and acceptable terms, rather than waiting for a finished proposal.

To advocates, patient groups, and families:

Your voice remains the clearest evidence of why this work is urgent, and the most effective check against models that lose sight of the child-first mission as capital scales. Continue to hold funders, industry, and government to account on delivery and help ensure that as new financing structures emerge, children and young people affected by cancer, and their families, retain a voice in how they are governed.

To convenors, academic institutions, industry leaders, and cross-sector platforms:

No single actor can assemble the capital, deal flow, and governance a solution at this scale requires. We need organisations with the standing to bring philanthropy, government, and private capital to the same table, and the credibility to sustain that coalition over the years a blended vehicle would take to build. C-Further is positioning itself to play this role for early-stage discovery, but the later-stage vehicle this paper describes will only succeed with a convenor bringing equivalent ambition to the clinical-development stage.

We call upon the ecosystem to take up this critical challenge to shape a new market for children & young people with cancer. We must ensure that children are not the ones who suffer due to our inaction.

We would like to thank our advocacy panel for their input into this report and continued guidance, embedding lived experience in all that we do.

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