International AIDS Society
Stronger Together Against HIV

Roundtable: Pharma collaboration and regulatory issues

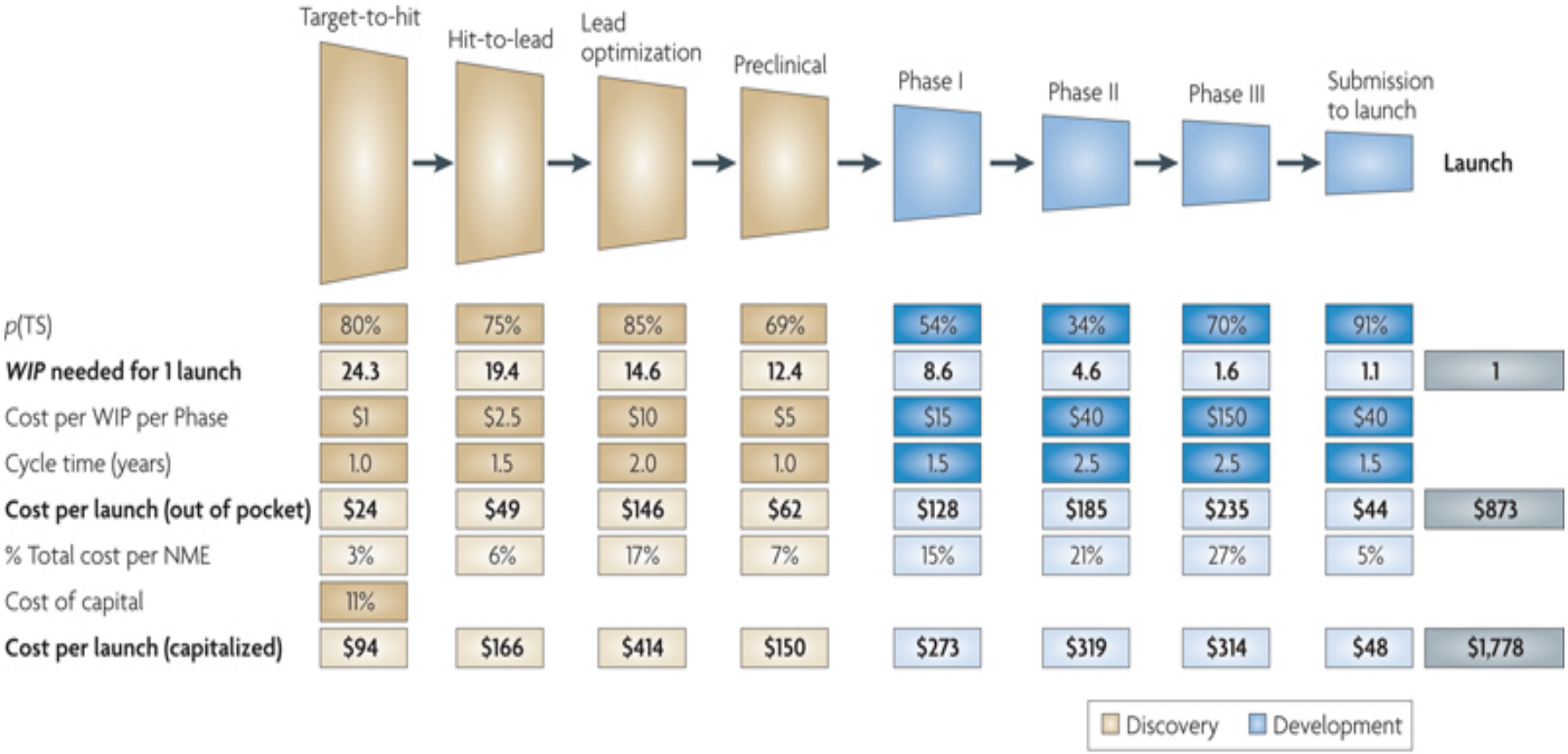
Veronica Miller
Guenter Kraus

IAS 2013 Towards an HIV Cure Symposium

towards an HIV cure
people focused science driven

Traditional NME Timeline

towards an HIV cure
people focused science driven



	Target-to-hit	Hit-to-lead	Lead optimization	Preclinical	Phase I	Phase II	Phase III	Submission to launch	Launch
p(TS)	80%	75%	85%	69%	54%	34%	70%	91%	
***WIP* needed for 1 launch**	24.3	19.4	14.6	12.4	8.6	4.6	1.6	1.1	1
Cost per WIP per Phase	$1	$2.5	$10	$5	$15	$40	$150	$40	
Cycle time (years)	1.0	1.5	2.0	1.0	1.5	2.5	2.5	1.5	
Cost per launch (out of pocket)	$24	$49	$146	$62	$128	$185	$235	$44	$873
% Total cost per NME	3%	6%	17%	7%	15%	21%	27%	5%	
Cost of capital	11%								
Cost per launch (capitalized)	$94	$166	$414	$150	$273	$319	$314	$48	$1,778

Discovery Development

Nature Reviews | Drug Discovery

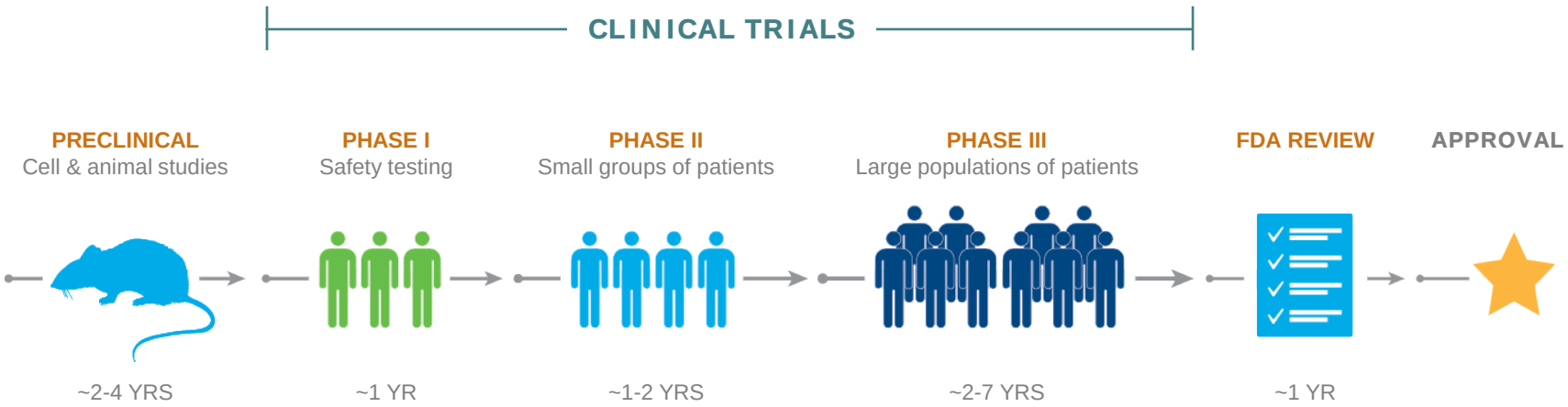
International AIDS Society
Stronger Together Against HIV

A Guide to FDA Approval Designations

towards an HIV cure
people focused science driven

There are two ways medicine can be approved by the FDA:

1 STANDARD APPROVAL



Source: Genentech

International AIDS Society
Stronger Together Against HIV

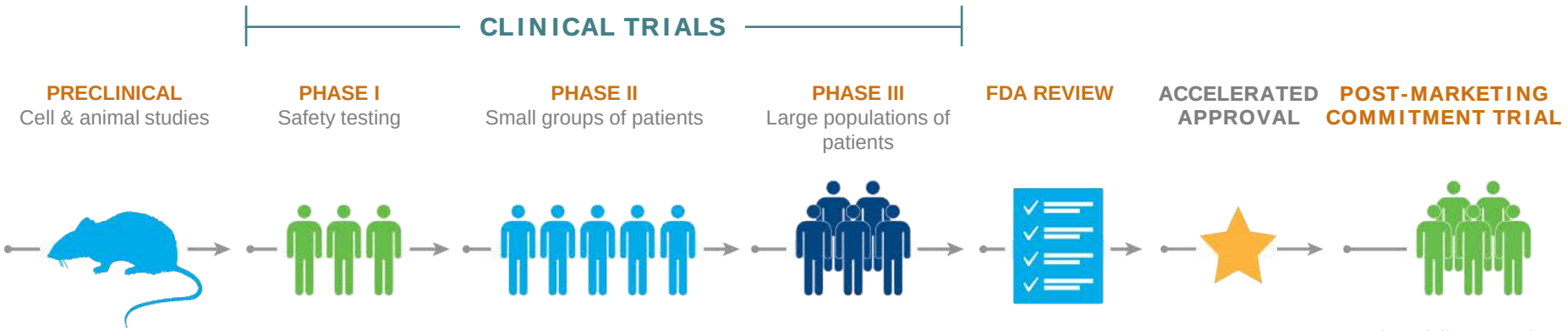
A Guide to FDA Approval Designations

towards an HIV cure
people focused science driven

There are 2 ways medicine can be approved by the FDA:

2 ACCELERATED APPROVAL

If **EARLY TRIAL RESULTS** are especially promising, the FDA can grant **ACCELERATED APPROVAL** to an investigational medicine. Allowing patients access while ongoing Phase III studies confirm safety and efficacy.



Source: Genentech

International AIDS Society
Stronger Together Against HIV

Codevelopment of Two or More Unmarketed Investigational Drugs for Use in Combination*

towards an HIV cure
people focused science driven

Conduct the same clinical pharmacology studies for each of the individual drugs in the combination as would be done if the drugs were being developed separately.

Combined Phase 1 to characterize the safety and pharmacokinetics of the individual components and then the combination.

Phase 2 should accomplish the following to the extent needed for a given combination :

•Demonstrate the contribution of each component of the combination to

The guidance is not intended to apply to biological products regulated by CBER

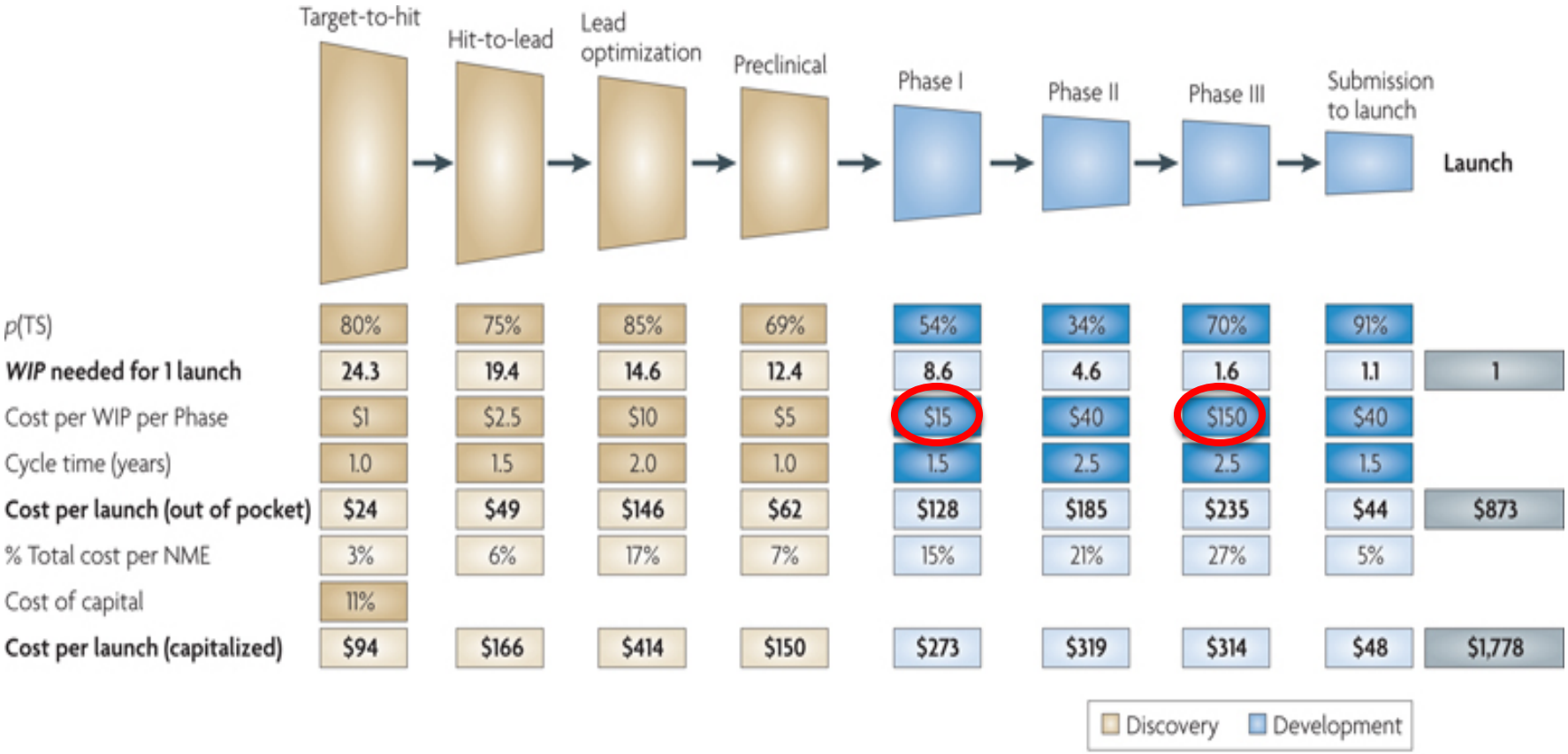
•Optimize the dose or doses of the combination

*9567dft.doc CDER

International AIDS Society
Stronger Together Against HIV

Traditional NME Timeline

towards an HIV cure
people focused science driven



p(TS)	80%	75%	85%	69%	54%	34%	70%	91%	
***WIP* needed for 1 launch**	**24.3**	**19.4**	**14.6**	**12.4**	**8.6**	**4.6**	**1.6**	**1.1**	**1**
Cost per WIP per Phase	$1	$2.5	$10	$5	$15	$40	$150	$40	
Cycle time (years)	1.0	1.5	2.0	1.0	1.5	2.5	2.5	1.5	
Cost per launch (out of pocket)	**$24**	**$49**	**$146**	**$62**	**$128**	**$185**	**$235**	**$44**	**$873**
% Total cost per NME	3%	6%	17%	7%	15%	21%	27%	5%	
Cost of capital	11%								
Cost per launch (capitalized)	**$94**	**$166**	**$414**	**$150**	**$273**	**$319**	**$314**	**$48**	**$1,778**

Discovery Development

Nature Reviews | Drug Discovery

International AIDS Society
Stronger Together Against HIV

Planning for Success

Almost 10 Phase I molecules ($15 million each) can be developed for the same cost as conducting a single full development program, ideally through to proof-of-concept.

Predictable biomarkers and/or clinical endpoints will be essential for such POC studies and to

Ensure safety of the enrolled individuals.

Today's Drug Regulatory Environment

towards an HIV cure
people focused science driven

- Pressure to facilitate/enhance drug discovery and translational research

President's Council of Advisors on Science and Technology Releases Report on Innovation in Drug Discovery and Development

The United States should set a goal of doubling the output of innovative new medicines that meet critical public health needs over the next 10 to 15 years, while continuing to increase drug

The report concludes there are two critical needs related to drug discovery and development that must be addressed to advance innovation:

(1) Scientists need better methodologies and tools for translating basic biological insights into validated therapeutic targets and leads—a gap in the drug discovery and development pipeline that academic scientists often view as "too applied" and pharmaceutical companies often eschew as "too basic" to justify private investment.
(2) Pharmaceutical developers and regulators need to incorporate new efficiencies into clinical trials of candidate medicines—complex and costly human studies that today constitute fully 40 percent of the biopharmaceutical industry's R&D budget.

Today's Drug Regulatory Environment

towards an HIV cure
people focused science driven

- Greater flexibility to address existing and emerging needs

√ e.g. Limited populations regulatory pathway

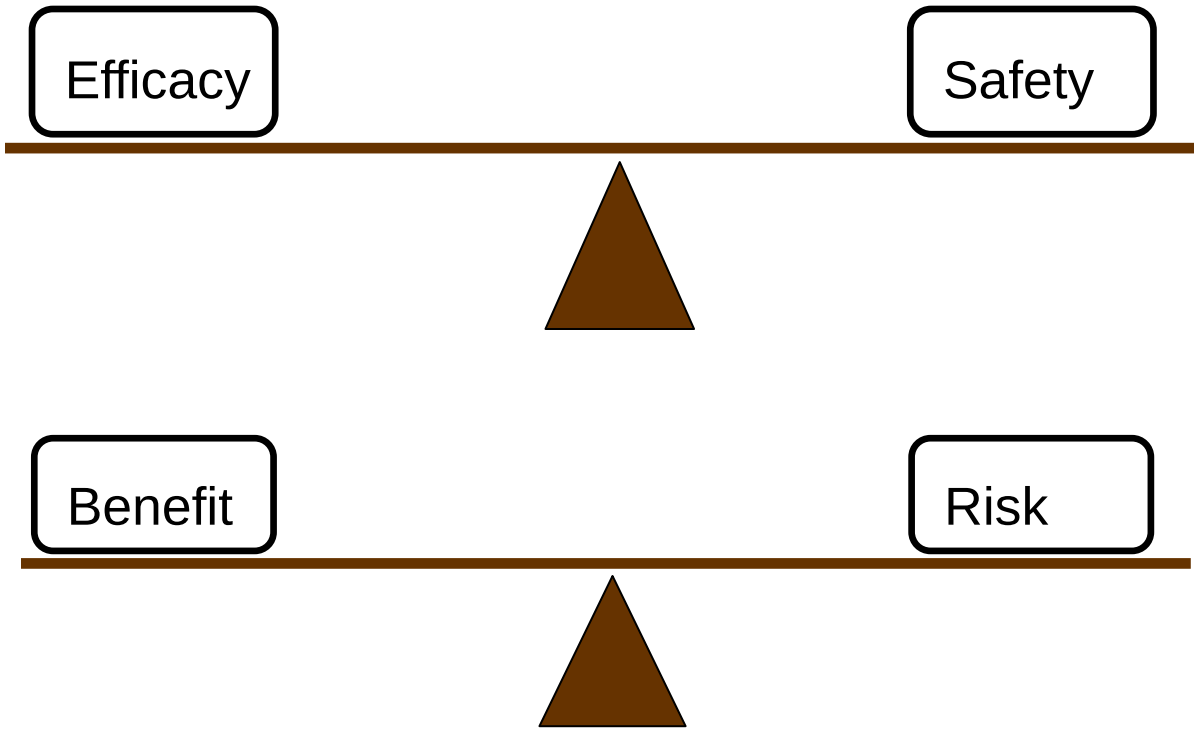
- Collaborative models

√ Pre-competetive space

√ e.g. Biomarkers Consortium

- Structured approaches to benefit-risk

International AIDS Society
Stronger Together Against HIV



Benefit-risk assessment: basis for FDA's decisions in pre-market and post-market review process

FDASIA

- Food and Drug Administration Safety and Innovation Act
  - Public Law 122-144
  - July 9, 2012
- Section 905 amends Section 505(d) of FD&C Act
  - “implement a structured risk-benefit assessment framework…….”

In PDUFA V, FDA also committed to a new initiative called Patient-Focused Drug Development with the goal of obtaining the patient perspective on certain disease areas during the five year period of PDUFA V. Assessment of a product's benefits and risks involves an analysis of the severity of the condition treated and the current treatment options available for the given disease. This information is a critical aspect of FDA's decision-making as it establishes the context in which the regulatory decision is made. FDA believes that drug development and FDA's review process could benefit from a more systematic and expansive approach to obtaining the patient perspective on disease severity and current available options in a therapeutic area.

towards an HIV cure
people focused science driven

Advances in Regulatory Science at the Food and Drug Administration

Bruce M. Psaty, MD, PhD
Steven N. Goodman, MD, MHS, PhD
Alasdair Breckenridge, MD

JAMA, May 22/29, 2013—Vol 309, No. 20 **2103**

tures applicable to a broad range of drug
"analysis of condition" and "current trea
tions provide an important context for
potential contributions of the new drug t
test the health of individuals and popu

Table. US Food and Drug Administration Benefit-Risk Framework

Decision Factor	Evidence and Uncertainties	Conclusions and Reasons
Analysis of condition		
Current treatment options		
Benefit		
Risk		
Risk management		

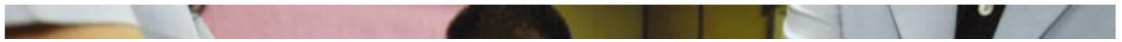
Adapted from US Food and Drug Administration.[2]

International AIDS Society
Stronger Together Against HIV

NATURE | VOL 423 | 8 MAY 2003 | www.nature.com/nature

AIDS researchers seek criteria for vaccines

Erika Check, Washington



Advocates [illegible] plain, in pa[illegible] stalling resea[illegible] clear expecta[illegible] needs to do.

That statement will not satisfy everyone. But Dan Kuritzkes, director of AIDS research at the Partners AIDS Research Center at Massachusetts General Hospital, says that the FDA's comments will help scientists. "I think we came out with a much clearer sense of what the potential indications might be for therapeutic vaccines," such as a lower viral load or an extended time off treatment, Kuritzkes says.

shop, Carol Weiss, a scientist at the FDA's [illegible] and Review, gave [illegible]eatment needs to [illegible]e in a clinically [illegible]d, adding that the [illegible]How durable, she

The “Forum Meeting”

towards an HIV cure
people focused science driven

SPECIFIC AIMS

• Facilitate and advance HIV cure research by clarifying and resolving regulatory issues through multi-stakeholder dialogue

√ Provide an ongoing neutral and independent platform for targeted discussions with multi-stakeholder experts

√ Provide a productive mechanism for broader, public input on questions of acceptable risk, ethics, informed consent and appropriate populations

International AIDS Society
Stronger Together Against HIV

The “Forum Meeting”

towards an HIV cure
people focused science driven

Specific Objectives

Review, discuss, propose

1) Regulatory pathways for therapeutic vaccines and other immunomodulatory agents, alone, or in combination, with other strategies

2) Measure of reduction of viral DNA defining cure

3) Criteria for analytic treatment interruption

Establish working groups as needed

International AIDS Society
Stronger Together Against HIV