Introduction and Overview of the Clinical Network Award

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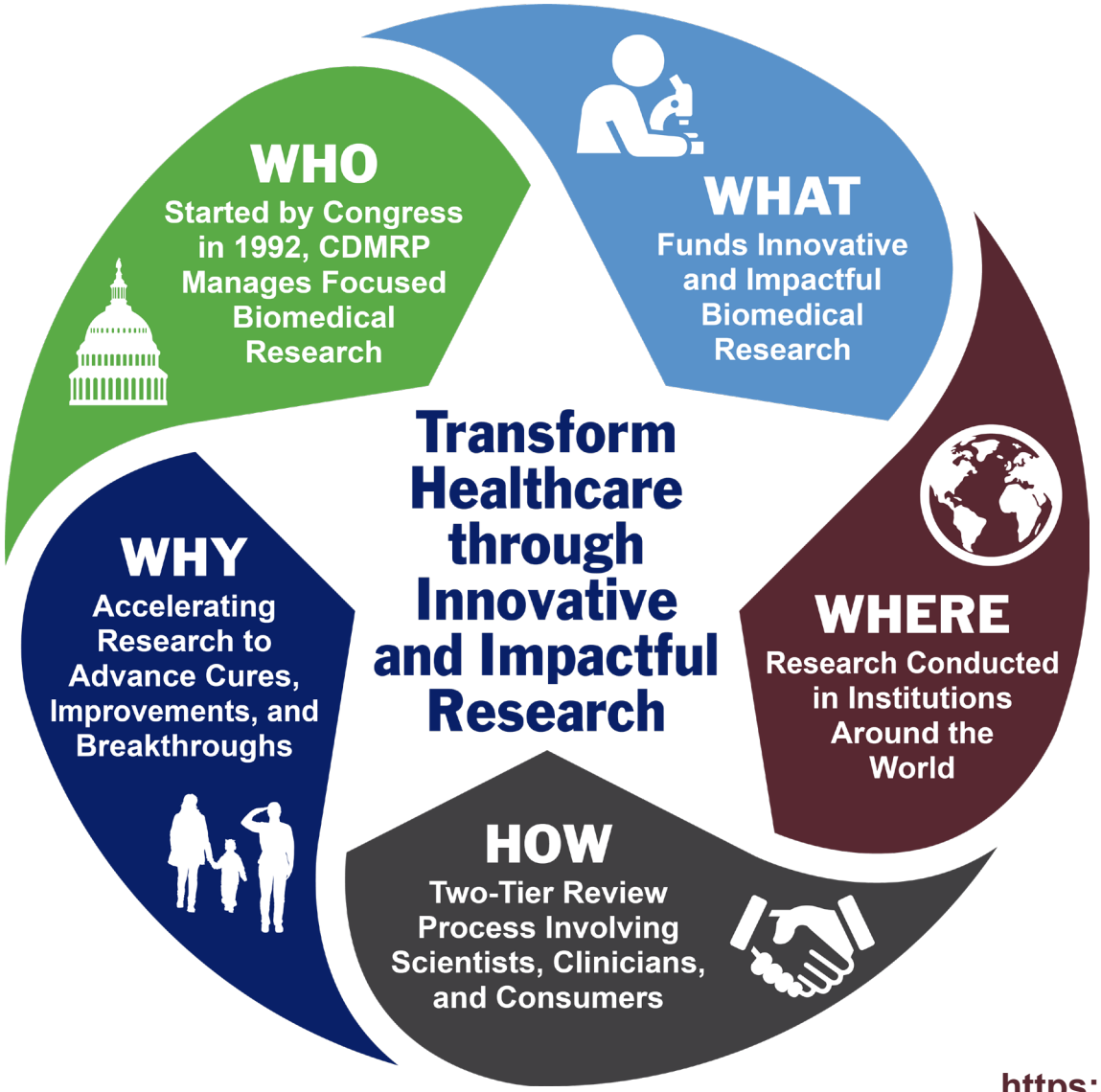
*Transforming Healthcare through Innovative and **Impactful** Research*

CDMRP
DEPARTMENT OF DEFENSE
CONGRESSIONALLY DIRECTED MEDICAL RESEARCH PROGRAMS

About the Congressionally Directed Medical Research Programs (CDMRP)



https://cdmrp.health.mil

CDMRP FY23 Appropriations

Research Program	FY23 $M	Research Program	FY23 $M
Alcohol and Substance Use Disorders	$4.0	Orthotics and Prosthetics Outcomes	$15.0
Amyotrophic Lateral Sclerosis	$40.0	Ovarian Cancer	$45.0
Autism	$15.0	Pancreatic Cancer	$15.0
Bone Marrow Failure	$7.5	Parkinson's	$16.0
Breast Cancer	$150.0	Peer Reviewed Alzheimer's	$15.0
Chronic Pain Management	$15.0	Peer Reviewed Cancer (20 Topics)	$130.0
Combat Readiness Medical	$5.0	Peer Reviewed Medical (50 Topics)	$370.0
Duchenne Muscular Dystrophy	$10.0	Peer Reviewed Orthopaedic	$30.0
Epilepsy	$12.0	Prostate Cancer	$110.0
Hearing Restoration	$5.0	Rare Cancers	$17.5
Joint Warfighter Medical	$25.0	Reconstructive Transplant	$12.0
Kidney Cancer	$50.0	Spinal Cord Injury	$40.0
Lung Cancer	$25.0	Tick-Borne Disease	$7.0
Lupus	$10.0	Toxic Exposures	$30.0
Melanoma	$40.0	Traumatic Brain Injury and Psychological Health	$175.0
Military Burn	$10.0	Tuberous Sclerosis Complex	$8.0
Multiple Sclerosis	$20.0	Vision	$20.0
Neurofibromatosis	$25.0	**TOTAL = $1.52B**	

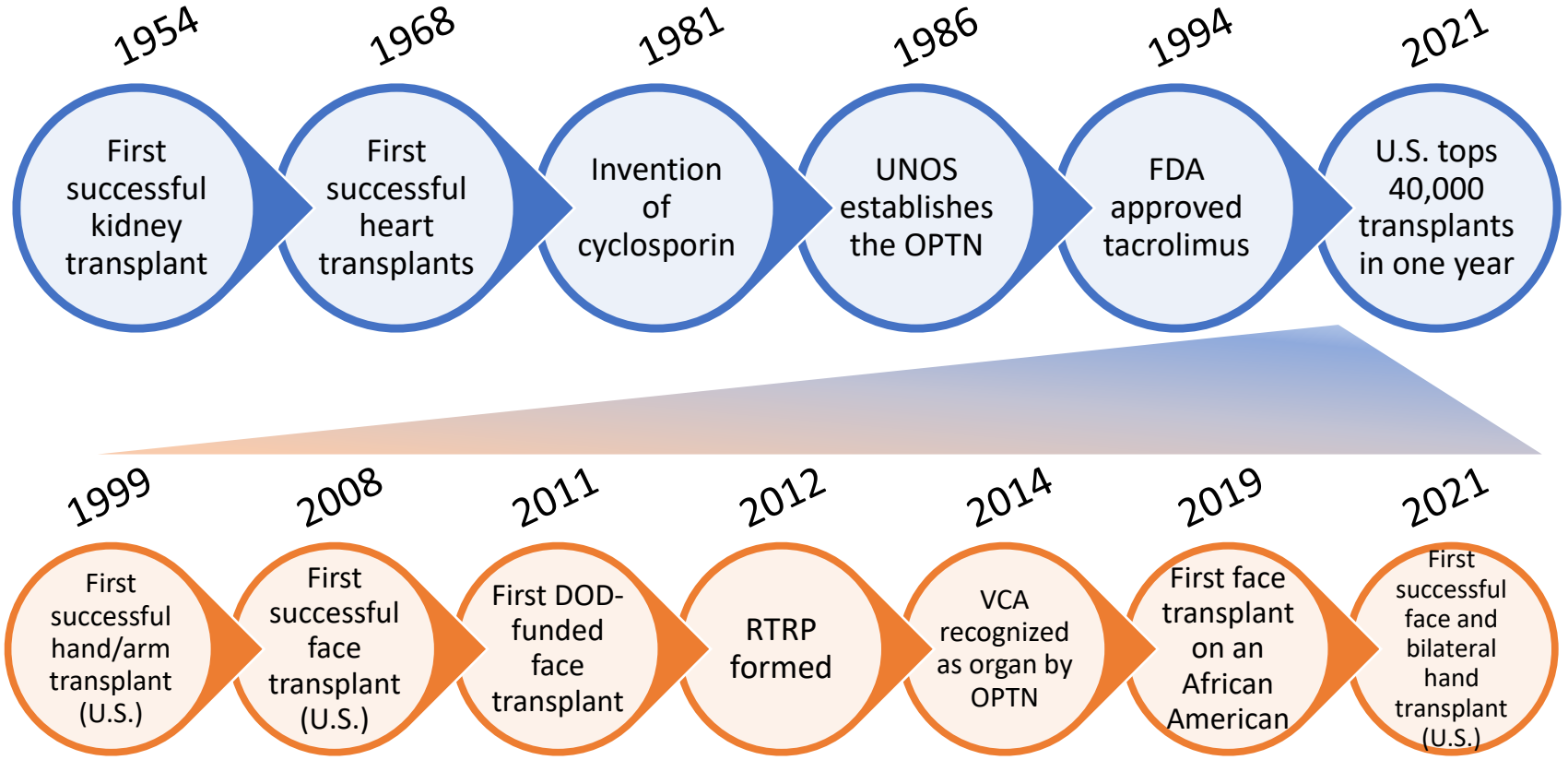
RTRP Program Overview

- History – The Reconstructive Transplant Research Program (RTRP) was established in fiscal year 2012 (FY12) with a $15 million (M) appropriation from Congress
  - $141M total for FY12 – FY23
- Vision – Reconstructive transplant: an accessible and realistic choice
- Mission - Advance science and standardized clinical practice of vascularized composite allotransplantation to improve access, safety, and quality of life for catastrophically injured service members, Veterans, and American civilians.

What is Reconstructive Transplantation?

- A treatment option for catastrophic loss of composite tissue (e.g., collection of multiple tissue types integrated to function as a single unit)
- Also known as vascularized composite allotransplantation (VCA)
- Involves the surgical transplantation of composite tissue (e.g., nerve muscle, bone, skin, vasculature) from a deceased donor to a recipient with a catastrophic tissue injury
- Generally considered a life-enhancing procedure, rather than life-saving, though some would argue against this assessment

History of Organ Transplant



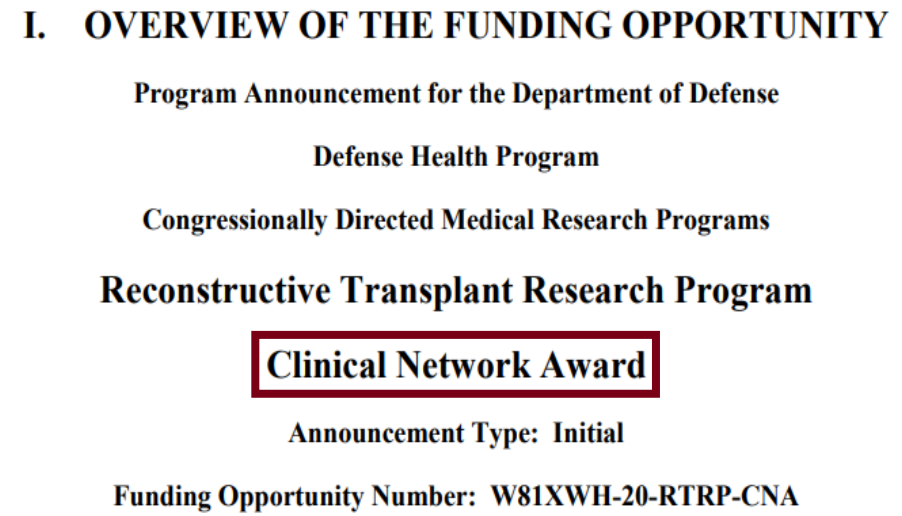
Organ Type	Total Number of Transplants Performed in the U.S.	Number of People Waitlisted in the U.S.
Kidney	27,332 (in 2023)	48,589
Upper Limb (uni+bilateral)	37	3
Craniofacial	19	4

Scope of the Problem: Clinical Challenges

- No standardized procedure (each VCA Center has its own guidelines)
- Procedure not covered by third-party payers
- High costs of procedure and lifelong care

Strategic Guidance: Feedback from Stakeholders

- Stakeholders Meeting held November 2019
  - Highlighted a need for more clinical studies and to standardize protocols and clinical practice guidelines for VCA procedures



I. OVERVIEW OF THE FUNDING OPPORTUNITY

Program Announcement for the Department of Defense

Defense Health Program

Congressionally Directed Medical Research Programs

Reconstructive Transplant Research Program

Clinical Network Award

Announcement Type: Initial

Funding Opportunity Number: W81XWH-20-RTRP-CNA

Clinical Network Award

Intent

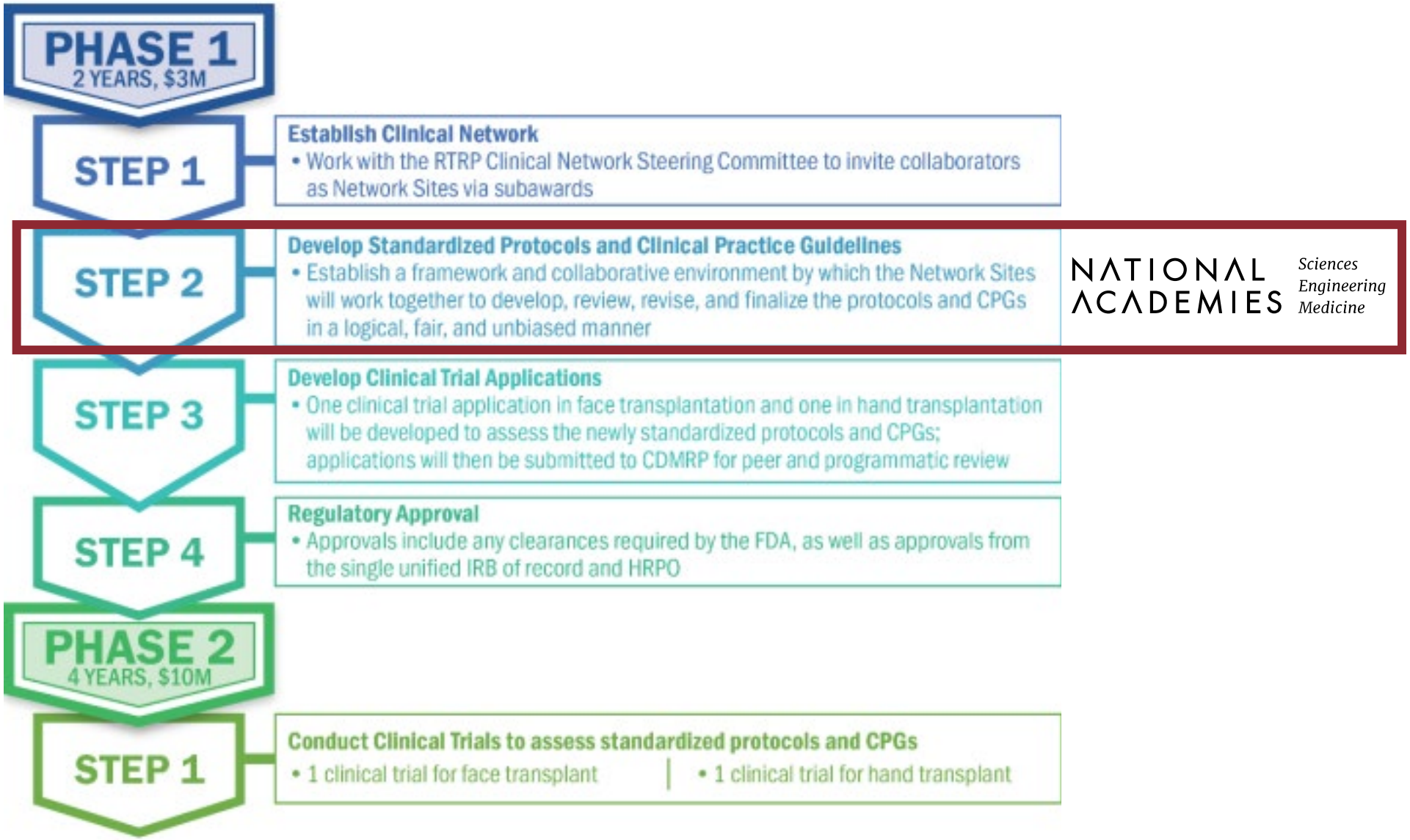
- To promote a major multi-institutional network of VCA centers and associated collaborators for the purpose of standardizing clinical protocols and clinical practice guidelines (CPGs) for face and hand transplantation and assessing those protocols in multi-institutional clinical trials.
- To bring together investigators from as many VCA centers as possible for both face and hand transplantation to establish a consensus in the field of reconstructive transplantation for these protocols and CPGs.
- To ensure a fair and equitable process through which the Clinical Network works together to achieve goals in a logical and unbiased manner, to include avoiding and mitigating conflicts of interest that may arise during the process.

Focus Areas

Applications must specifically address the standardization and assessment of protocols and/or CPGs for **ALL** of the following Focus Areas for both face and hand transplantation.

1. Patient inclusion/exclusion criteria
2. Patient education
3. Surgical procedures
4. Immunosuppression and/or immunoregulation
5. Outcome metrics
6. Quality of life measures
7. Rehabilitation
8. Patient reporting (e.g., registry)

Clinical Network Award



NASEM Statement of TASK

- Develop a framework to assist the Clinical Network in achieving consensus and standardization for each of the eight focus areas in both hand and face transplantation.
  - Including processes to ensure consensus is achieved in a nonbiased manner.
- Establish a set of principals and strategies the Clinical Network can utilize to develop, review, revise, and finalize VCA protocols and SOPs for both hand and face transplantation to ensure a fair and equitable process where all participants serve as equal partners.
  - Including considerations for mitigating and resolving conflicts of interest.

Focus Areas

For both face and hand transplantation:

1. Patient inclusion/exclusion criteria
2. Patient education
3. Surgical procedures
4. Immunosuppression and/or immunoregulation
5. Outcome metrics
6. Quality of life measures
7. Rehabilitation
8. Patient reporting (e.g., registry)

Anticipated Impact

Potential to transform the VCA field

- Unify the VCA field toward a common goal and increase collaboration
- Standardize VCA procedures across VCA Centers
- Advance face and hand transplant from experimental status to standard of care, providing impetus for third-party payer coverage, thereby increasing accessibility for more individuals
- Increase number of face and hand transplant procedures, which in turn provides a greater number of recipients available for study participation
- Success could entice more researchers to join the VCA field, thereby bringing new ideas to revitalize and reinvigorate the field

Questions?
For more information, please visit:

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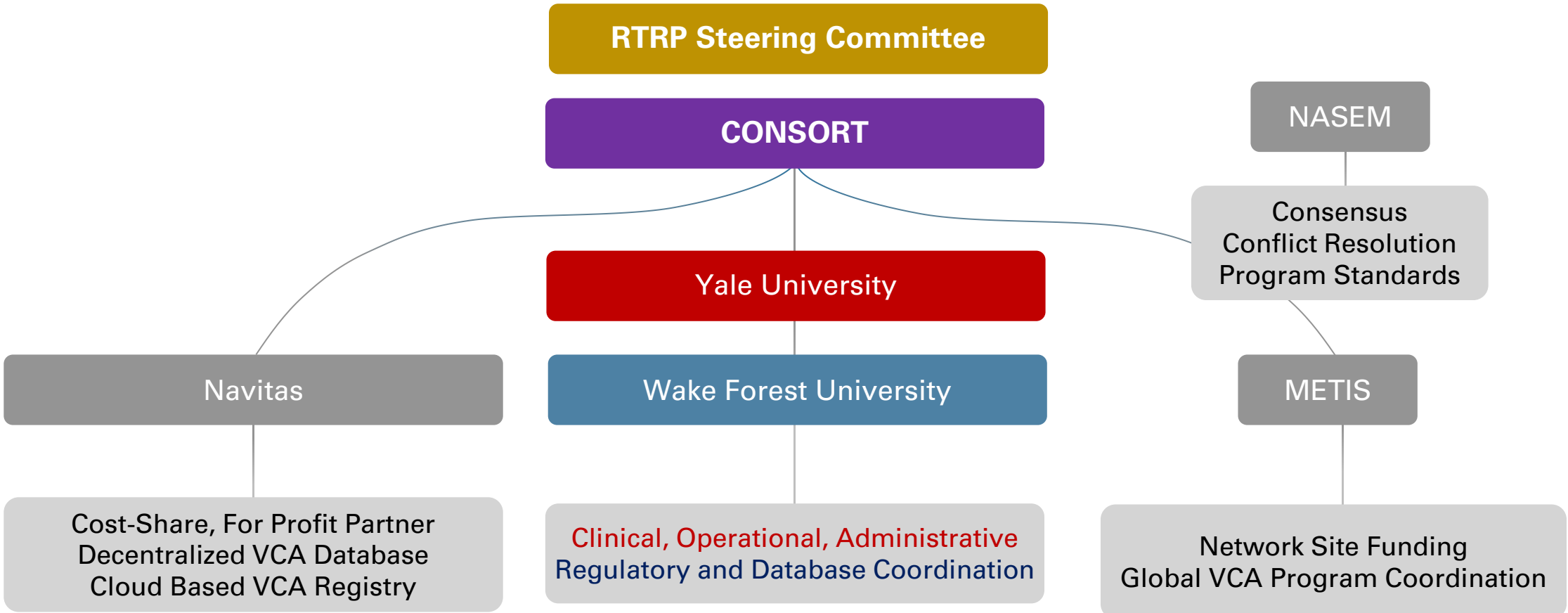
CONSORT

CLINICAL ORGANIZATION NETWORK FOR STANDARDIZATION
OF RECONSTRUCTIVE TRANSPLANTATION

Overall Project Organization



Bo Pomahac, MD
Network Director

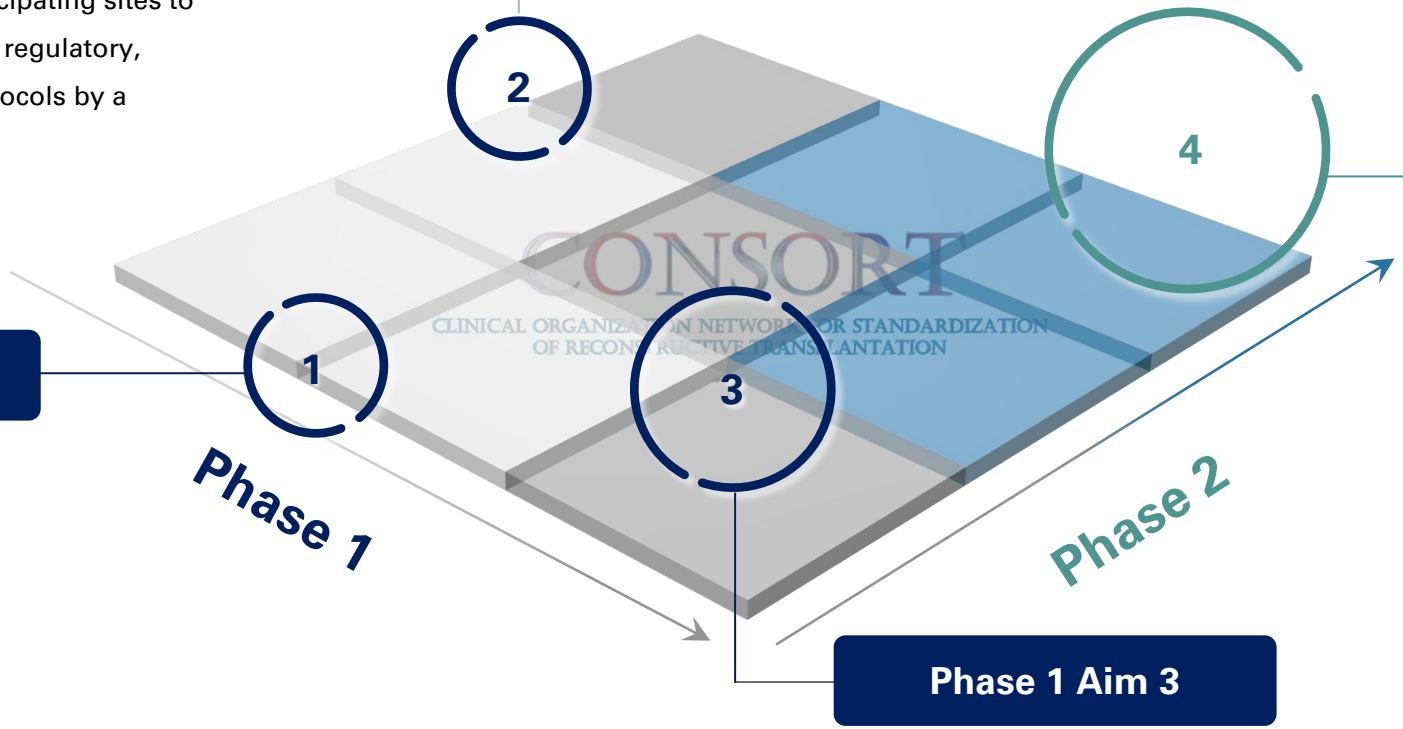
Vijay Gorantla, MD
Network Co-Director

Col. Michael Davis, MD
Chief Programmatic Liaison

Specific Aims

Phase 1 Aim 2

Implement agreements between participating sites to allow sharing, review and approval of regulatory, intellectual and material property protocols by a unified, central IRB and OHRO.



Phase 2 Aim 1

Assess and validate standardized protocols and SOPs for hand and face transplantation in multi-institutional clinical trials across selected VCA Network Sites

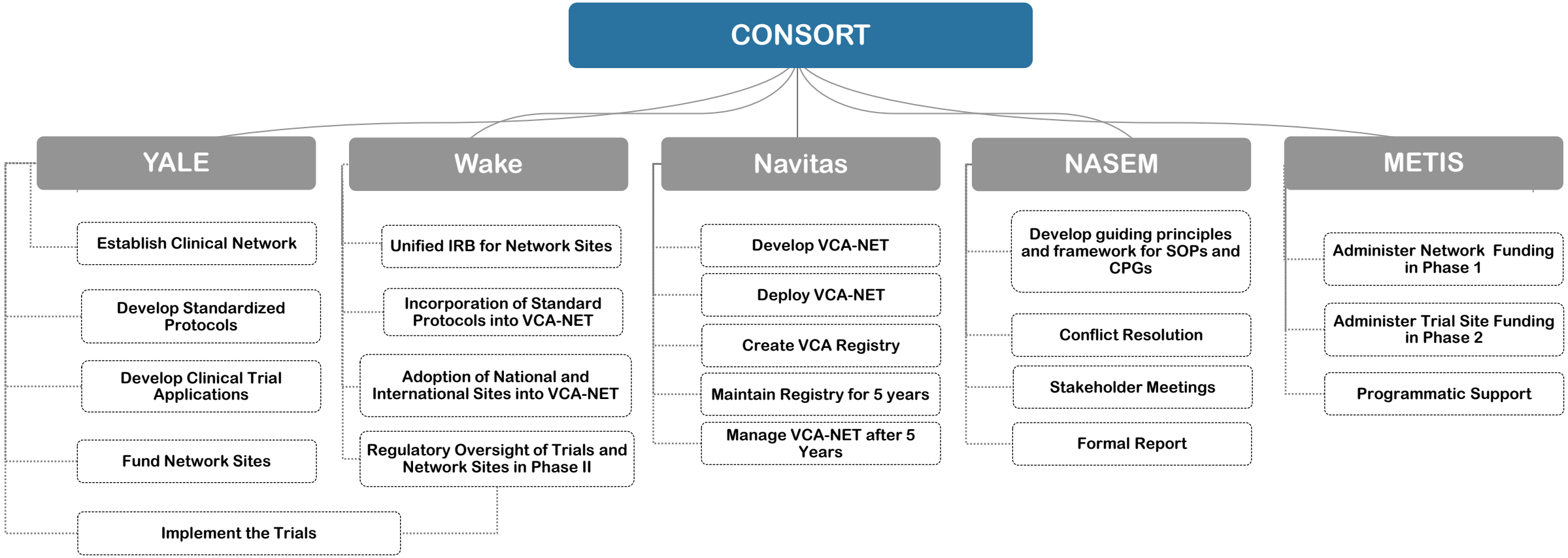
Phase 1 Aim 1

Establish (through collaborative consensus among VCA teams), procedural and protocol standards that impact program and patient success and outcomes in hand and face transplantation.

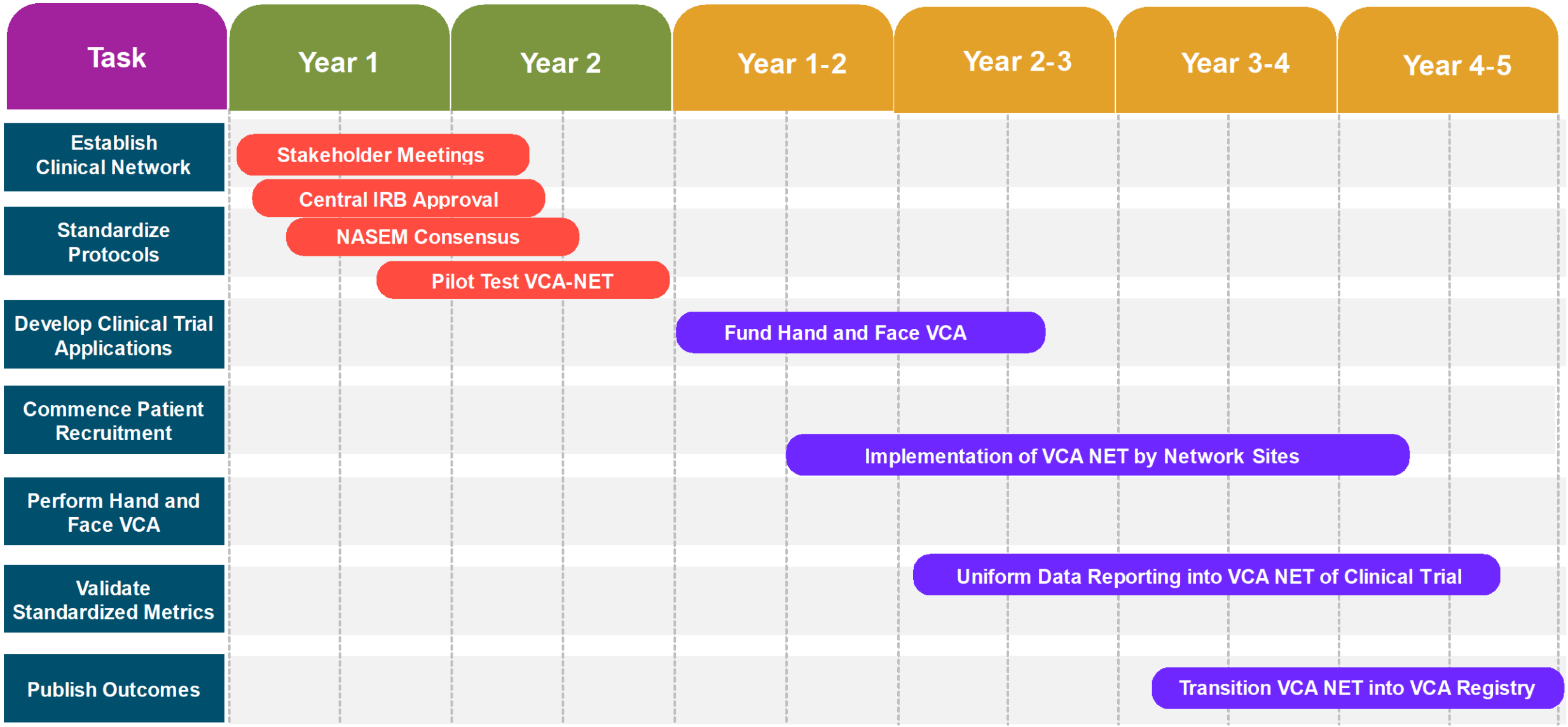
Phase 1 Aim 3

Design, develop and deploy VCA-NET, which is a purpose-built electronic clinical trial management system (eCTMS), with standardized domains that incorporate the unique complexity of hand and face transplant metrics.

Roles and Responsibilities

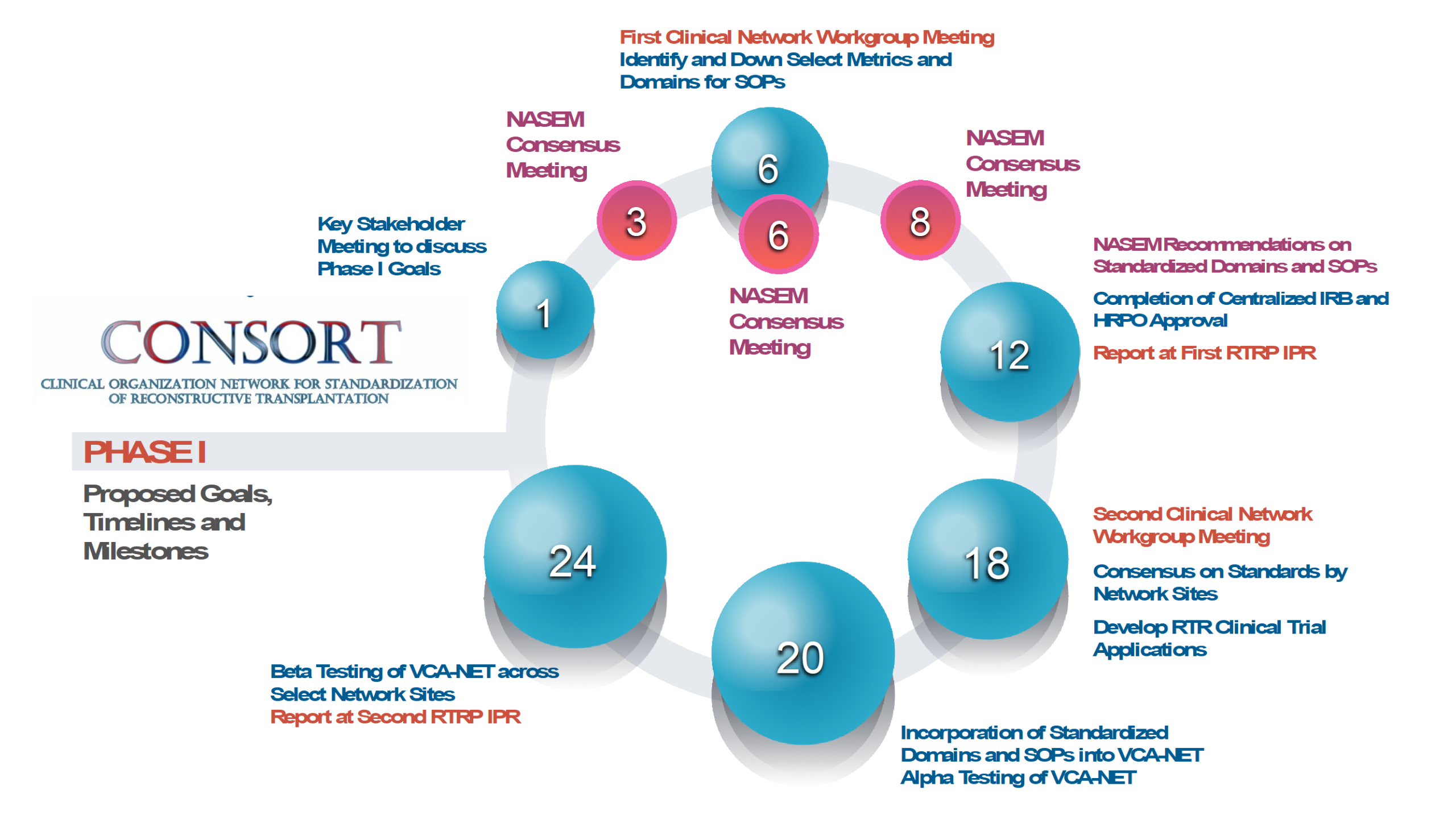


Timeline


Task
Year 1
Year 2
Year 1-2
Year 2-3
Year 3-4
Year 4-5
Establish Clinical Network
Standardize Protocols
Develop Clinical Trial Applications
Commence Patient Recruitment
Perform Hand and Face VCA
Validate Standardized Metrics
Publish Outcomes
Stakeholder Meetings
Central IRB Approval
NASEM Consensus
Pilot Test VCA-NET
Fund Hand and Face VCA
Implementation of VCA NET by Network Sites
Uniform Data Reporting into VCA NET of Clinical Trial
Transition VCA NET into VCA Registry

CONSORT

CLINICAL ORGANIZATION NETWORK FOR STANDARDIZATION
OF RECONSTRUCTIVE TRANSPLANTATION


First Clinical Network Workgroup Meeting
Identify and Down Select Metrics and Domains for SOPs
NASEM Consensus Meeting
NASEM Consensus Meeting
Key Stakeholder Meeting to discuss Phase I Goals
NASEM Consensus Meeting
NASEM Recommendations on Standardized Domains and SOPs
Completion of Centralized IRB and HRPO Approval
Report at First RTRP IPR
CONSORT
CLINICAL ORGANIZATION NETWORK FOR STANDARDIZATION OF RECONSTRUCTIVE TRANSPLANTATION
PHASE I
Proposed Goals, Timelines and Milestones
Second Clinical Network Workgroup Meeting
Consensus on Standards by Network Sites
Develop RTR Clinical Trial Applications
Beta Testing of VCA-NET across Select Network Sites
Report at Second RTRP IPR
Incorporation of Standardized Domains and SOPs into VCA-NET
Alpha Testing of VCA-NET
1
3
6
6
8
12
18
20
24

Execution of Clinical Network Objectives

Phase II - Enrollment and Outreach

ENSURE in Phase I

- Adoption of consensus standards in Phase I
- Obtain IRB, OHRO approvals in Phase I
- Completion of CONSORT By-Law Agreements in Phase I

EVALUATE

- Program status on existing enrolled patients
- Program capabilities on referral, access and enrollment of patients
- Fund VCA programs to perform a total of 10-12 hand/face transplants
- Confirm equitable inclusion of minorities and women

EXPAND

- Generalizability of data collection per SOPs and CPGs in Phase II by inclusion of international sites (such as Canada, UK, EEU, India and Latin America)

Execution of Clinical Network Objectives

Network Site Compensation in Phase I and Phase II

Incentivize Program Participation and Expert Contribution in Phase I

RECOGNIZE — 1

- Contribution from SMEs during development of SOPs and CPGs by NASEM

ENCOURAGE — 2

- Participation of National and International teams in adopting consensus standards (SOPs and CPGs) into their existing protocols

Peer-Select Qualified US Based Programs for Hand or Face Transplantation in Phase II

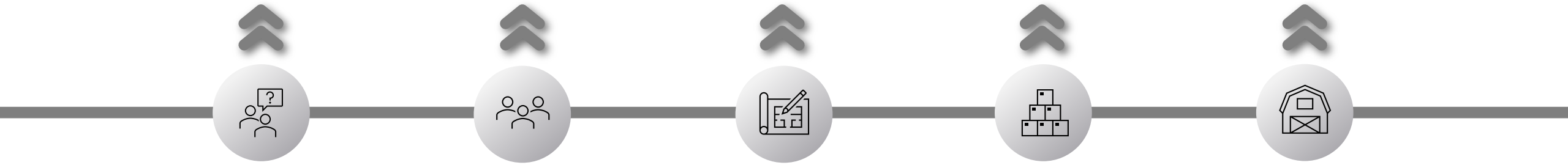
FUND — 3

- Funding VCA programs to perform a total of 10-12 hand and face transplants in Phase II (4 years of POP with possibility of NCE)

SUPPORT — 4

- Programs willing to participate as enrollment and referral sites for VCA patients during Phase II

PURPOSE	STAKEHOLDERS	PROCESS	RESOURCES	KNOWLEDGE PRODUCT
Fair, equitable, unbiased development of SOPs and CPGs will be achieved with the guidance of NASEM	Collaboration and communication will be promoted among Network Sites to facilitate achievement of objectives	Compensate Network Sites in Phase 1 (protocol/CPG development) and Phase 2 (Clinical Trials) Maximize enrollment	Leverage infrastructure, institutional support and cost-share opportunities to deliver RTRP-CNA objectives	Maximize short and long-term return on investment for RTRP-CNA through development of VCA-NET and global VCA Registry for use by the VCA community and realize global adoption of developed standards for generalizable impact
WHY	WHO	HOW	WHAT	WHERE



Thank You!

QUESTIONS?