From Approval to Access: Lessons from HIV Antiretrovirals for Accelerating Casgevy Equity in Sub-Saharan Africa

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Abstract

Background: Casgevy (exagamglogene autotemcel; exa-cel), the inaugural CRISPR-Cas9 gene therapy for sickle cell disease (SCD), received authorization from the United States Food and Drug Administration in December 2023, with a list price of US$2.2 million per patient. Sub-Saharan Africa (SSA), which accounts for approximately 75–80% of the global annual SCD births, lacks a regulatory approval pathway, procurement plan, and cost-effectiveness evidence to support the adoption of the Casgevy. A similar disparity was observed in 1996 when combination antiretroviral therapy (ART) was approved in high-income countries at US$10,000–15,000 per patient-year, with no access to SSA. By 2004, however, generic ART became available in the region for US$140 per patient-year.

Objective: This study aimed to investigate the mechanisms that expedited the timeline for HIV treatment access in SSA and assess their applicability in achieving equitable access to Casgevy.

Methods: A comprehensive review of peer-reviewed literature, grey literature, and policy documents was conducted across five comparative domains: disease burden geography, pricing at approval, manufacturing complexity, political will and advocacy, and feasibility of tiered pricing.

Results: The structural parallels between the HIV and SCD crises are significant: both disproportionately impact SSA, both initially involved prohibitive pricing, and both present pricing and manufacturing challenges that necessitate political solutions. However,

there are critical differences between the two. Generic ARV manufacturing relies on standard small-molecule chemistry, whereas the production of Casgevy involves autologous hematopoietic stem cell collection, ex vivo CRISPR editing, and GMP vector production, a process that cannot currently be reduced to a generic formulation. Political mobilization for HIV was driven by advocacy from high-income countries, whereas SCD advocacy remains comparatively under-resourced in low-income countries.

Conclusions: Achieving sustained access to Casgevy in SSA is feasible under an optimistic yet realistic scenario that includes voluntary licensing of manufacturing expertise, tiered pricing models similar to the Advance Market Commitment, PEPFAR-analog financing, and investment in regional cell therapy infrastructure. The ARV precedent illustrates that political will, rather than technical feasibility, is the primary constraint on ARV use.

Keywords: Casgevy; exagamglogene autotemcel; sickle cell disease; sub-Saharan Africa; antiretroviral therapy; health equity; gene therapy;

1. Introduction

Sickle cell disease (SCD) ranks among the most prevalent monogenic disorders globally, affecting approximately 7.74 million individuals in 2021, with the highest burden observed in sub-Saharan Africa (SSA), where 75–80% of annual SCD births occur [1]. In SSA, child mortality due to SCD remains alarmingly high, with 50–90% of affected children dying before the age of five in many regions lacking newborn screening and hydroxyurea programs [1]. Despite this epidemiological challenge, curative therapies have historically been inaccessible to patients in Africa.

The approval of Casgevy (exagamglogene autotemcel; exa-cel) by the United States Food and Drug Administration in December 2023 represents a significant milestone. Casgevy is the first CRISPR-Cas9-based therapeutic approved for human use and the first curative option for SCD that does not necessitate a matched allogeneic donor [2]. In the pivotal CLIMB SCD-121 phase 3 trial, 29 out of 30 evaluable patients (97%) achieved freedom from severe vaso-occlusive crises (VOC) for at least 12 consecutive months, with 100% freedom from VOC-related hospitalization [2]. These results indicate unprecedented efficacy for SCD therapeutics. However, Casgevy's US list price of approximately US$2.2 million per patient renders it entirely inaccessible within SSA's health systems [3].

This disparity between scientific advancement and equitable access is not unprecedented. In 1995–1996, combination antiretroviral therapy (ART) transformed HIV infection from a fatal condition to a manageable chronic illness in high-income countries at a cost of US$10,000–$15,000 per patient-year. In SSA, where the majority of the global HIV burden is concentrated, access is virtually nonexistent [4]. The mechanisms that bridged the access gap over the subsequent eight years — from the Doha Declaration to generic scale-up — fundamentally reshaped the global health landscape [5]. By 2004, generic ART was available in SSA at US$140

per patient-year, and the PEPFAR was facilitating treatment for millions [6]. This review examines the lessons the HIV access narrative can offer regarding pathways to achieving Casgevy equity in SSA. We compared the two cases across five domains and proposed a structured policy framework to expedite Casgevy access in the SSA. The critical question is not whether access will eventually be realized but how swiftly it can be accelerated and which policy mechanisms provide the most effective leverage.

2. Methods

This narrative review was designed as a policy analysis framed by comparative analogy. Narrative reviews are appropriate when the objective is to synthesize heterogeneous evidence — spanning clinical medicine, health economics, and political science — into a coherent conceptual framework for policymakers. No formal systematic protocol or PRISMA-ScR registration was undertaken, consistent with the review's stated scope [7].

Literature was identified through targeted retrieval from PubMed, MEDLINE, Google Scholar, and institutional grey literature repositories, including publications from the World Health Organization, Médecins Sans Frontières, UNAIDS, the Institute for Clinical and Economic Review, and Vertex Pharmaceuticals. Search terms included combinations of: "HIV antiretroviral access," "Doha Declaration," "sub-Saharan Africa medicines equity," "sickle cell disease gene therapy," "Casgevy exagamglogene," "compulsory licensing generic pharmaceuticals," and "PEPFAR access to medicines." Papers published until May 2026 were eligible. No language restrictions were applied, although all cited papers were in English.

Comparative analysis was structured across five pre-specified domains derived from the access-to-medicines literature: (1) disease burden geography, (2) pricing at regulatory approval, (3) manufacturing complexity, (4) political will and advocacy, and (5) tiered pricing feasibility. For each domain, we characterized the historical HIV experience, assessed the contemporary SCD situation, and evaluated the degree of structural analogousness.

3. Background

3.1 The Global Burden of Sickle Cell Disease and the SSA Paradox

SCD results from a point mutation in the HBB gene encoding the beta-globin chain of hemoglobin, producing abnormal hemoglobin S (HbS), which polymerizes under deoxygenation conditions and causes erythrocyte sickling, vascular occlusion, hemolysis, and progressive multi-organ damage [1]. The condition is inherited in an autosomal recessive pattern, with the highest carrier frequencies in malaria-endemic regions, where heterozygous carriage confers partial protection against Plasmodium falciparum.

The consequent geographic distribution of SCD births is profoundly asymmetric to the distribution of curative capacity. SSA

generates the majority of global SCD births, yet less than half of children with SCD in low- and middle-income countries (LMICs) survive to adulthood, a figure exceeding 90% in high-income countries (HICs) [8]. This gap is attributable not to disease biology but to differential access to newborn screening, penicillin prophylaxis, transcranial Doppler surveillance, and disease-modifying therapy. Hydroxyurea, available since 1998 and off patent, reduces VOC frequency, acute chest syndrome, and mortality [8]; however, its uptake in SSA remains limited by supply chain inconsistency, clinician awareness, and adherence support infrastructure.

Gene therapy and allogeneic hematopoietic stem cell transplantation (HSCT) have emerged as curative modalities. HSCT achieves cure rates exceeding 90% in matched sibling donor transplants but is limited by donor availability (fewer than 20% of patients have an HLA-matched sibling) and transplant-related morbidity [9]. The advent of autologous gene therapy eliminates donor constraints entirely. However, global cellular therapy capacity is heavily concentrated in HICs, with only a few SSA centers possessing the infrastructure to contemplate HSCT, let alone ex vivo gene editing [9].

3.2 **Casgevy: Mechanism, Efficacy, and the Price Barrier**

Casgevy (exa-cel) represents a CRISPR-Cas9 gene therapy developed by Vertex Pharmaceuticals and CRISPR Therapeutics. This therapy specifically targets BCL11A, a transcriptional repressor of γ-globin expression. By disrupting the erythroid-specific enhancer of BCL11A in autologous CD34+ hematopoietic stem and progenitor cells (HSPCs) through CRISPR, the repression of gamma-globin is alleviated, thereby restoring the production of fetal hemoglobin (HbF), which does not polymerize and thus prevents sickling [2].

The CLIMB SCD-121 trial included 44 patients aged 12–35 years with severe sickle cell disease (SCD), characterized by at least two vaso-occlusive crisis (VOC) episodes annually in the two years prior to screening [2]. Among the 30 patients with adequate follow-up for efficacy assessment, 29 (97%; 95% CI 83–100) achieved the primary endpoint of being VOC-free for a minimum of 12 consecutive months, and all 30 (100%) were free from VOC-related hospitalization [2]. The median follow-up duration at the time of publication was 19.3 months, with durability data extending up to 48 months. No cancer incidences were reported, and the safety profile was consistent with that of busulfan myeloablative conditioning [2]. Notably, the CLIMB SCD-121 trial did not include any patients from sub-Saharan Africa (SSA), despite this region having the majority of the global SCD population. This omission raises significant concerns regarding the applicability of efficacy data to African patients, who may present with different disease severity profiles, malaria comorbidities, and nutritional statuses [3].

The list price of US$2.2 million for Casgevy is structured as a one-time therapy cost but surpasses the entire annual healthcare budget of many SSA health systems on a per-patient basis. A recent cost-effectiveness analysis adapted for Uganda indicated that

Casgevy could be cost-effective from a societal perspective, even in low- and middle-income countries (LMICs), but only if the price is significantly reduced. This finding underscores the theoretical potential for equitable access while highlighting the substantial gap between the current list price and an affordable threshold [10].

4. Five-Domain Comparative Analysis: HIV ART versus Casgevy

Table 1 provides a summary of the five-domain comparison. The following sections elaborate each domain in sequence.

Domain	**HIV ART (1996 baseline)**	**Casgevy SCD (2023 baseline)**	**Analogousness**
Disease burden geography	SSA: ~68% of global burden	SSA: ~75–80% of global SCD births	High
Pricing at approval	US$10–15k/patient-year	US$2.2M one-time/patient	Partial
Manufacturing complexity	Standard organic chemistry; generic scalable	Ex vivo cell therapy; GMP; autologous — not conventionally genericisable	Low
Political will & advocacy	High-income advocacy + SSA civil society; MSF; ACT UP	Nascent; SCD advocacy underfunded vs HIV	Low–moderate
Tiered pricing feasibility	Tiered pricing + generic competition reduced costs >95%	Voluntary licensing of process; AMC-style mechanisms possible	Moderate

4.1 Disease Burden Geography

In 1996, when antiretroviral therapy (ART) was approved, sub-Saharan Africa (SSA) represented approximately 68% of the global HIV burden [11]. By December 2023, at the time of Casgevy's approval, SSA accounted for 75–80% of all global sickle cell disease

(SCD) births [1]. In both instances, the region bearing the majority of the disease burden had no feasible means of accessing the newly approved therapies at the prevailing prices. Structural epidemiological injustice is evident: therapies transformative for diseases associated with global poverty are priced for high-income countries.

However, a crucial difference lies in the burden's reversibility. HIV, a communicable disease, has a dynamic burden in SSA that can be mitigated through preventive measures. In contrast, the SCD burden is largely determined by birth rates and remains relatively stable over decades as genetic carrier frequencies change slowly. Consequently, the number of patients with SCD requiring intervention will remain substantial in the foreseeable future, presenting a paradoxically more stable market than HIV did in the mid-1990s. This persistent demand could unexpectedly serve as a potential mechanism for negotiating market-based pricing.

4.2 **Pricing at Approval**

In 1996, the cost of antiretroviral (ARV) combination therapy ranged from US$10,000 to US$15,000 per patient annually [4]. In contrast, Casgevy, a one-time therapy, is priced at US$2.2 million per patient. These costs are not directly comparable; ARV costs represent an annual recurring expense, whereas Casgevy involves a single payment. When evaluated in net present value terms over a 30-year period, the ARV lifecycle cost at US$12,500 per year surpasses US$170,000, which is less than one-tenth of the Casgevy's list price. Consequently, the affordability challenge for Casgevy is approximately an order of magnitude greater than that for ARV therapy, even before considering additional infrastructure costs, such as hospitalization for myeloablative conditioning, stem cell collection, and monitoring.

In high-income countries (HICs), pharmaceutical pricing for gene therapy increasingly employs outcome-based payment models and annuitized financing mechanisms. Vertex Pharmaceuticals has established outcome-based agreements with several payers in the United Kingdom and the United States [12,13]. However, the feasibility of implementing similar financing mechanisms in sub-Saharan African (SSA) health systems remains uncertain, as these systems typically lack the actuarial capacity, regulatory infrastructure, and health technology assessment bodies necessary to negotiate such agreements [10].

4.3 **Manufacturing Complexity**

The manufacturing asymmetry between antiretroviral therapy (ART) and Casgevy represents a significant structural distinction between the two. Antiretroviral drugs are small-molecule compounds produced using established organic chemistry methods. Indian generic manufacturers, notably Cipla, Ranbaxy, and Aurobindo, successfully reverse-engineered ARVs on a large scale once patent restrictions were lifted or waived, allowing the production of combination fixed-dose tablets at substantially reduced costs [11]. The

primary barrier to generic ARV production was legal rather than scientific because the technical challenges were minimal.

In contrast, the production process for Casgevy is technically complex, highly individualized, and lacks a direct analogy to conventional generic manufacturing processes. Each batch of Casgevy is derived from a single patient's CD34+ hematopoietic stem and progenitor cells (HSPCs), which are mobilized using plerixafor, collected via apheresis, edited ex vivo using CRISPR-Cas9, subjected to quality control and release testing, and infused after the patient's myeloablative busulfan conditioning [2]. This entire process necessitates GMP-certified laboratory facilities, trained hematologists and stem cell transplant physicians, critical care infrastructure for busulfan conditioning, and 4–6 weeks of inpatient monitoring post-administration. However, such capabilities are not available at scale in sub-Saharan Africa (SSA) [9].

Two potential manufacturing pathways warrant consideration in this regard. First, regional hub models, similar to the WHO-supported mRNA vaccine technology transfer program established post-COVID-19, could localize at least the cell collection and editing steps within SSA, thereby reducing logistics costs and patient travel burdens to the West [14]. Second, the development of in vivo gene editing platforms, including extracellular vesicle-mediated CRISPR delivery and in vivo prime editing, may eventually eliminate the need for ex vivo manufacturing altogether, facilitating a single-injection curative approach that is more conducive to decentralized production and distribution [15].

4.4 **Political Will and Advocacy**

The HIV access movement was initiated by an unprecedented coalition of patient advocates, civil society organizations, academic researchers, and supportive politicians. Entities such as the Treatment Action Campaign in South Africa, ACT UP in the United States, and Médecins Sans Frontières (MSF) exerted public pressure, rendering the high prices of antiretroviral drugs politically unsustainable [6]. The 2001 anthrax crisis in the United States, during which the US government threatened Bayer with a compulsory license for ciprofloxacin, highlighted a significant political contradiction: the same government that defended pharmaceutical patent rights internationally challenged them domestically. Advocacy groups exposed this contradiction, significantly advancing the Doha negotiations [4].

Advocacy for Sickle Cell Disease (SCD) operates within a structurally distinct environment. SCD disproportionately affects Black patients in both Sub-Saharan Africa (SSA) and the African diaspora in high-income countries (HICs) and has historically received less funding than diseases with similar prevalence and morbidity [3]. In the United States, the advocacy ecosystem for SCD, led by organizations such as the Sickle Cell Disease Association of America, is considerably smaller and less resourced than the HIV advocacy infrastructure that existed in 2001. In SSA, SCD advocacy is still in its early stages, with limited organized civil society infrastructure at the national and regional levels. Bridging this advocacy gap is essential for achieving the political mobilization that

facilitated the HIV revolution.

4.5 **Tiered Pricing Feasibility**

Tiered pricing, which involves setting lower prices in low-income markets than in high-income markets, was informally applied to antiretrovirals (ARVs) prior to the advent of generic alternatives and later became formalized through voluntary licensing agreements and the procurement frameworks of the Global Fund [6,16]. The Advance Market Commitment (AMC) mechanism, developed for pneumococcal vaccines through the Global Alliance for Vaccines and Immunization (GAVI), illustrated that donor-funded price guarantees could motivate manufacturers to produce affordable quantities for low- and middle-income country (LMIC) markets without affecting pricing in high-income countries (HICs) [17].

In the case of Casgevy, tiered pricing faces distinct structural challenges. As Casgevy is a service-intensive therapy rather than a storable product, differential pricing must encompass the entire delivery ecosystem and not just the drug itself. For instance, a Casgevy program in Sub-Saharan Africa (SSA) that imposes a one-time therapy fee of US$500,000 but necessitates an additional US$200,000 in infrastructure per patient does not offer a significantly more affordable option than the US-list price. Genuine tiered pricing for gene therapy in LMICs necessitates differential pricing of the drug, manufacturing expertise, and clinical delivery infrastructure as a comprehensive package, a model without direct precedent.

However, several analogous mechanisms warrant consideration. The expansion of UNITAID's Medicines Patent Pool to include gene therapy process patents should be explored. AMC-style commitments from GAVI, the Gates Foundation, or successor mechanisms to the President's Emergency Plan for AIDS Relief (PEPFAR) could support volume purchases at predetermined prices, providing demand certainty that encourages manufacturers to invest in their capacity. Additionally, outcome-based payments distributed over five to ten years with donor co-financing could transform the upfront cost barrier into an annuitized payment stream, making it more feasible for SSA health budgets.

5. **A policy Freamework for Casgevy Access in SSA**

Based on the five-domain analysis, we propose a policy framework organized into five parallel workstreams. These workstreams are interdependent, as advancements in one facilitate progress in the others, and none can succeed independently. They are presented as a set of concurrently essential policy investments rather than as a sequential programme.

Workstream 1: Expand the Evidence Base for SSA Patients

No patients from sub-Saharan Africa (SSA) were included in the CLIMB SCD-121 trial [2]. This omission represents both ethical shortcomings and practical obstacles. The absence of efficacy data for African patient populations, who may exhibit distinct

baseline HbF levels, comorbidity profiles (such as malaria, malnutrition, and different hemoglobin F quantitative trait loci), and pre-treatment disease severity, impedes regulatory approval in SSA countries and hinders clinicians' ability to provide informed patient counseling. Establishing a dedicated clinical trial program in SSA, ideally co-led by institutions such as the Muhimbili University of Health and Allied Sciences (Tanzania) or the Komfo Anokye Teaching Hospital (Ghana), is urgently required [18]. The inclusion of African patients should be a mandatory criterion for future regulatory evaluations and for any manufacturer aiming to enter SSA market. In the absence of this evidence base, other workstreams lack essential clinical foundations.

Workstream 2: Voluntary Licensing of Manufacturing Know-How

The Medicines Patent Pool (MPP) has effectively negotiated voluntary licenses for medications targeting HIV, hepatitis C, and tuberculosis from originator companies, facilitating low-cost generic production for low- and middle-income countries (LMICs) [19]. It is recommended that UNITAID and the MPP engage in discussions with Vertex Pharmaceuticals and CRISPR Therapeutics to explore a voluntary license for the gene-editing process applicable to sickle cell disease (SCD), specifically in LMIC markets. This approach would not allow for conventional generic competition but would enable authorized regional manufacturers or academic institutions to produce comparable therapy under license. The COVID-19 mRNA Technology Transfer Programme, which successfully transferred mRNA vaccine manufacturing expertise to six African manufacturers [14], exemplifies the viability of process licensing as a mechanism for enhancing access to medicines. In contrast to small-molecule generics, transfer in this context does not involve a chemical formula but a comprehensive production system, including cell collection protocols, CRISPR editing parameters, quality release standards, and conditioning regimen guidance. This distinction underscores the increased importance of voluntary participation by originators compared to the antiretroviral (ARV) era.

Workstream 3: Build Regional Cell Therapy Infrastructure

Minimum viable Casgevy delivery capability necessitates several key components: apheresis capacity, GMP cell processing, myeloablative conditioning with busulfan pharmacokinetics-guided dosing, 4–6 weeks of inpatient critical care, and a long-term follow-up infrastructure [9]. A pragmatic strategy involves identifying existing centers of excellence in hematology and transplantation, such as the Bone Marrow Transplant Unit at Groote Schuur Hospital in South Africa and the emerging hematology programs in Nigeria and Tanzania, and investing in systematic capacity upgrades. This approach is analogous to investing in ART delivery infrastructure through PEPFAR's clinical platforms. Instead of pursuing universal national coverage from the outset, a hub-and-spoke model should be developed. In this model, two to four regional centers of excellence would function as manufacturing and clinical delivery hubs, with referral networks extending into countries lacking transplant-capable hospitals. Such infrastructure investment must be regarded as a public health commitment rather than a commercial calculation, as it cannot be achieved through market mechanisms alone.

Workstream 4: Financing Innovation

The Global Fund model, which consolidates donor contributions to procure medicines at negotiated prices, necessitates modification for gene therapy, where the product is intrinsically linked to a service-delivery system. A viable financing structure comprises three interconnected components: a donor commitment akin to an Advance Market Commitment (AMC) that ensures the purchase of a specified volume of Casgevy procedures at a predetermined price for low- and middle-income countries (LMICs); outcome-based payments co-financed by donors and national governments, which distribute costs over several years instead of requiring a lump-sum payment upon delivery; and integration with existing sub-Saharan Africa (SSA) health financing mechanisms, such as the Africa CDC-led Africa Health Initiative [10]. The precedent set by antiretroviral (ARV) drugs is instructive regarding scale: the 99% price reduction from the 1996 list price to the 2004 generic price was achieved not through incremental negotiation but by fostering a competitive supply. According to Casgevy, traditional manufacturing competition is not feasible; however, competition among hub-model delivery systems, coupled with volume-based pricing agreements, can achieve similar price regulation. Policymakers should challenge the notion that gene therapy is intrinsically too costly for LMICs; the cost-effectiveness analysis conducted in Uganda indicates that, at a scaled price, Casgevy is cost-effective from a societal perspective, even in low-income settings [10].

Workstream 5: Advocacy and Political Mobilisation

The success of the HIV access movement is largely due to its effectiveness in making the price–access disparity politically visible and morally unacceptable within the political discourse of high-income countries (HICs). To achieve a similar level of mobilization for sickle cell disease (SCD), investment is necessary in three critical areas: First, civil society organizations in sub-Saharan Africa (SSA) that advocate for SCD must be sufficiently resourced and integrated into international health policy networks, as isolated national advocacy has historically been insufficient to influence global pharmaceutical pricing. Second, advocacy efforts within diaspora communities in the United States and the United Kingdom, where significant populations of African heritage with SCD are part of HIC political systems, represent a politically potent yet underutilized opportunity [3]. Third, collaborations between academia and advocacy groups must transform the clinical urgency, as evidenced by the fact that 75–80% of global SCD births occur in regions without realistic access to proven curative therapies, into sustained, evidence-based political pressure similar to that which advanced the Doha Declaration. Framing the Casgevey equity as a civil rights issue, given the disproportionate burden of SCD on Black populations globally, offers a compelling political narrative with established precedents in HIV advocacy. The HIV precedent demonstrates that political will is the crucial factor that converts all other efforts from mere intention into tangible outcomes.

6. Discussion

The primary thesis of this review posits that the revolution in HIV antiretroviral (ARV) access provides a validated framework for achieving equity in gene therapy, albeit with some limitations. Three insights are directly applicable to this study. First, the access gap in both scenarios reflects the political economy rather than scientific infeasibility; the obstacles are related to pricing and manufacturing infrastructure, not inherent technical limitations. Second, while voluntary licensing and procurement mechanisms are necessary, they are insufficient on their own; their success is contingent upon political will and diplomatic influence, as demonstrated by Uganda's experience, where donor dependency restricted the ability to utilize access provisions despite formal legal rights [20]. Third, advocacy-driven political mobilization, rather than spontaneous market adjustments, was the immediate catalyst for the breakthrough in HIV access.

However, these three insights do not seamlessly translate. First, the manufacturing complexity of Casgevy implies that process licensing alone cannot ensure affordable access without substantial infrastructure investment; what needs to be transferred is not merely a formula but an entire production system, encompassing proprietary CRISPR reagents, cell handling protocols, and quality release systems. This scenario is more akin to vaccine technology transfer than to the manufacturing of generic drugs. Second, the pricing model for Casgevy, characterized by a one-time lump-sum therapy rather than a recurring annual prescription, is fundamentally incompatible with the procurement and financing systems that facilitated generic ARV access. This necessitates new financing structures that are currently absent in Sub-Saharan Africa (SSA). Third, the political advocacy network for sickle cell disease (SCD) is currently significantly smaller and less organized than the HIV advocacy infrastructure that propelled access reform.

The five-domain analysis indicates that the most significant structural parallels between HIV antiretroviral therapy (ART) and Casgevy lie in the geography of disease burden and the feasibility of tiered pricing, where the political and economic rationale for access reform is directly applicable to ART. The greatest divergence is found in manufacturing complexity, where the autologous nature of Casgevy production fundamentally restricts the generic pathway that led to the collapse of ARV prices. This asymmetry suggests that the policy toolkit for Casgevy access must differ in nature, relying more on process licensing, hub-model infrastructure investment, and innovative financing mechanisms than on market competition, which delivers affordable ARVs.

The optimistic scenario for Casgevy access in SSA hinges on a factor that the HIV analogy cannot assure: manufacturing innovation. Should in vivo gene editing advance sufficiently to provide a single-injection curative solution for SCD, the manufacturing constraint would be eliminated, rendering the product genuinely genericizable and significantly reducing the access challenge [15]. Conversely, if ex vivo CRISPR therapy remains the sole viable curative option, achieving equitable access will necessitate sustained political commitment over multiple decades, precisely the type of commitment that the ARV precedent demonstrates is attainable when political will is mobilized.

7. Limitations

This review has several limitations. First, as a narrative review lacking a systematic search methodology, it is prone to selection bias in the literature referenced. Second, the policy framework proposed in Section 5 is inherently speculative and will be influenced by unpredictable political and technological developments. Third, the comparison between HIV and SCD, although structurally informative, involves two conditions that are biologically, pharmacologically, and epidemiologically distinct. The analogy has limitations that have been explicitly identified but may not be comprehensive. Finally, the cost estimates provided in this review are approximate and intended to demonstrate feasibility rather than serve as precise economic forecasts.

8. Conclusion

The HIV antiretroviral access revolution showed that global health equity is politically achievable despite the structural barriers of manufacturing concentration, pricing, and commercial interest. The mechanisms behind it—voluntary licensing, manufacturing competition, advocacy-driven mobilization, and innovative financing—form a documented, replicable toolkit.

For Casgevy and SCD in SSA, this toolkit requires adaptation for the gene-therapy era. Process licensing must replace generic manufacturing methods. AMC-style demand commitments must replace the open competition. Regional cell therapy hubs must replace the tablet manufacturing scale-up. A new generation of SCD advocacy must make the access gap morally and politically intolerable in HIC.

Sub-Saharan Africa bears most of the world's sickle cell disease (SCD) burden. Access to curative therapy will depend less on science and more on political choices made by governments, multilateral institutions, manufacturers, and civil society in the next decade. The ARV precedent shows that such choices can succeed.

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9. Authors' Contributions

O.G.A. conceived and designed the review, developed the search strategy, performed study selection and data charting, and drafted the manuscript. A.B.A. contributed to study selection, data charting, and interpretation. M.E.O. contributed to data charting, tabulation, and critical revision. D.T.I. contributed to screening, interpretation, and critical revision. All authors read and approved the final manuscript.

10. Conflict of Interest

The authors declare that they have no financial or non-financial conflicts of interest relevant to this work.

11. Ethical Statements

This study is a scoping review of previously published literature and did not involve human participants, human data, or animals directly.

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