

Global HIV Vaccine Enterprise
Strategic Plan

2018-2023



Foreword

For over a decade, the Global HIV Vaccine Enterprise (the Enterprise) has played a unique and essential role as a neutral convener and facilitator, committed to identifying gaps and mobilizing stakeholders to accelerate HIV vaccine development. Among its many achievements, the Enterprise has helped to realize the untapped collaborative potential of HIV vaccine researchers and was instrumental in establishing the Collaboration for AIDS Vaccine Discovery (CAVD) and Center for HIV/AIDS Vaccine Immunology (CHAVI), two networks that remain central to advancing preclinical and translational HIV vaccine R&D.

The International AIDS Society (IAS) is thrilled to be hosting the Enterprise as it builds on this legacy of impact in HIV vaccine research and development. Hosting the Enterprise at IAS will ensure that the pursuit of an HIV vaccine takes a place of prominence in IAS' mission to reduce the global impact of HIV.

The Enterprise's 2018-2023 Strategic Plan aims to address several pivotal questions: How can we maintain the momentum of scientific collaborative efforts while orienting the vaccine community around emerging priorities in late-stage product development? How can we support the vaccine space to respond optimally to results from current efficacy trials? How can we best leverage the IAS' track record in convening and engaging a diverse range of stakeholders to advance the interests of the HIV vaccine community? How can we heighten political support and expand the Enterprise?

In the spirit of the Enterprise, development of this 5-year strategy has been a highly collaborative effort. We would like to thank the dozens of stakeholders we consulted, our Strategic Advisory Group and the IAS Governing Council, whose insights, ideas and review have helped us to tackle these questions and produce a plan that will challenge, energize and inspire the vaccine community. We look forward to working in partnership with many different stakeholders to make this strategy a reality and strengthen our collective commitment towards accelerating the development of an effective HIV vaccine.



Context

A Bold New Era for the Enterprise

The alliance of funders and stakeholders that established the Enterprise over a decade ago understood the potential to accelerate HIV vaccine development through coordination, collaboration, knowledge-sharing and mobilization of resources. Today, as the Enterprise transitions to the IAS, we have an opportunity to affirm the Enterprise’s mission in the context of a transformed landscape—and to engage new stakeholders and funders in a diversified, resilient and truly global alliance relentlessly committed to developing an HIV vaccine as quickly as possible.

Nothing has changed for the Enterprise...

While the field is arguably more collaborative than ever before, there remains a profound need for a neutral convener to facilitate connections aimed at overcoming silos and tackling the field’s most complex issues.

... and yet, everything has changed for the Enterprise.

With multiple efficacy-stage programmes underway and new vaccine concepts in the clinical pipeline, the field has built considerable momentum toward the end goal. This sense of possibility is matched only by a growing sense of urgency that the field remains inadequately prepared for the final—and most complex—leg of the vaccine development journey. There is now a need for an Enterprise committed to fueling dialogue, developing resources and facilitating solutions that help the field maintain product development momentum, plan for success and diversify the coalition of partners critical to achieving the end goal.

This document describes the context and framework for the Enterprise’s new five-year strategy. We begin with an overview of the field’s critical issues.

We Need Even More Collaboration

Vaccine Candidates Face a Complex and Uncertain Path to Market

The field is enjoying an unprecedented level of late-stage clinical activity, with multiple vaccine efficacy trials underway (P5, Janssen) or soon to begin (PrepVacc) in southern Africa (Fig. 1). In parallel, HVTN 703 and 704 are assessing passive immunization of a broadly-neutralizing antibody (bNAb). While exciting, these trials are exposing gaps in the field’s ability to respond to and prepare for the realities of late-stage development.

First, conducting efficacy trials in the future will be challenged by the evolving nature of the epidemic. As use of pre-exposure prophylaxis (PrEP) and other prevention tools increases and HIV incidence declines, the cost and complexity of vaccine trials will rise in order to maintain statistical power.

Second, several issues must be tackled to set the stage for future vaccine access. There is a need to build local regulatory capacity for licensing an HIV vaccine in high-incidence countries and to understand policymakers’ desired vaccine

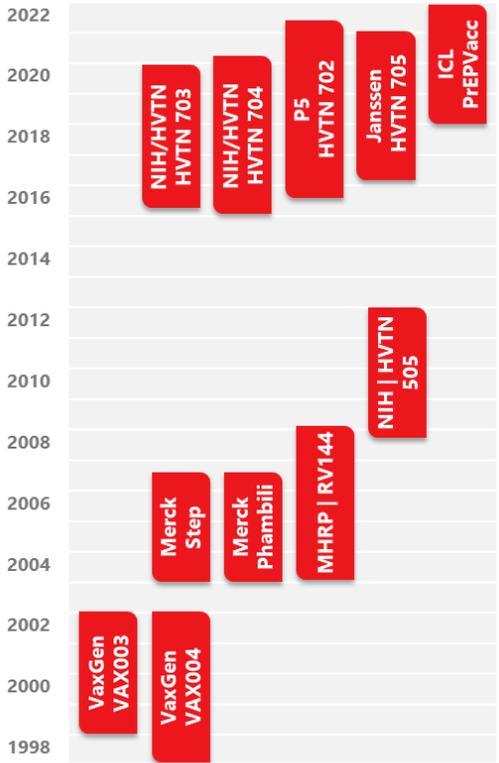
characteristics, including efficacy levels. Developers will need to create manufacturing capacity, either directly or through technology transfer to third parties, to ensure stable, cost-effective vaccine supply. Finally, access will hinge on stakeholder engagement and careful planning to identify target populations, forecast demand and determine optimal deployment channels—challenges that may be exacerbated by the multi-dose regimens currently in development.

Planning for and enabling the success of late-stage candidates will require broad stakeholder engagement and alignment to clarify and accelerate the path to market.

Strengthening the Pipeline Will Require a Focus on Scientific Gaps

Early-stage HIV vaccine candidates align with a few high-level strategies (eliciting bNAbs, stimulating non-neutralizing antibodies or inducing T cell-mediated control of HIV) based on current (and incomplete) knowledge of the potential capacity of the immune response to protect against HIV infection. To improve and diversify the range of concepts in the pipeline we need to improve our understanding of immunology and optimize preclinical research tools.

Figure 1. HIV Vaccine & Biologics Efficacy Trials



Data Source: AVAC

It will be critical to learn more about immune responses—including mucosal immunity, microbiome responses and bNAb generation, among others—and determine which responses are correlated with vaccine-induced protection. With late-stage programmes planning correlates analyses following efficacy readouts in 2021-2022, there is an opportunity for the field to prepare for sharing and interpretation of results to inform early-stage vaccine efforts.

There is also a need to increase the predictive accuracy of animal models and continue to improve and standardize immune response assays. And while the field has benefited from research and clinical networks in the US and Europe, there is still room for increased collaboration, information-sharing and exchange of vaccine components.

Fortifying the pipeline will require field-wide innovation and increased collaboration to encourage diverse approaches, including ‘mixing and matching’ vaccine components.

Funding Has Been Stagnant and Shouldered by Only a Few Funders

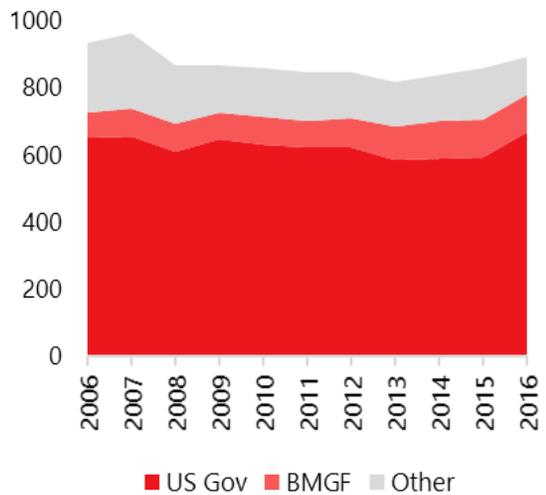
Funding for HIV vaccine R&D has been relatively flat (and thus declining in real

dollars) for the past decade, and ~85% has come from the US Government and the Bill & Melinda Gates Foundation (BMGF; Fig. 2). The field will need more resources to accelerate progress and support early- and late-stage R&D efforts.

Attracting funding will require knowledge of the objectives of various (potential) funders. Some governments have been reluctant or unable to fund HIV vaccine R&D due to other priorities taking precedence or to constraints related to integrating HIV vaccine work within broader HIV or infectious disease portfolios. International development agencies are often focused on community-based programme delivery and may not have latitude or appropriate vehicles to invest in HIV vaccine R&D. Most industry players have not invested substantially, especially before efficacy readouts, given the perceived lack of commercial potential—though Janssen’s pursuit of a ‘global’ vaccine could transform this view and stimulate wider industry funding.

Stakeholders must work together to optimize resource use and to increase funding and broaden the support base by aligning investor priorities with potential impact.

Figure 2. HIV Vaccine R&D Funding
(US\$ Millions)



Data Source: AVAC
Other includes European Commission, Ragon Foundation, Swedish Research Council, ANRS, UK MRC and industry.

Focusing the Enterprise on Areas of Greatest Unmet Need and Potential Impact

Engagement with stakeholders has sharpened our focus on critical issues that would benefit most from greater co-ordination, invigorated collaboration and facilitated, multi-stakeholder approaches (highlighted cells; Fig. 3).

Figure 3. Priority Issues in the HIV Vaccine Field

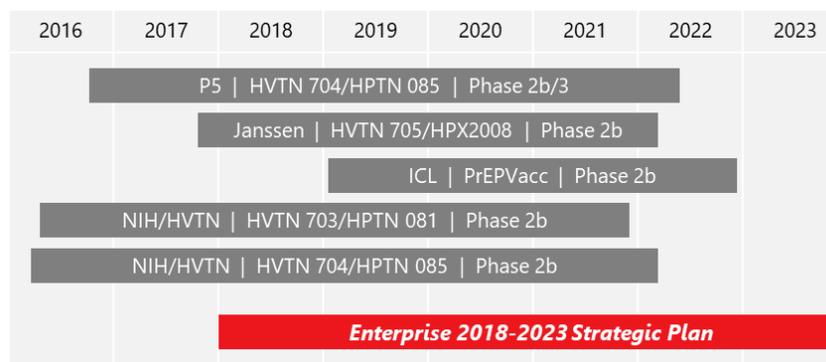
Basic/Pre-Clinical Research	Clinical Research	Product Development	Implementation/Deployment
Linking immunology research (e.g. bNAbs, microbiome) with vaccine design efforts (e.g. immunogen, adjuvant)	Exploring trial design strategies to mitigate PrEP/low incidence	Conceiving new models to fund late stage vaccine development	Modelling public health impact in key regions and populations
	Enabling adaptive trial designs to rapidly test candidates	Mapping HIV vaccine regulatory pathways in sub-Saharan Africa	Understanding acceptability in different populations/regions
Facilitating study of novel vaccine delivery technologies	Piloting combination prevention trials	Demand forecasting to inform volume, cost and price estimates	Mapping potential deployment channels in different regions
Improving accuracy of animal models (e.g. NHP)	Advancing pediatric and adolescent trials	Enhancing product development know-how across the field	
Integrating vaccine, prevention and cure research efforts/findings		Enhancing vaccine manufacturing capabilities (e.g. env protein)	
Standardizing sampling methods and assays (e.g. ADCC, mucosal sampling, microbiome)			
Aligning on a field wide/portfolio strategy for next-gen candidates			
Increasing funding for HIV vaccine research and development			
Monitoring the evolving epidemic in different regions and populations			
Integrating with other vaccine efforts in disease areas with common interests (e.g. TB, malaria)			

The Enterprise Has a Timely Opportunity to Support a Complex Ecosystem

The Enterprise's 5-year strategy coincides with the completion of several vaccine and biologics efficacy trials (Fig. 4), sharpening our focus on helping the field prepare for potential outcomes and respond to the knowledge, opportunities and expectations these studies yield. Stakeholders across the HIV vaccine ecosystem are working to address many of these priorities (Fig. 5) and the Enterprise has an opportunity to amplify and accelerate mutually reinforcing efforts by fostering co-ordination and collaboration and helping the field work together as effectively as possible.

N.B. Selected logos are illustrative and do not reflect the dozens of academic institutions and groups contributing to HIV vaccine R&D. Activities associated with HVTN, AVAC and WHO represent examples of ongoing work to address field-wide priorities. CHAVI (later CHAVI-ID) will be re-established as the Consortia for HIV/AIDS Vaccine Development (CHAVD).

Figure 4. Enterprise Strategy in the Context of Study Timelines



Data Source: AVAC; PrEPVacc estimated start date is approximate

Figure 5. A Diverse Ecosystem Tackling Field-wide Priorities



A Renewed Sense of Mission

The transition to IAS is an important milestone for the Enterprise and an opportunity to reaffirm our mission and realign our focus to meet the needs of a field that has changed dramatically since our formation over a decade ago.

The next section provides an outline of our updated, 5-year strategic framework, which has been designed to ensure that the Enterprise is optimized to support the most critical issues, risks and challenges faced by the field.

Our Strategy

A safe and effective vaccine available to the world: This is the vision that inspires the Enterprise.

Attuned to the challenges of the field today, the Enterprise aspires to support a global alliance of stakeholders to achieve a common vision: a safe and effective HIV vaccine that is available to the world.

To this end, our 5-year ambition emphasizes the Enterprise's critical role in bringing stakeholders together to address the needs, risks and complexities critical to accelerating HIV vaccine development.

OUR AMBITION

The Global HIV Vaccine Enterprise unites stakeholders to share knowledge, foster collaboration, enable solutions and expand support critical to the development of—and future access to—an HIV vaccine.

The Enterprise Approach

Because the Enterprise is neither a funding body nor a direct participant in R&D, it is uniquely poised to serve as a neutral convener of the field, driven by the following guiding principles:



Facilitate stakeholder alignment in a neutral & impartial manner



Focus on complex issues that cannot be addressed by any single entity



Identify issues and coordinate responses **proactively** & efficiently



Mobilize collaborative action and decision-making toward solutions



Promote accountability of the field to its collective resolve

Our Commitments

To realize this ambition, we will build on the Enterprise's proven and enduring role as a neutral convener that brings stakeholders together to tackle critical issues (see "The Enterprise Approach" box). Over the next 5 years, we will concentrate our efforts on the pursuit of three pivotal **COMMITMENTS**:

1. PROPELLING THE VACCINE PIPELINE

Strengthen strategies to align, amplify and accelerate development of candidate vaccines.

2. PREPARING FOR SUCCESS

Tackle priorities essential to clarifying the roadmap for future access to a vaccine.

3. EXPANDING RESOURCES & ENGAGEMENT

Enlist a diverse community of partners to support and contribute to the field.

Each commitment will be advanced by two **GOALS** that provide focus for Enterprise-led activities, while preserving flexibility to work with the broader HIV vaccine community in defining how the Enterprise's specific contribution can add the greatest value.

The Enterprise recognizes that the needs of the HIV vaccine field will evolve over the next 5 years, and it will work through ongoing stakeholder engagement and with strategic guidance from the Enterprise Advisory Group (comprised of leading HIV vaccine experts, funders and stakeholders who represent the field's needs, priorities and diversity) to identify, prioritize and invest in activities with the greatest potential for impact.

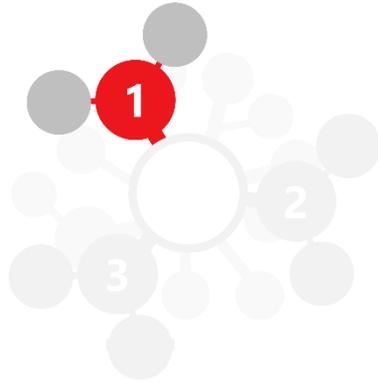
We will build momentum in year one by focusing our efforts on **NEAR-TERM ACTIVITIES**. Activities will be sequenced strategically and annual implementation plans—with detailed activities, timelines and deliverables—will be developed to direct and monitor our efforts.

Our commitments are also associated with **GUIDEPOSTS** (pages 11-13) describing immediate and intermediate Enterprise-driven outcomes as well as field-wide **IMPACTS** (page 14) against which we can help monitor and report on to gauge the field's progress over the coming years (page 14).

On the next page we present a high-level illustration of our strategic model. The 'hub and spoke' architecture is meant to convey the spirit of collaboration that underpins our work and is instrumental to the success of the HIV vaccine field.

Our Strategic Framework





Near-Term Activities

- Review existing incidence and PrEP uptake data and develop plans to increase understanding of and sustain dialogue around the impact of prevention modalities on vaccine development and testing.
- Assess available resources and develop an integrated PD education programme.

Guideposts

- Diverse stakeholders accessing events, tools and information to enhance PD knowledge.
- The field is increasingly accessing Enterprise-hosted resources to support trial design.
- Stakeholders are developing frameworks and toolkits and reaching consensus to guide PD.
- Funders/developers are integrating knowledge of the global pipeline into portfolio decisions.
- Collaborations are emerging to test new vaccine concept/component combinations.

Commitment 1

PROPELLING THE VACCINE PIPELINE

Strengthen strategies to align, amplify and accelerate development of candidate vaccines.

The Enterprise can help the field maintain scientific, pipeline and product development momentum in the context of unprecedented late-stage clinical activity. Two issues are particularly salient.

First, as the evolving prevention landscape transforms the dynamics of the epidemic worldwide, vaccine trials are becoming more complex. We must prepare for and adapt to new ethical, epidemiological and clinical realities that will drive trial design and implementation to ensure that promising vaccine candidates efficiently reach advanced stages of development.

Second, with diverse stakeholders (industry, academia, government, NGOs) contributing to HIV vaccine development, we must strengthen knowledge-sharing to enrich the field's product development mindset, identify synergies of effort and foster more collaboration—most notably in learning from trial outcomes, improving research tools (e.g. animal

models, immune assays) and in designing and refining vaccine concepts, particularly if correlates of protection are validated.

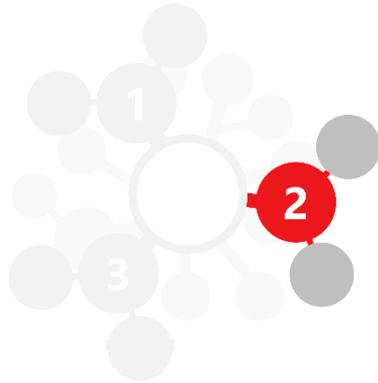
This commitment will help to fortify partnerships by reinforcing a common product development language; nurturing innovative vaccine concepts; and supporting future vaccine trials.

GOAL 1.1 Tackle issues in trial design and implementation. Working with trial networks, communities and policymakers, and aligning with complementary efforts, we will foster collaborative solutions to sustain the field's ability to conduct efficient clinical trials in an evolving prevention landscape.

GOAL 1.2 Enhance product development knowledge and collaboration. We will host workshops and toolkits that sharpen the field's product development mindset and enable the scientific dialogue needed to promote collaborative efforts around novel combinations of concepts/components and improving research tools.

"All the science in the world doesn't get you a vaccine... It's the end game you have to think about."

—Vaccine R&D Leader, Industry



Near-Term Activities

- Engage efficacy-stage programmes to define common access planning challenges.
- Convene stakeholders to discuss ideas for catalyzing new funding models.

Guideposts

- Stakeholders view the Enterprise as an important partner in mobilizing ideas and solutions around vaccine access.
- Stakeholders are engaged in dialogue on licensure pathways and capacity-building, beginning in Sub-Saharan Africa.
- The field has defined a target product profile that reflects health system and community priorities.
- Perspectives on potential business models for late-stage vaccines have been documented and are driving action.

Commitment 2

PREPARING FOR SUCCESS

Tackle priorities essential to clarifying the roadmap for future access to a vaccine.

With late-stage vaccine programmes anticipating efficacy results in 2021-2022, there is a critical need to mobilize now to prepare for all potential trial outcomes, including vaccine efficacy scenarios. The Enterprise has an important role to play in helping the field align on strategies to overcome potential barriers to licensure, scale-up and access to a safe and efficacious vaccine.

Preparing for success means planning for any outcomes of current and future trials; understanding regulatory pathways—particularly in countries with limited capacity for and experience with vaccine licensure; aligning on preferred product characteristics to focus product improvement efforts; developing access strategies aligned with regional needs and resources; and identifying ways to encourage at-risk investment needed for manufacturing scale-up and deployment.

This commitment will help to ensure that, as a field, we are ready to make a safe and

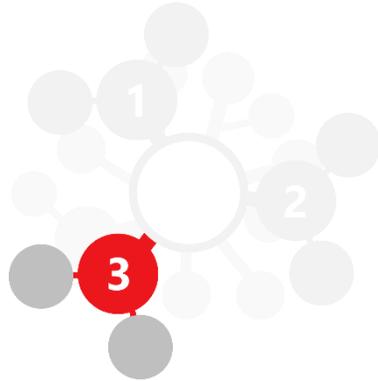
efficacious HIV vaccine readily available for the populations that need it most.

GOAL 2.1 Clarify regulatory and access pathways. Working with the WHO, regulators, policymakers, communities and product developers and funders, we will facilitate mapping of regulatory and licensure pathways for an HIV vaccine and help advance efforts to forecast demand and define deployment channels. Initial efforts in this area may focus on Sub-Saharan Africa as it is the epicenter of the epidemic and efficacy trial activity.

GOAL 2.2 Devise new business models for late-stage product development. We will convene diverse stakeholders—product developers, industry, research funders, international finance and development agencies, the investment community, local and regional authorities—to catalyze dialogue around novel business models that address the imperatives and risks of late-stage HIV vaccine R&D, scale-up and rollout.

“Scoping out what would be required—and designing business models to fund it—if successful results emerge from efficacy studies would be very meritorious.”

—Leader, HIV Vaccine Product Development Partnership



Near-Term Activities

- Build on 2018 Stakeholders' Meeting to create a platform for sustained engagement.
- Work with advocates to align on approaches to reinforce and amplify case for investment.

Guideposts

- The field is supported by a broader funding and partner base and growth in total resources.
- Industry is an increasingly active participant in Enterprise programmes and initiatives.
- Europe, Asia and Latin America are more engaged in Enterprise programmes.
- Industry's contribution to vaccine development is growing.

Commitment 3

EXPANDING RESOURCES & ENGAGEMENT

Enlist a diverse community of partners to support and contribute to the field.

Expanding and diversifying investments in HIV vaccine R&D remains a key priority for the field. The Enterprise has a role to play in engaging new funders, making the scientific case for investment and mobilizing political commitment.

Unlocking new funding for the field is complex and dependent on the efforts of multiple actors. The Enterprise will work closely with the IAS Resource Mobilization team and partners to apply focus, create venues for information-sharing among current and potential funders, and amplify the case for support.

As the Enterprise, we will ensure that our programmes tackle issues of foremost priority for funders and the field, positioning the Enterprise as an essential partner in mitigating risk, aligning fragmented efforts and amplifying the potential of finite resources. Enhancing engagement in the Enterprise will be

critical to our capacity to design, incubate and scale programmes that create value.

When we are successful, the field will be propelled by a broader pool of committed funders and by an Enterprise that is widely recognized for helping diverse stakeholders achieve greater impact.

GOAL 3.1 Strengthen political commitment and encourage new investment. We will bring scientific rigour to collaborative advocacy efforts aimed at influencing political priorities; driving greater investment in HIV vaccine R&D; deepening engagement with a range of potential funders in the EU, Asia and beyond; and working toward ensuring that industry's seat at the table fosters opportunities for collaborative action.

GOAL 3.2 Diversify engagement and expand collaborative action. We will engage relevant stakeholders in designing and delivering programmes that reflect diverse priorities, perspectives and contributions, advance opportunities for collaboration and optimize resources.

"There is a role for scientific advocacy... I don't think we can have too many people saying the world needs an HIV vaccine."

—Leader, Vaccine Research Institute

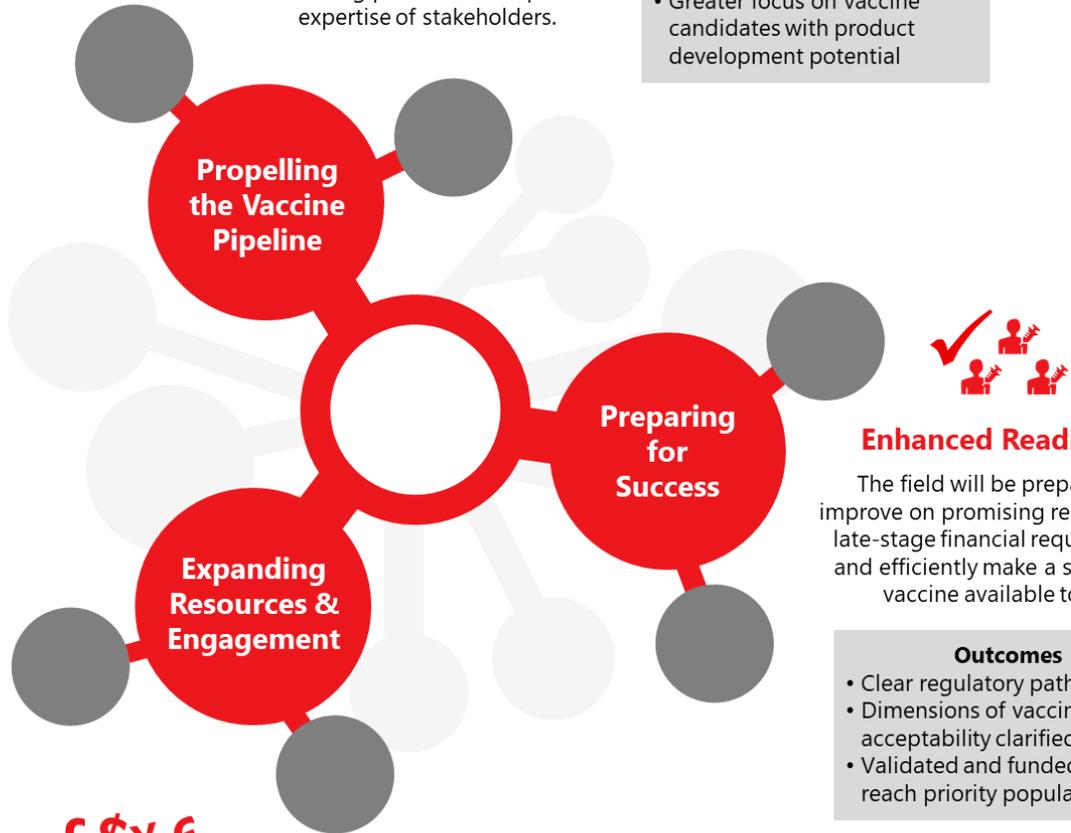


Robust Portfolio

The field will be sustained by a pool of concepts that reflect the innovative potential of the field and the strong product development expertise of stakeholders.

Outcomes

- Increased number of worthy candidates in clinical trials
- More multi-component vaccine concepts in pipeline
- Greater focus on vaccine candidates with product development potential



Enhanced Readiness

The field will be prepared to improve on promising results, meet late-stage financial requirements and efficiently make a successful vaccine available to all.

Outcomes

- Clear regulatory pathways
- Dimensions of vaccine acceptability clarified
- Validated and funded plans to reach priority populations



Diversified Funding

The field's R&D priorities will be propelled by an enriched and diversified community of funders, partners and donors.

Outcomes

- Increased funding for field
- Greater number, type and geographic range of funders
- More resources contributed by industry

Impact

Over the past decade, the Enterprise has played an important role as a neutral convener to accelerate HIV vaccine R&D.

Our 2018-2023 Strategic Plan recognizes the enduring need for a neutral convener—and it emboldens this role by positioning the Enterprise to help the field tackle key challenges, including preparing for the possibility of success while sustaining innovative product development momentum.

Our plan will support collaborative solutions to enable three field-wide impacts against which we—and other stakeholders—will measure the field's progress: a **ROBUST PORTFOLIO** of promising vaccine concepts; **ENHANCED READINESS** for the path forward for a successful vaccine; and **DIVERSIFIED FUNDING** for the field.

Our success will enable the field to build on available data to advance the most promising vaccine concepts and make the best use of resources. Product developers, regulators and health systems will be ready to make a successful vaccine available to populations that need it most. And the field's R&D priorities will be propelled by an expanded community of engaged funders, partners and donors.

This is a unique and exciting moment for the HIV vaccine development field, characterized by renewed momentum and unprecedented promise for the development of a vaccine. This Strategic Plan will solidify the Enterprise's value to the field and propel our shared vision to develop a safe and effective HIV vaccine available to the world.

