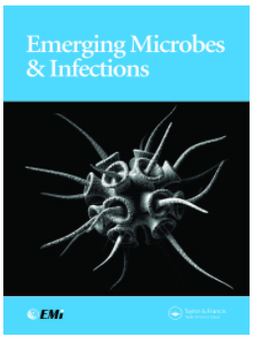

Emerging Microbes & Infections

ISSN: 2222-1751 (Online) Journal homepage: www.tandfonline.com/journals/temi20

Biotech's role in advancing HIV vaccine development

Roger Tatoud, Christian Brander, Carey Hwang, Jo Kennelly, Shan Lu, Kevin O'Neil, Jeffrey T. Safrit, Iris Benhayoun, Julieta Firmat & Nelli Barriere

To cite this article: Roger Tatoud, Christian Brander, Carey Hwang, Jo Kennelly, Shan Lu, Kevin O'Neil, Jeffrey T. Safrit, Iris Benhayoun, Julieta Firmat & Nelli Barriere (2024) Biotech's role in advancing HIV vaccine development, Emerging Microbes & Infections, 13:1, 2384460, DOI: 10.1080/22221751.2024.2384460

To link to this article: https://doi.org/10.1080/22221751.2024.2384460

Emerging Microbes & Infections
2024, VOL. 13, 2384460 (6 pages)
https://doi.org/10.1080/22221751.2024.2384460

COMMENT

OPEN ACCESS Check for updates

Biotech's role in advancing HIV vaccine development

Roger Tatoud [a], Christian Brander [b], Carey Hwang[c], Jo Kennelly[d], Shan Lu [e], Kevin O'Neil[f], Jeffrey T. Safrit[g], Iris Benhayoun[e], Julieta Firmat [h] and Nelli Barriere[h]

[a]Origena Consulting, Ferney Voltaire, France; [b]AELIX Therapeutics, Catalonia, Spain; [c]Vir Biotechnology, San Francisco, CA, USA; [d]Malaika Vx, Toronto, Canada; [e]Worcester HIV Vaccine, Worcester, MA, USA; [f]Uvax Bio, Newark, DE, USA; [g]ImmunityBio, San Diego, CA, USA; [h]International AIDS Society, Geneva Switzerland

ABSTRACT

HIV vaccine development has been hindered by significant challenges over four decades. Despite persistent efforts, all efficacy trials to date have yielded disappointing results. This has pushed the field back to the discovery phase and created uncertainty about the future involvement of large pharmaceutical companies. Currently, the HIV vaccine landscape is dominated by startup biotech firms, which face a complex array of obstacles. These include evolving HIV prevention methods, waning interest in vaccine research, and difficulties securing sustainable funding. This viewpoint explores the challenges faced by these biotech companies and the support mechanisms necessary for their continued involvement in HIV vaccine development. By leveraging insights from both pharmaceutical and biotech sectors, we propose a multi-faceted approach that includes enhanced communication, fostering innovation, and implementing strategic funding models.

ARTICLE HISTORY Received 10 May 2024; Revised 17 July 2024; Accepted 19 July 2024

KEYWORDS HIV; HIV vaccine; research and development; biotech; pharmaceutical industry

Introduction

Advances in the prevention, treatment, and care for HIV have significantly transformed the global HIV response [1]. HIV is no longer considered a life-threatening condition, but a manageable, long-term chronic illness when adequate treatment and care are accessible. Effective prevention methods, such as pre-exposure prophylaxis, are now available, and it's recognized that individuals with an undetectable HIV viral load do not transmit the virus. The current global focus of the HIV response is on developing sustainable national strategies ending the HIV pandemic as a threat to public health and individual well-being, prioritizing the right to health for everyone [2]. However, challenges persist in accessing antiretroviral (ARV) therapy and ARV-based prevention in many areas and the reliance on continuous drug supply underscores the importance of continued research and development of HIV vaccines.

Yet, the HIV vaccine product development field has not made real progress in 40 years despite advancements in novel vaccine technology and an improved understanding of immune responses in people living with HIV, and in-depth structural analysis of key protective antigen HIV-1 envelope protein [3–6]. Remarkably, following repeated set back, large pharmaceutical companies are no longer involved in vaccine development, and HIV vaccine development now rests largely with academic researchers and a few small biotech companies. As of 2023, nine biotech companies have been identified as actively contributing to the development of the next generation of HIV vaccines (Table 1).

In this perspective, we draw from the experience of pharmaceutical and biotech companies engaged in or previously involved in HIV vaccine development to discuss the difficulties faced by biotech and enablers that could support their continued participation in HIV vaccine research and development.

Pioneering and powering HIV vaccine R&D

On 18 August 1987, the US Food and Drug Administration approved the first phase 1 clinical trial for an HIV vaccine. The vaccine tested, called VaxSyn, was developed by MicroGeneSys, a biotechnology company based in Connecticut, USA. It involved inserting the HIV gp160 envelop gene into baculovirus for production in insect cells. MicroGeneSys

CONTACT Roger Tatoud r.tatoud@outlook.com
Supplemental data for this article can be accessed online at https://doi.org/10.1080/22221751.2024.2384460.

Table 1. Landscape of Biotech actively involved in HIV vaccine R&D in 2024.

	Company information	Product	Application	Clinical stage
AELIX Therapeutics	• Spain • Founded 2015 • Spin-off of HIVACAT	• HTI immunogen:	• Therapeutic vaccine	• NCT03204617 Phase 1 • NCT04364035 Phase 2
	Key results: No related serious adverse events. HTI vaccine induce strong, polyfunctional and broad CD4 and CD8 T-cell responses. All participants experienced detectable viral rebound during ATI. In post-hoc analyses, HTI vaccines were associated with a prolonged time off ART in vaccinees without beneficial HLA class I alleles [7].			
Emmune	• USA • Founded 2018	• Synthetic antibody delivered via an adeno-associated virus (AAV)	• Preventive and Therapeutic vaccine	• Phase 1
	Key results: The eCD4-Ig inhibitor binds strongly to HIV-1's Env protein and irreversibly inactivates it. eCD4-Ig neutralises 100% of a diverse range of neutralization-resistant HIV-1 strains. When delivered to macaques using an adeno-associated virus, eCD4-Ig protects them from multiple virus challenges [8].			
Gritstone Bio	• USA • Founded 2018	• Self-amplifying mRNA (samRNA) • Simian adenoviral vectors	• Therapeutic vaccine	• Preclinical
	Key results: Simian immunodeficiency virus (SIV) ChAd and samRNA vaccines in combination with immune modulators induced a strong immune response [9].			
ImmunityBio	• USA • Founded 2014	• IL-15 superagonist		• NCT04340596 Phase 1 • NCT04505501 Phase 2
	Key results: N-803 (Anktiva) activates T cells and NK cells as tools for fighting HIV. In combination with bNAbs, 9/13 rhesus macaques were able to control virus without antiretroviral therapy following a treatment interruption. This approach is currently being evaluated in 2 separate clinical trials [10].			
LinkinVax	• France • Founded in 2020 • Spin-off of the Vaccine Research Institute	• Dendritic cell-targeting vaccine	• Therapeutic vaccine	• NCT04842682 Phase 1
	Key results: Safe and induced early, potent and durable anti-Env and V1/V2 IgG and polyfunctional CD4 T-cell responses, markers associated with reduced risk of infection in RV144 [11].			
Malaika Vx	• Canada • Founded 2020	• Recombinant vector • Lipid nano particle	• Preventive vaccine	• Preclinical
	Key results: Simian immunodeficiency virus (SIV) VSV (and LNP vaccines in production) induced strong T cell immune response [12].			
Minka Therapeutics	• France • Founded in 2008	• Env peptide	• Therapeutic vaccine	• NCT02041247 Phase 2
	Key results: Vaccination was well tolerated with no serious adverse events. In high responders, a robust increased of CD4 count was associated with a significant and sustained reduction of PD-1 expression on CD4+ T cells through week 48. PD-1 expression was correlated with level of anti-3S Abs and expression of NKp44L in CD4+ T cells [13].			
Uvax Bio	• USA • Founded 2018 • Spin-off of Scripps Research	Two protein nanoparticle vaccines displaying prefusion-optimized (UFO) envelope glycoprotein from HIV-1 BG505.	• Preventive vaccine	• U1111-1299-3168 Phase 1
	Key results: Clinical study fully enrolled and in progress [14].			
Vir Biotechnology	• USA • Founded 2016	• Recombinant vector	• Preventive vaccine	• NCT04725877 Phase 1 • NCT05854381 Phase 1
	Key results: No safety signals and no vector shedding or viremia were reported. In addition, no sustained HIV insert specific T cell responses were observed at all doses tested with initial vector. (Vir Biotechnology Corporate Update and Reports First Quarter 2023 Financial Results May 4, 2023). Phase 1 study with less attenuated vector currently in Phase 1.			
Worcester HIV Vaccine	• USA • Founded 2018 • Spin-off of University of Massachusetts Medical School	• DNA prime protein-boost	• Preventive vaccine	• NCT00061243 Phase 1 • NCT03409276 Phase 1 • NCT04927585 Phase 1b
	Key results: Vaccination regimen was safe, well-tolerated, and demonstrated uniquely robust immunogenicity. PDPHV is the first HIV vaccine showing a broad range of cross-reactive immune responses in one vaccine design. IgG/IgG3 responses against gp70 V1V2 were higher in HVTN124 than any other previously reported HIV vaccine efficacy trials [15].			

conducted over 10 clinical trials, but the vaccine failed to provide protection [16] or therapeutic benefits [17]. MicroGeneSys later became Protein Science Corp, before being acquired by Sanofi-Pasteur. Wyeth-Ayerst, MicroGeneSys' development partner, was later acquired by Pfizer. At the time, other biotech companies like Genentech, Genetic Systems, and Oncogene were also working on HIV vaccine candidates [18].

A decade later, many companies, both small and large, were actively involved in developing and testing HIV vaccines highlighting the vibrant environment for clinical development of an HIV vaccine and underscoring the critical role played by startup biotech in the early days of HIV vaccine research (Supplementary Table 1) [19]. As vaccine candidates progressed along the product development path and the costs of research increased substantially, large companies took a more prominent role in the search for an HIV vaccine, although small biotech companies continued to develop innovative technologies and candidates. Four decades later, the search for an HIV vaccine continues. Ten phase II and III clinical trials evaluating

various vaccination approaches have all failed to show effectiveness [3–5].

Nowadays, biotech companies remain more agile and can quickly adapt to scientific advancements. Their higher risk tolerance allows them to invest in cutting-edge technologies like self-amplifying mRNA and dendritic cell vaccines, using focused expertise to achieve breakthroughs. They are expanding HIV vaccine development from prevention to therapy and potential cures. By prioritizing unconventional vaccine candidates that stimulate less studied immune responses and using innovative immunization platforms and adjunct therapies, they open new possibilities for discovery. Despite promising results, their efforts are fraught with challenges, compounded by the intrinsic complexities of creating an HIV vaccines [20].

Challenges and opportunities

Small and medium enterprises (SME) played a significant role in driving innovation in the past half-century in the development of new biomedical products, processes, methods as well as in improving existing ones [21]. Small biotech companies have the flexibility to explore research paths that larger pharmaceutical companies, being more risks adverse, might avoid investing in. However, biotech companies also have vulnerabilities that can pose challenges to opportunities (Box 1). Biotech companies also encounter challenges due to the unique nature of HIV vaccine R&D (Box 2).

Box 1. Rapid SWOT analysis of biotech involved in HIV vaccines R&D.

STRENGHTS

- Scientific foundation
- Innovation & creativity
- Technology focussed
- Problem solving

WEAKNESSES

- Product development plan
- Business acumen
- Timeline management
- Supporting data
- Timeliness
- Funding and viability

OPPORTUNITIES

- Ideation
- Filling the gap in current mainstream pipeline
- Partnerships with industry, funders, and other biotech

THREATS

- Success of HIV prevention today
- Market opportunity
- No public funding mechanism
- Fragmented development
- Intellectual property
- Business risk perception

Box 2. Challenges encountered by biotechnology company engaged in HIV R&D.

Technology-related

- Attractiveness and relevance of the technology for HIV vaccine
- Freedom to operate.
- Access to diverse vaccine components (for example vectors, delivery systems, adjuvants).
- Generating compelling preclinical data for regulators, investors, and funders after initial proof of concept.
- Feasibility to conduct clinical research (access to trials networks).
- Product maturity and scalability.

Business acumen

- Compelling business case and business plan, go/no-go criteria.
- Expertise in product development.
- Portfolio development and management.
- Competitive advantage.
- Exit strategy.

Funding

- Gap in early/late public/private investment.
- Timescale for return on investment.
- Funding for long-term and sustained growth.
- Maintaining interest and funding momentum.

Securing funding is the primary barrier for initiating, sustaining, and growing a small biotech company. Major factors affecting funding for small biotech include: progress in HIV prevention and treatment, the perception that HIV is a distant problem (both in time and space), the belief that an HIV vaccine is no longer a public health priority for public health policy makers, the thinking it seems to be an unattainable goal by the pharmaceutical industry, a cautious attitude towards supporting innovation by funders, and a lack of funding processes and mechanisms suitable for biotech companies. Further, there is an imbalance between early and late public and private funding: early research is largely funded by the not-for-profit sector, public and philanthropic, and late research requires the involvement of the for-profit sector [22]. Altogether, the funding landscape is a complex patchwork further complicated by contracts and intellectual property agreements.

Current philanthropic and public funding opportunities remain limited in focus with limited interest in novel vaccinal approaches and disruptive technology. Funding mechanisms often lack transparency and consistency, with funders being averse to risks; innovation does not seem to reach funders and research is dependent on funders' interest and strategy.

In parallel, the greatest challenge for attracting private investment is to address the perceived lack of scientific momentum resulting from inconsistent communication of research development that tends to overly praise the potential for success and downplay the reality of failure and to convince backers that an HIV vaccine remains a necessity and is feasible. The

Table 2. Recommendations to support Biotech's continuous involvement in and contribution to HIV vaccine R&D.

AREAS	RECOMMENDATIONS	PROPOSED ACTIONS
FINANCING	**Establish a Global R&D Translation Fund**	• Create or use existing investment tools like equity, loans, and grants to support translational research. • Support in priority early-stage biotech companies tackling specific and practical challenges of HIV vaccine development. • Provide tailored, long-term funding that bridge funding gaps alongside the product development path. • Invest in ventures integrating innovative science in a corporate framework to facilitate financing growth.
	Reevaluating funding strategies of non-profit organizations	• Align non-profit funding strategies with the unmet needs for a HIV vaccine. • Encourage non-profit funding agencies to break away from the themes that have been explored and funded for the last 40 years, without compelling success.
BUSINESS DEVELOPMENT AND MANAGEMENT	**Establish business training programmes**	• Create opportunities for industry to provide strategic advice, mentorship programmes, and networking opportunities with potential partners and investors.
	Strengthen inventor-led startup pathways	• Foster alternative pathways for biotech-led product development such as bootstrapping academic-led startups that provides training to gain a "real-world" market perspective on their discoveries and innovations and cultivate important strategic alliances [23, 26].
	Facilitate the establishment of partnerships and strategic alliances	• Build partnerships between early-stage biotech, inventor-led startups, and interested growth financing organizations. • Protect legacy investments in the science and technology. • Ensures that scientific innovations and technological advancements reach their full potential. • Encourages prioritizing the joint pursuit of public health outcomes.
	Structure support around clear, performance-based milestones.	• Align financial disbursements with progress in vaccine development, ensuring that funds are utilized effectively and that companies are motivated to achieve key development milestones.
	Implement a new model based on an accelerator approach	• Support the de-risking of products during their development by providing intensive mentorship, focused training, access to a peer group of startup founders, and exposure to investors.
INTELLECTUAL PROPERTY	**Assist early-stage biotech in developing robust intellectual property (IP) strategies**	• Support patent filing, IP management, and negotiation of licencing agreements, ensuring that companies can safeguard their innovations and leverage them for growth financing while facilitating future partnerships and licencing agreements.
CLINICAL RESEARCH	**Provide support for navigating regulatory pathways and designing effective clinical trials**	• Facilitate access to regulatory consultants, assist with regulatory submissions, and support in establishing partnerships for conducting clinical trials in relevant populations. • Engage with investigators to explore potential alternative to trials designs.
POLICY AND ADVOCACY	**Demonstrate the overall value of an HIV vaccine.**	• Conduct product and market characterization to guide product development and quantify the potential for return • Develop product development tools such as Preferred Products Characteristics (PPC), Target Product Profile (TPP) and Full Value of Vaccine Assessment (FVVA) which compiles and analyses critical data and evidence that highlight the health, economic, and societal benefits of a preventative vaccine. • Identify research gaps and areas where incremental progress by biotech companies would be particularly valuable.
	Engage in advocacy and policy dialogue	• Enhanced and improve communication of HIV vaccine R&D and of the shortcomings of relying on ARV-based prevention and therapies for the control of the epidemic. • Make the case for the pressing need to develop an HIV preventative vaccine, especially for people living in resource-limited settings, women and children, and marginalized groups.
	Embed access and equity considerations into the funding and support model	• Integrate plans for affordability, accessibility, and delivery in low- and middle-income countries from the earliest stages of vaccine development.
RESEARCH COORDINATION AND DISSEMINATION	**Build on trusted neutral conveners**	• Enhance communication among stakeholders by providing a space for multi-stakeholder engagement, improving the dissemination of scientific achievements, overcoming the negativity surrounding HIV vaccine and increasing exposure to new and potentially disruptive approaches to HIV vaccines R&D.

primary pathways to product development for biotech is to secure backing from pharmaceutical companies or venture capital (VC). VC firms tend to be risk averse, looking for evidence of market demand, a strong founding team, technology maturity and a clear path to meaningful milestones, which are all the more challenging when considering HIV vaccine development [23]. The perceived uncertainty about the value of an HIV vaccine and corollary market opportunity contribute to the vaccine investment hesitancy. Product development risks, as well as VC firms' timeline for return on investment, are not compatible with the time required to develop and clinically test HIV vaccine candidates.

Developing an HIV vaccine is a complex and lengthy process. The potential of a product relies on clinical data being available to support investment. The gap between preclinical and first in human studies – the so-called valley of death – remains a major barrier to product development and a catch-22 situation where product developers need to generate data that will support request for funding. Another obstacle is that product development will require the conduct of large and costly safety and efficacy trials, the conduct of which has become complicated by evolving standards of care and the availability of effective prevention in the form of preexposure prophylaxis. The cost of two of the most recent efficacy trials run above USD 100 million (RV144 USD 119 m [24], HVTN702 USD 104 million [25]) and such investment requires long term vision and planning. Furthermore, it is assumed that an HIV vaccine will require the combination of several product and technologies, raising the spectre of freedom to operate. In a complex intellectual property environment and with developers weary of potential reputational risk to their product these additional obstacles, although not unsurmountable, add to the challenges to secure funding from various sources.

Given the challenges encountered by biotech, we identified specific actions that could result in tangible enhancements to support and maintain the contributions of SMEs engaged in HIV vaccine R&D. These actions are categorised according to themes that align with the product development path (Table 2).

Conclusion

Successful biotech startups can have positive impact on society by addressing previously insurmountable scientific and medical issues. In the current HIV prevention landscape, biotech startups play an important role in advancing an HIV vaccine by addressing specific scientific challenges, promoting innovation, and contributing to sustained and diversified efforts in vaccine R&D. The primary goal is to accelerate the transition of promising products from academia to biotech and industry.

However, this is contingent upon the development of a viable business model that enables them to undertake the monumental task of creating an HIV vaccine. This not only increases the likelihood of attracting private investors and achieving success, but also broadens the scope of research funded by non-profit organizations. Overcoming the challenge of sustainable funding remains a significant obstacle for early-stage product development and late-phase efficacy studies. A paradigm shift is necessary to devise funding mechanisms and structures applicable in an environment where the role and market potential of HIV vaccines are clearly defined, and biotech companies are fully integrated into a global research environment.

Disclosure statement

RT: The author declares that they have no competing interests. CB: Co-founder, shareholder and CSO at AELIX Therapeutics. CH: Employee and stockholder of Vir Biotechnology, Inc. JK: Founder, Executive Chair, Malaika Vx, Inc. SL: Editor-in-Chief of EMI; recuses himself from the editorial review of this manuscript. KO: Employee at Uvax Bio. JTS: Employee and stockholder of ImmunityBio. IB: Employee at Worcester HIV Vaccine. JF: The author declares that they have no competing interests. NB: The author declares that they have no competing interests.

Funding

This work was supported by the International AIDS Society HIV Vaccine Industry Partnership Group, through contributions from its 2023 and 2024 Gold Partners (Gilead Sciences, MSD and ViiV Healthcare), Silver Partners (Janssen) and Bronze Partners (AccuBio, Beckman Coulter Life Sciences, ImmunityBio, MalaikaVx, Roche, Sanofi, Vir Biotechnology and Worcester HIV Vaccine).

Author contributions

RT drafted the manuscript, and all other authors reviewed and approved the final version.

ORCID

Roger Tatoud https://orcid.org/0000-0002-3999-8264
Christian Brander https://orcid.org/0000-0002-0548-5778
Shan Lu https://orcid.org/0000-0002-8417-7588
Julieta Firmat https://orcid.org/0009-0008-6261-7918

References

[1] Landovitz RJ, Scott H, Deeks SG. Prevention, treatment and cure of HIV infection. Nat Rev Microbiol. 2023;21:657–670. doi:10.1038/s41579-023-00914-1.
[2] Joint United Nations Programme on HIV/AIDS. HIV response sustainability primer [Internet]. Geneva; 2024 [cited 2024 Feb 7]. Available from: https://www.unaids.org/en/resources/documents/2024/20240117_HIV_response_sustainability.
[3] Lee JH, Crotty S. HIV vaccinology: 2021 update. Semin Immunol. 2021;51:101470. doi:10.1016/j.smim.2021.101470.
[4] Kim J, Vasan S, Kim JH, et al. Current approaches to HIV vaccine development: a narrative review. J Int AIDS Society. 2021;24:e25793. doi:10.1002/jia2.25793.
[5] Nkolola JP, Barouch DH. Prophylactic HIV-1 vaccine trials: past, present, and future. Lancet HIV. 2024;11:e117–e124. doi:10.1016/S2352-3018(23)00264-3.
[6] Jefferys R. The HIV vaccines and passive immunization pipeline report 2023. [cited 2024 Jun 18].

Available from: https://www.treatmentactiongroup.org/wp-content/uploads/2023/07/pipeline_HIV_VAX_2023_final.pdf.

[7] Bailón L, Llano A, Cedeño S, et al. Safety, immunogenicity and effect on viral rebound of HTI vaccines in early treated HIV-1 infection: a randomized, placebo-controlled phase 1 trial. Nat Med. 2022;28:2611–2621. doi:10.1038/s41591-022-02060-2.

[8] Gardner MR, Kattenhorn LM, Kondur HR, et al. AAV-expressed eCD4-Ig provides durable protection from multiple SHIV challenges. Nature. 2015;519:87–91. doi:10.1038/nature14264.

[9] Rappaport A, Bekerman E, Boucher G, et al. Heterologous ChAd/samRNA vaccine induces robust T-cell responses in macaques. Abstract 323. [Internet]. Conference on Retroviruses and Opportunistic Infections (CROI), Seattle, Washington, USA; 2023 [cited 2024 Jun 18]. Available from: https://www.croiconference.org/abstract/heterologous-chad-samrna-siv-vaccine-induces-robust-t-cell-responses-in-macaques/.

[10] Lim S-Y, Lee J, Osuna CE, et al. Induction of durable remission by dual immunotherapy in SHIV-infected ART-suppressed macaques. Science. 2024;383:1104–1111. doi:10.1126/science.adf7966.

[11] Lelievre J-D, Moog C, Wiedermann A, et al. CD40.HIVRI.Env vaccine induces strong and durable immune responses: ANRS VRI06 trial. Abstract 324 [Internet]. Conference on Retroviruses and Opportunistic Infections (CROI), Seattle, Washington, USA; 2023 [cited 2024 Jun 18]. Available from: https://www.croiconference.org/abstract/cd40-hivri-env-vaccine-induces-strong-and-durable-immune-responses-anrs-vri06-trial/.

[12] Li H, Omange RW, Liang B, et al. Vaccine targeting SIVmac251 protease cleavage sites protects macaques against vaginal infection. J Clin Invest. 2020;130:6429–6442. doi:10.1172/JCI138728.

[13] Vieillard V, Combadière B, Tubiana R, et al. HIV therapeutic vaccine enhances non-exhausted CD4+ T cells in a randomised phase 2 trial. npj Vacc. 2019;4:1–9. doi:10.1038/s41541-018-0094-0.

[14] Zhang Y-N, Paynter J, Antanasijevic A, et al. Single-component multilayered self-assembling protein nanoparticles presenting glycan-trimmed uncleaved prefusion optimized envelope trimers as HIV-1 vaccine candidates. Nat Commun. 2023;14:1985. doi:10.1038/s41467-023-37742-z.

[15] Frank I, Li SS, Grunenberg N, et al. Safety and immunogenicity of a polyvalent DNA-protein HIV vaccine with matched Env immunogens delivered as a prime-boost regimen or coadministered in HIV-uninfected adults in the USA (HVTN 124): a phase 1, placebo-controlled, double-blind randomised controlled trial. Lancet HIV. 2024;11:e285–e299. doi:10.1016/S2352-3018(24)00036-5.

[16] Dolin R, Graham BS, Greenberg SB, et al. The safety and immunogenicity of a human immunodeficiency virus type 1 (HIV-1) recombinant gp160 candidate vaccine in humans. NIAID AIDS Vaccine Clinical Trials Network. Ann Intern Med. 1991 Jan 15;114(2):119–127. doi:10.7326/0003-4819-114-2-119.

[17] Tsoukas CM, Raboud J, Bernard NF, et al. Active immunization of patients with HIV infection: a study of the effect of VaxSyn, a recombinant HIV envelope subunit vaccine, on progression of immunodeficiency. AIDS Res Hum Retroviruses. 1998;14:483–490. doi:10.1089/aid.1998.14.483.

[18] Merz B. HIV vaccine approved for clinical trials. JAMA. 1987;258:1433–1434. doi:10.1001/jama.1987.03400110013003.

[19] Batson A, Ainsworth M. Private investment in AIDS vaccine development: obstacles and solutions. Bull World Health Organ. 2001;79(8):721–727.

[20] Ng'uni T, Chasara C, Ndhlovu ZM. Major scientific hurdles in HIV vaccine development: historical perspective and future directions. Front Immunol. 2020;11:590780. doi:10.3389/fimmu.2020.590780.

[21] Robinson R. Small pharma driving big pharma innovation. PharmaVoice [Internet]. 2020 Jan 1 [cited 2024 Feb 14]; Available from: https://www.pharmavoice.com/news/2020-01-pharma-innovation/612330/.

[22] Seyhan AA. Lost in translation: the valley of death across preclinical and clinical divide – identification of problems and overcoming obstacles. Transl Med Commun. 2019;4:18. doi:10.1186/s41231-019-0050-7.

[23] Marrus SK, Blaho JA. Increasing the success potential of promising biotech companies. Nat Biotechnol. 2023;41:154–155. doi:10.1038/s41587-022-01627-1.

[24] Burton DR, Desrosiers RC, Doms RW, et al. A sound rationale needed for phase III HIV-1 vaccine trials. Science. 2004;303:316–316. doi:10.1126/science.1094620.

[25] Cohen J. Another HIV vaccine strategy fails in large-scale study. Science. 2020. doi:10.1126/science.abb1480

[26] Canaria CA, Portilla L, Weingarten M. I-Corps at NIH: entrepreneurial training program creating successful small businesses. Clin Transl Sci. 2019;12:324–328. doi:10.1111/cts.12637.