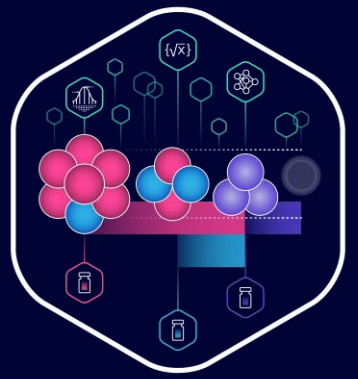
Welcome to ADAPT Proposers' Day!



Agenda (*all times ET*):

12:00 - Welcome & Opening Remarks
12:05 - Intro to ARPA-H & Resilient Systems Office
12:20 - ADAPT Program Overview
1:05 - Acquisition Details: The Submission Process
1:20 - Important Reminders
1:40 - Closing Remarks

Ask a Question

https://solutions.arpa-h.gov/Ask-A-Question

Questions not answered today will be answered on the ADAPT program website.

ARPA-H

The ARPA-H Model

Transforming Health for All

Dr. Jennifer Roberts
Resilient Systems Director

ARPA-H

Mission

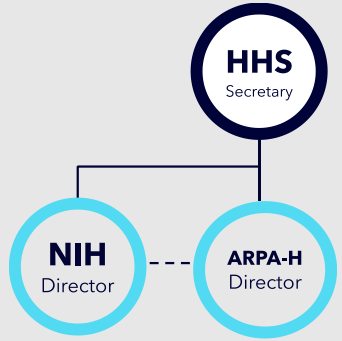
Accelerate better health outcomes for everyone.

ARPA-H

ARPA-H Key Features and Authorities

ARPA-H has unique structures and legal authorities that allow it to **function like a business – quickly, nimbly, and decisively**.

- ARPA-H is a **funding agency**
- **Independent** component of HHS within NIH; not an Institute
- No internal research labs; **disease agnostic**
- **$2.5B appropriations**; budget independent from NIH
- Generally **fund outcome-based contracts,** not grants; accelerated award timelines
- **Bottoms-Up Problem Centric Approach** to address the toughest challenges in health



Lean and nimble management structure with autonomy in decision-making.

ARPA-H Director **reports directly to HHS Secretary**

Term limits of 3-6 years bring urgency and idea flow.

Flexibility in hiring allows ARPA-H to recruit at levels competitive with industry.

Bottom-up decision-making. PMs have autonomy to make decisions quickly.

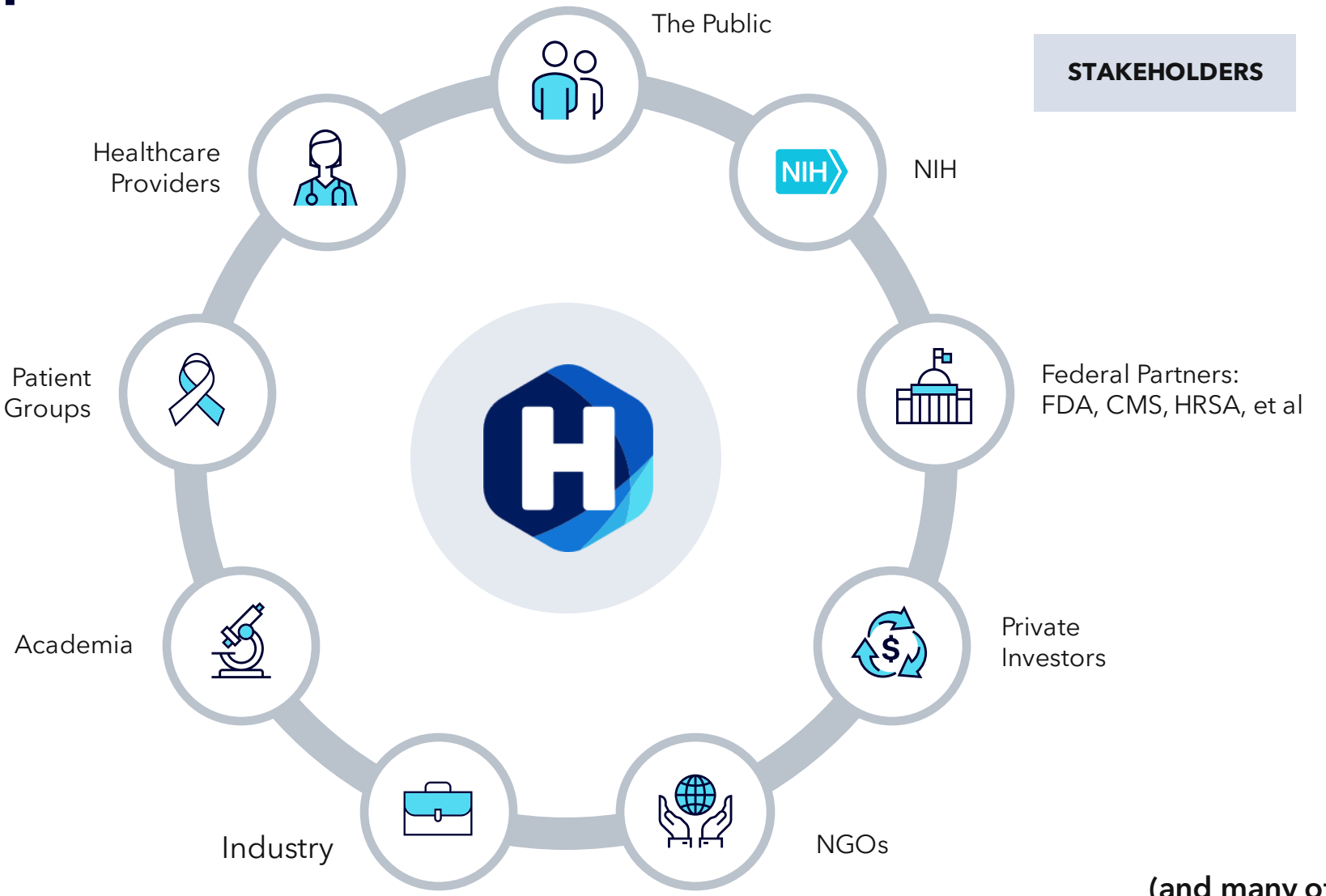
ARPA-H is a problems focused organization

ARPA-H

ARPA-H Health Ecosystem

CUSTOMERS

PERFORMERS



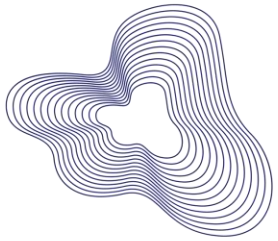
STAKEHOLDERS

(and many others …)

ARPA-H

Initial Mission Focus Areas

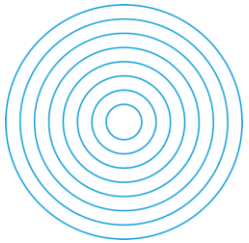
Further ARPA-H investment in these areas will generate **asymmetrical benefits** to the health ecosystem



Health Science Futures

Expanding what's technically possible

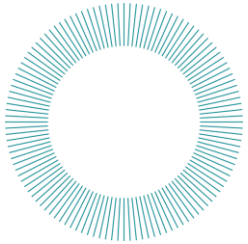
Accelerate advances across research areas and remove limitations that stymie progress towards solutions. These tools and platforms apply to a broad range of diseases.



Scalable Solutions

Reaching everyone quickly

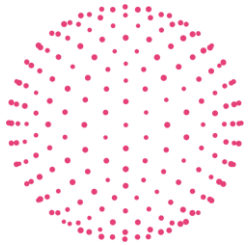
Address health challenges that include geography, distribution, manufacturing, data and information, and economies of scale to create programs that result in impactful, timely, and equitable solutions.



Proactive Health

Keeping people from being patients

Preventative programs will create new capabilities to detect and characterize disease risk and promote treatments and behaviors to anticipate threats to Americans' health, whether those are viral, bacterial, chemical, physical, or psychological.



Resilient Systems

Building integrated healthcare systems

Develop capabilities, business models, and integrations to endure crises such as pandemics, social disruption, and economic instability. Resilient systems need to sustain themselves between crises – from the molecular to the societal - to better achieve outcomes that advance American health and wellbeing.

Project Accelerator Transition Innovation

Ensuring programs survive in the wild

Translating scientific and technical breakthroughs into real world products and services, ensuring they result in better health outcomes for all Americans

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1. Socio-Technical System Innovation

Empower patients, providers, and communities by transforming the way healthcare is accessed, delivered, and supported.

Innovate user-centric digital health tools, platforms, technologies, and intervention models that improve outcomes across the health continuum, including prevention, diagnosis, and treatment.

2. Health Ecosystem Integration

Advance capabilities to integrate health-related systems, from the individual to population scale.

Strengthen the connectivity and interoperability of health data and devices to enable the safe, secure, and seamless exchange of information among healthcare providers, researchers, and stakeholders.

3. Adaptive & Antifragile Solutions

Enhance stability and adaptability across the health ecosystem.

Leverage AI and decentralized approaches to address evolving health challenges, bolster supply chains, optimize care quality, expand access, and enhance emergency responsiveness.

ARPA-H's Investment Portfolio Snapshot: What if...?

NITRO

Novel Innovations for Tissue Regeneration in Osteoarthritis

What if we could make our joints heal themselves?

REACT

Resilient, Extended, and Automated Cellular Therapies

What if your body could make its own medicine?

SPIKEs

Synthetic Programmable Bacteria for Immune Directed Killing in Tumor Environments

What if programable bacteria could be directed to kill cancer inside the body?

DIGIHEALS

Digital Healthcare Security

What if we had resilient healthcare infrastructure with advanced digital security for data, software, and devices?

PSI

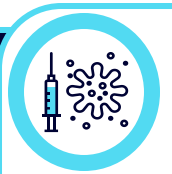
Precision Surgical Interventions

What if surgeries fixed problems flawlessly, the first time?

PARADIGM

Platform Accelerating Rural Access to Distributed and Integrated Medical Care

What if we could deliver advanced hospital-level care to every rural county in America?



HEROES

HEalthcare Rewards to Achieve Improved OutcomES for All

What if we could create a sustainable national healthcare market that rewards prevention?

DARTS

Defeating Antibiotic Resistance through Transformative Solutions

What if we could identify antibiotic-resistant bacteria in minutes?

CUREIT

Curing the Uncurable via RNA-Encoded Immunogene Tuning

What if uncurable diseases could be treated by tuning your immune system?

THEA

Transplantation of Human Eye Allografts

What if we could cure blindness?

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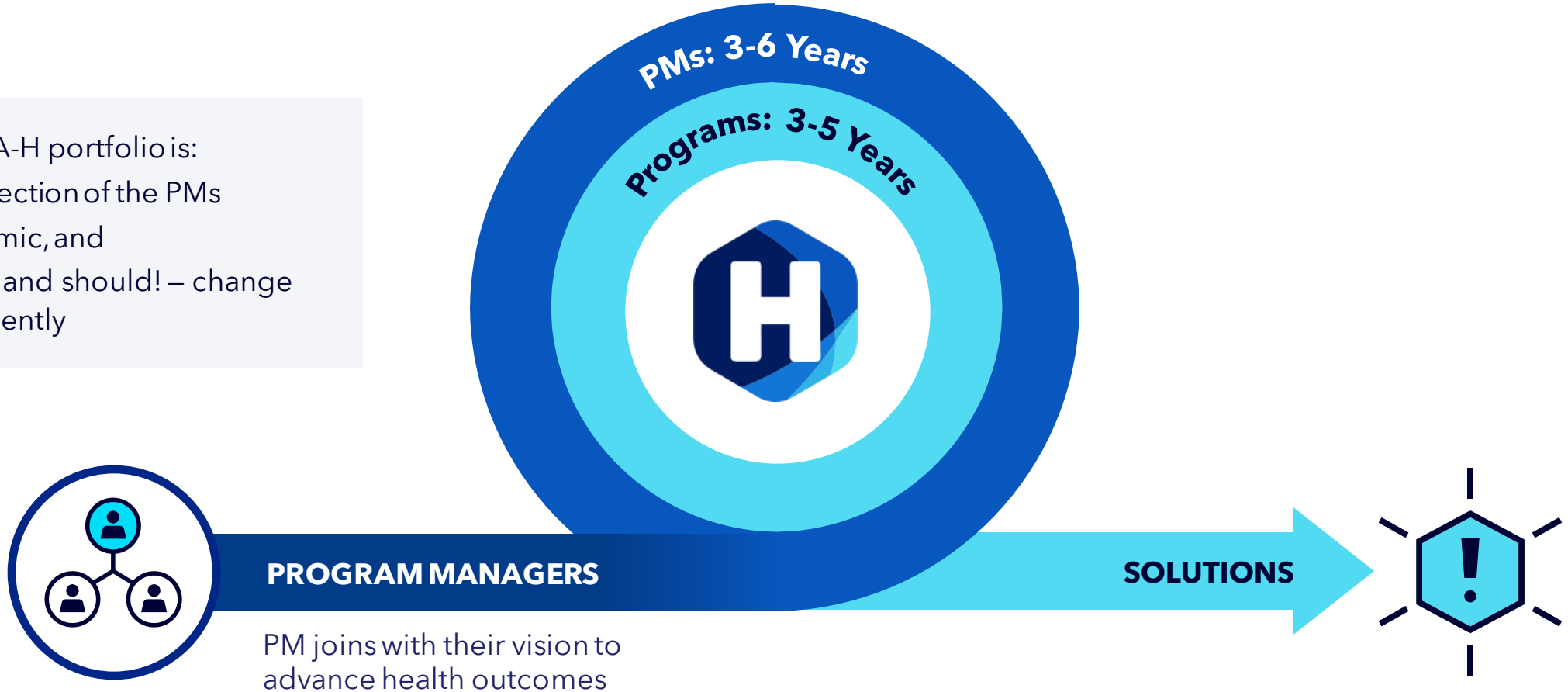
The Program and Program Manager Flywheel

The ARPA-H portfolio is:

(1) a reflection of the PMs

(2) dynamic, and

(3) will – and should! – change frequently



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Program Lifecycle

From ideas to solutions in the real world

DESIGN PROGRAMS

- ARPA-Hard and well-defined problems in health
- Heilmeier Framework
- High risk/High consequence
- Stakeholder Insights

BUILD A PERFORMER TEAM

- Solicit Solutions from the community
- Find the best non-traditionals, industry, and academics to solve
- Build new coalitions

EXECUTE & MEASURE

- Active program management against metrics; PM = CEO
- Stakeholder engagement throughout to ensure transition
- Pivot resources when needed

LEARN & GROW

- Capture and share insights
- Technical honesty
- Advance the state of the art; 10x+ improvement, no incremental change

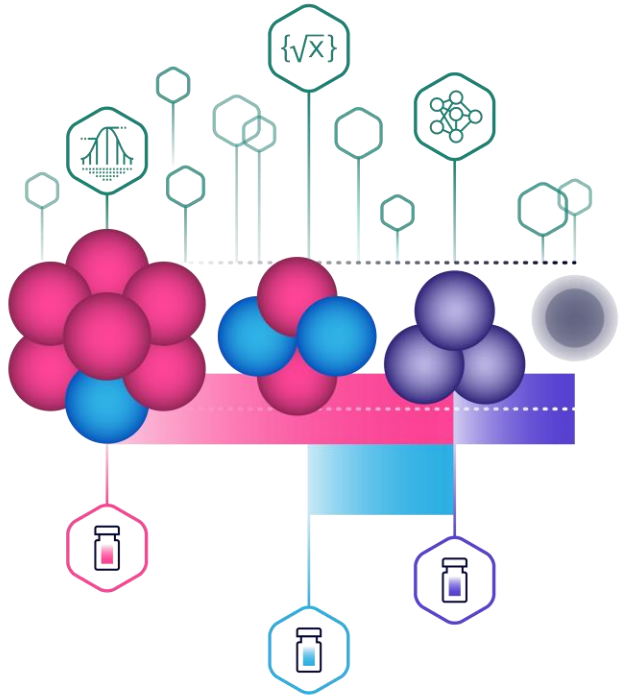
COMMERCIALIZE & TRANSITION

- Assist company formation or licencing
- Provide mentorship, connections to customers, investors
- De-risk investments

Proposers' Day
March 15th, 2024

ADAPT

ADvanced Analysis for Precision cancer Therapy



Andrea Bild, PhD
Program Manager
Resilient Systems Office
Advanced Research Projects Agency for Health

Ask a question

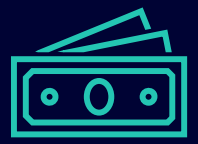
ARPA-H

What if we could adapt cancer treatments as tumors mutate and change?

ARPA-H

Metastatic cancer affects over 600,000 Americans every year

- **>90%** of metastatic cancer patients develop resistance to therapy.
- **>20%** of deaths in the US are attributable to advanced cancer.
- **1 in 3** individuals is expected to encounter cancer in their lifetime.



- **>$200 B** in economic burden of medical costs from cancer treatment in 2020.
- **>$35 B** in medical costs from metastatic breast cancer alone in 2020.
- **>$86 B** in projected annual costs of metastatic breast cancer by 2030.
- **>$48 B** in combined medical care costs for lung and colon cancers in 2020.

- **ADAPT** will revolutionize how we treat metastatic cancer patients by identifying and targeting resistant tumor traits, thereby matching the right drug to each tumor as it evolves.
- **ADAPT** will lead to effective tumor growth inhibition and increased patient survival time.

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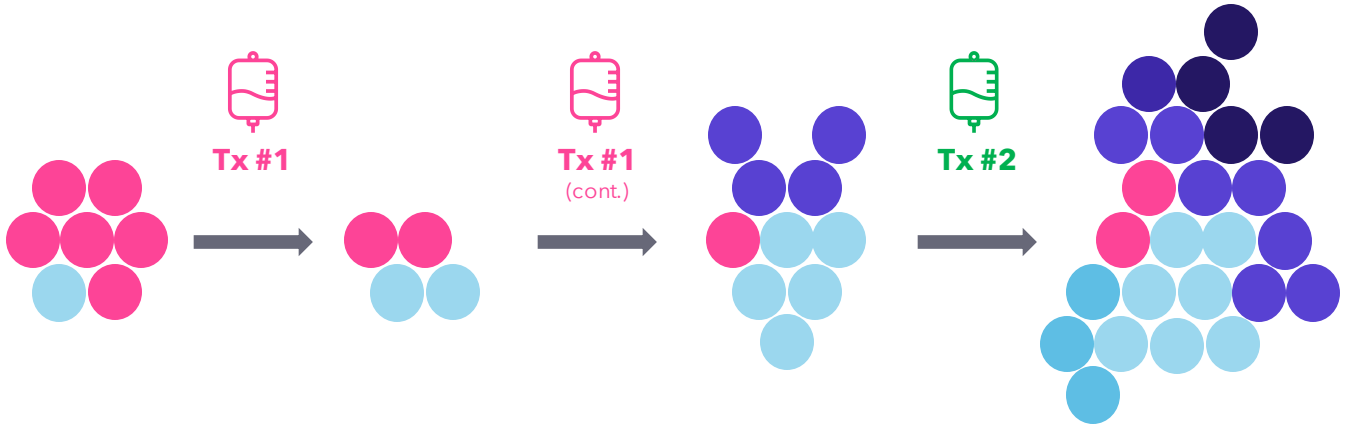
Cancer mutates quickly: ADAPT will identify and target these changes

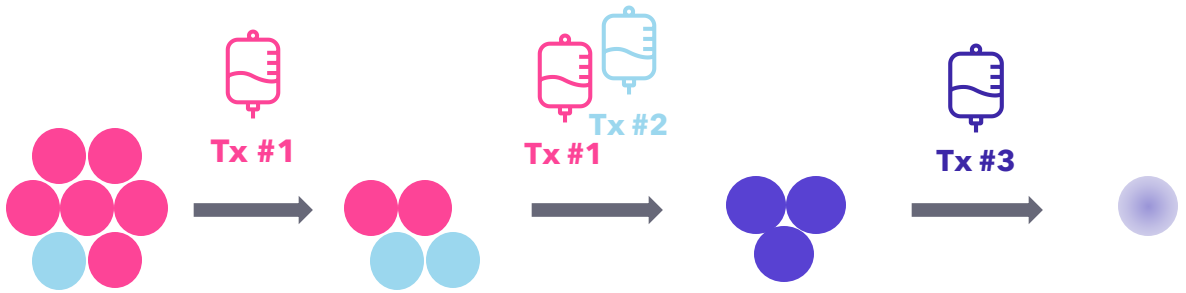
Current State

- Cancer changes during treatment. Therapies ***are not*** often informed by tumor changes or tailored to cancer resistance traits.
- There are only ***limited*** tumor measurements or biomarker analyses, which are most often performed ***prior to*** treatment.



ADAPT's "future state"

- Therapies ***will be*** informed by and tailored to observed cancer resistance traits.
- ***In-depth*** tumor measurements (biomarkers) will be taken ***before, during and after*** treatment.



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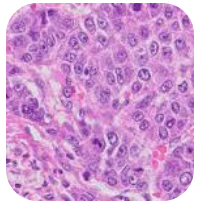
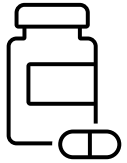
ADAPT's predictive biomarkers will identify the right therapy for the right patients at the right time

ADAPT will revolutionize the use of predictive biomarkers by dramatically improving the quantity available and the ability to predict effective and personalized therapies.

Today



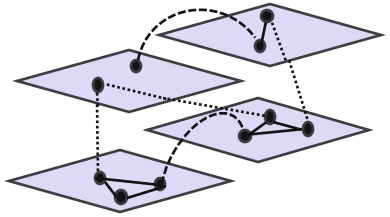
Single data type or single gene
(pathology or DNA sequencing)



Loosely informs treatment

Future Vision

Data Advances: New and **multi-modal data**



Computational Advances: New AI / ML / mathematical methods to build **multi-gene** biomarkers from multi-modal data

Biomarker for individualized therapy

<5% of cancer treatments are informed by multi-modal biomarkers based on multiple genes.

→ ADAPT will develop new biomarkers where **100%** use multi-modal data and are comprised of multiple genes

~10-50% of metastatic patients respond to standard therapies after initial treatment.

→ ADAPT aims to identify the right therapy so that **>80%** of metastatic patients respond to treatment.

Few clinical trial mechanisms to build and test biomarkers in near real-time

→ ADAPT will develop a clinical trial framework to identify, test, and validate predictive multi-modal biomarkers that inform patient treatments

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ADAPT technical areas

TA1: Therapy Recommendation Techniques

- **TA1.1: Multi-Modal Data Fusion** to integrate diverse data types & develop structures required for predictive models
- **TA1.2: Resistant Trait Modeling** including temporal modeling of tumor evolution
- **TA1.3: Biomarkers that Predict Drug Response** to identify and associate with effective therapies

TA2: Evolutionary Clinical Trial

- **TA2.1: Tumor Measurement Technologies** to gather more comprehensive tumor data to inform biomarker development
- **TA2.2: Evolutionary Trial Protocol** to dynamically adjust treatment based on patient-specific tumor evolution
- **TA2.3: Evaluation of TA1 Biomarkers** to provide real-world evidence for predictive biomarkers

TA3: Cancer Treatment & Analysis Platform

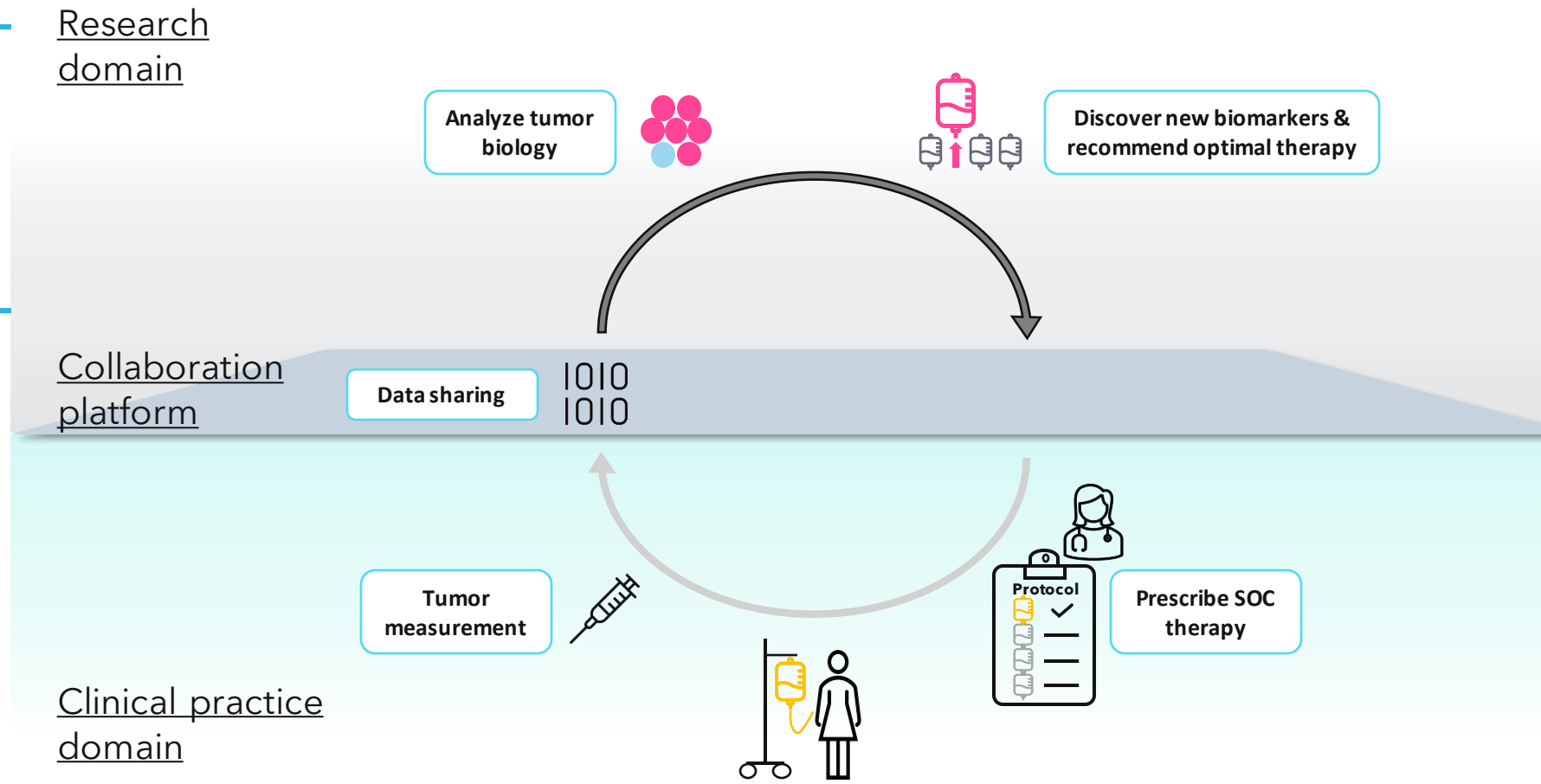
- **Cancer Data Linkage** to ensure compatibility and consistency
- **Data Architecture and Integration** enables rapid data availability, protocol distribution, and standardization of a new biomarker
- **Collaborative Platform & Testing Ground** to design, analyze, and share innovations from TA1 & TA2 (including biomarkers, tumor genomic profiles, health records, models, treatment strategies, and trial protocols)

ARPA-H

The ‘Adaptive Cancer Treatment Platform’ will develop biomarkers from patient data to predict the optimal cancer therapy for each patient.

TA1: Therapy Recommendation Techniques

Biomarkers and data analysis will identify resistant cancer traits and guide optimized treatments based on a tumor’s phenotype

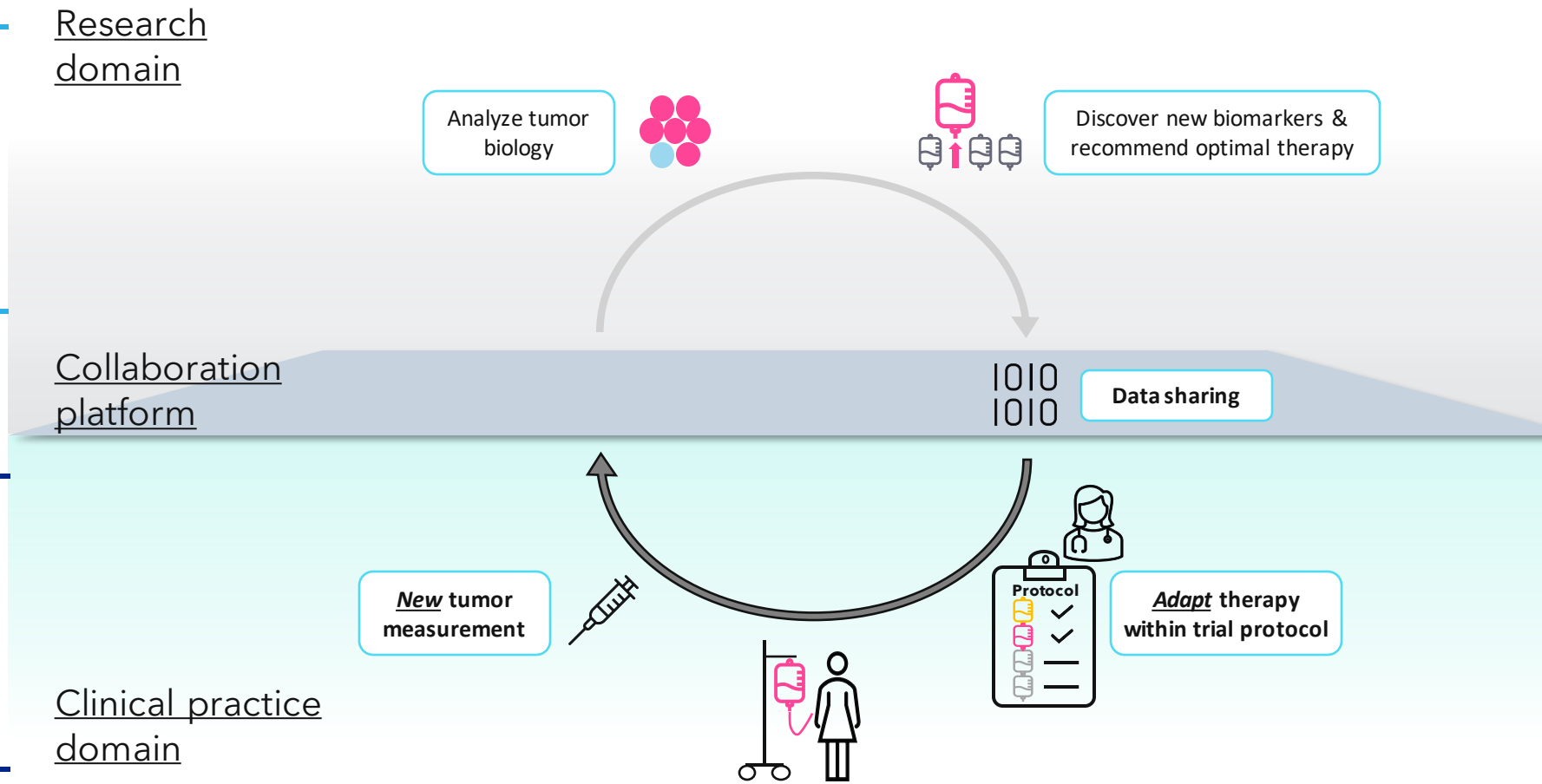


ARPA H

An evolutionary clinical trial will iteratively enable clinicians to dynamically adjust therapy based on near-real-time changes in tumor biology

TA1: Therapy Recommendation Techniques
Biomarkers and data analysis will identify resistant cancer traits and guide optimized treatments based on a tumor's phenotype

TA2: Evolutionary Clinical Trial
New clinical trial design will collect evidence across sequences of treatments so that adjustments can be optimized based on tumor progression



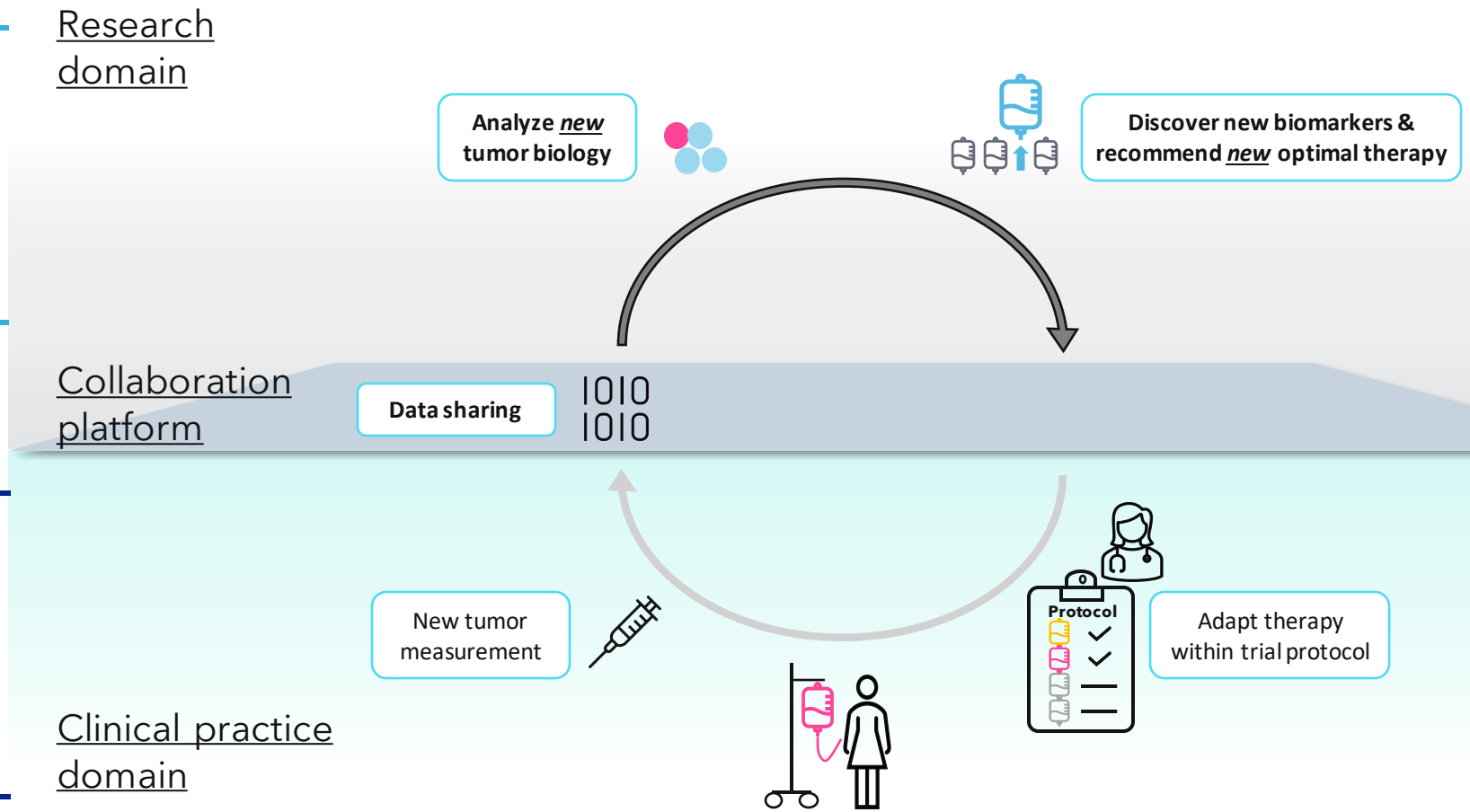
ARPA-H

Longitudinal tumor biology measurements will aid subsequent biomarker development, testing and implementation

TA1: Therapy Recommendation Techniques
Biomarkers and data analysis will identify resistant cancer traits and guide optimized treatments based on a tumor's phenotype

TA3: Treatment & Analysis Platform
Open-source collaboration space accelerates the development and sharing of data, models, and trial protocols between research and clinical practice

TA2: Evolutionary Clinical Trial
New clinical trial design will collect evidence across sequences of treatments so that adjustments can be optimized based on tumor progression



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New biomarkers can identify next line therapies based on acquired traits during tumor evolution

TA1: Therapy Recommendation Techniques
Biomarkers and data analysis will identify resistant cancer traits and guide optimized treatments based on a tumor's phenotype

TA3: Treatment & Analysis Platform
Open-source collaboration space accelerates the development and sharing of data, models, and trial protocols between research and clinical practice

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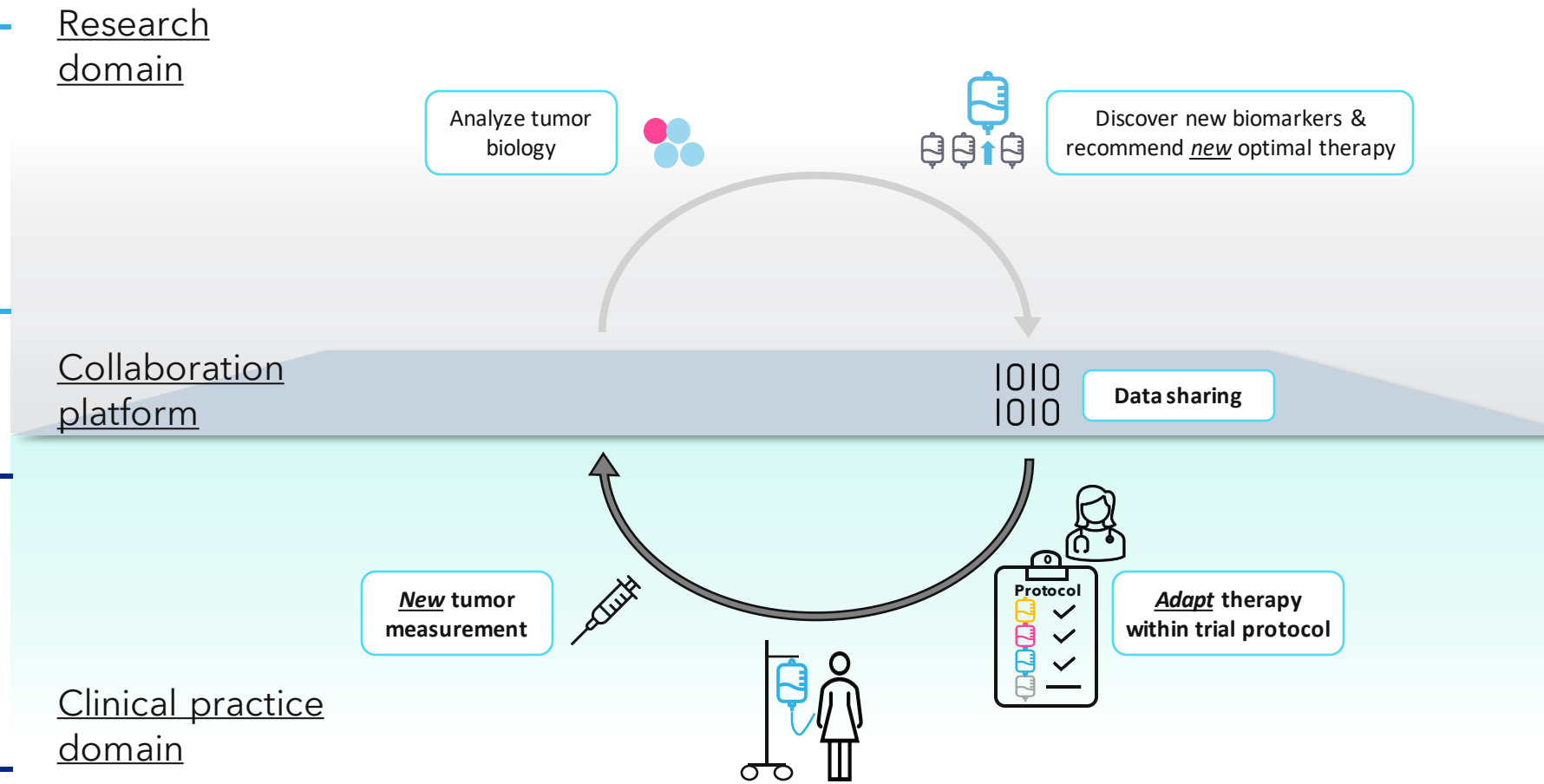

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This cycle enables a new approach in the treatment of cancer patients where data rapidly, consistently, and accurately informs patient care.

TA1: Therapy Recommendation Techniques
Biomarkers and data analysis will identify resistant cancer traits and guide optimized treatments based on a tumor's phenotype

TA3: Treatment & Analysis Platform
Open-source collaboration space accelerates the development and sharing of data, models, and trial protocols between research and clinical practice

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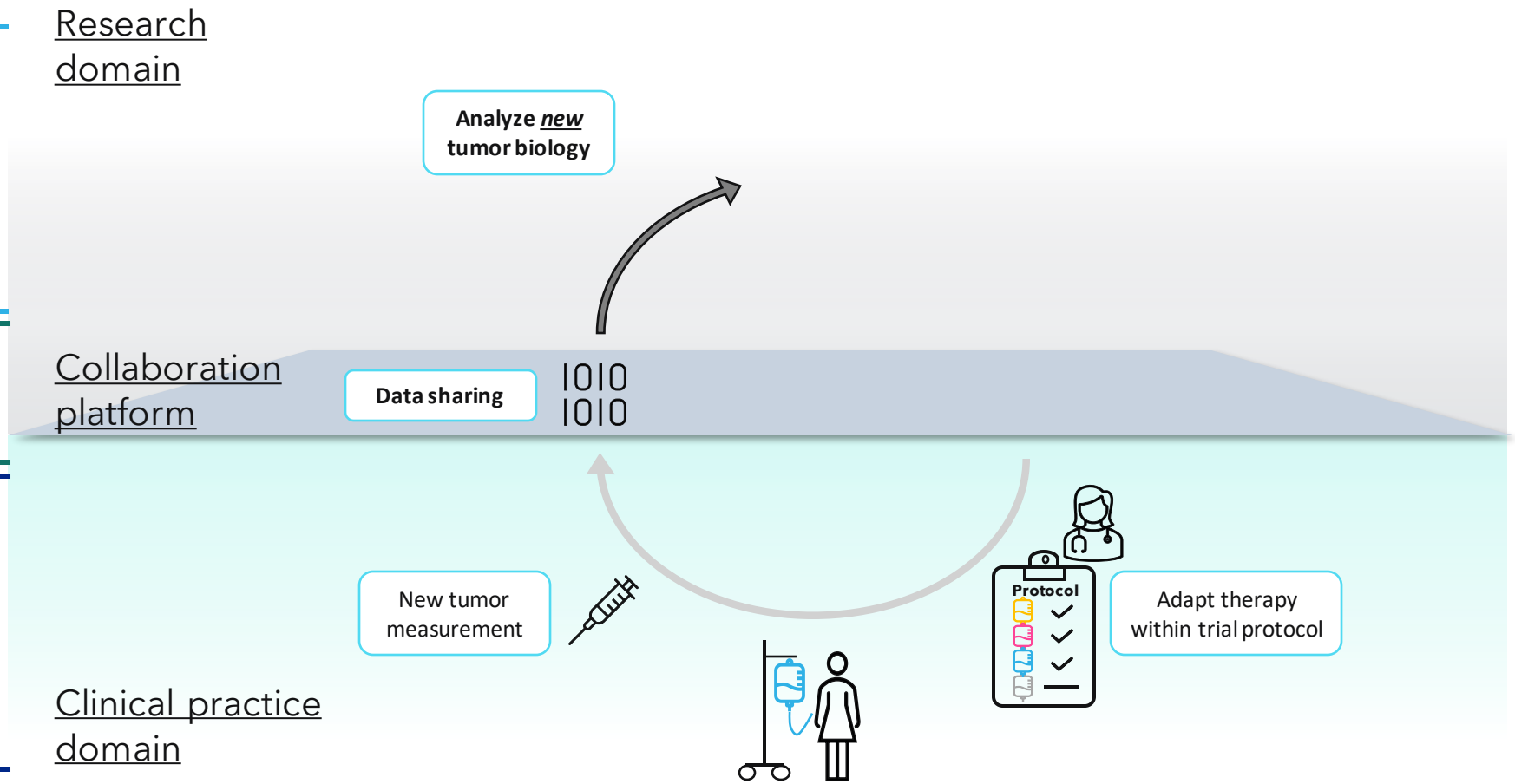

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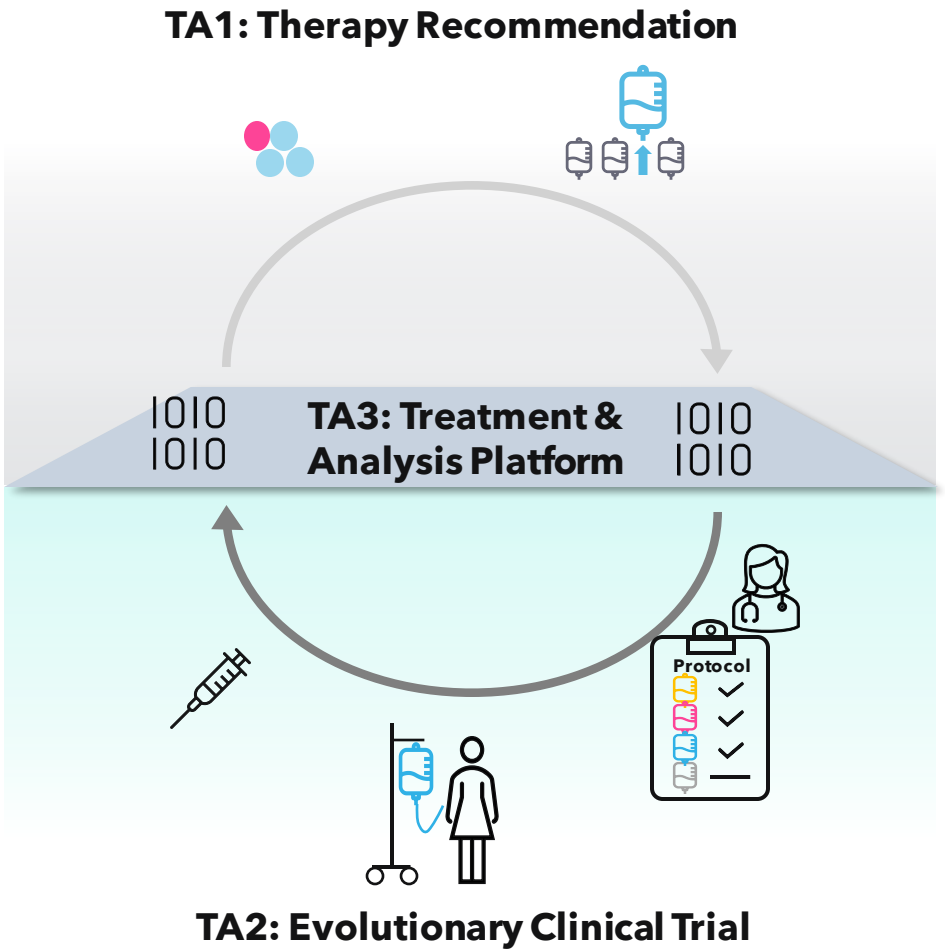
Advances to the Current State of the Art

1. Develop methods and data to track cancer resistance and identify personalized therapies at the speed of relevance

2. Develop, test, and apply multi-modal, multi-gene drug response biomarkers within a clinical trial infrastructure in near real time.

3. Modular evolutionary protocol enabling study of multiple cancer types & treatment lines.

4. An infrastructure for researchers and clinicians to work together, share data and protocols, and carry out integrated translational studies.



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TA1: Therapy Recommendation Techniques

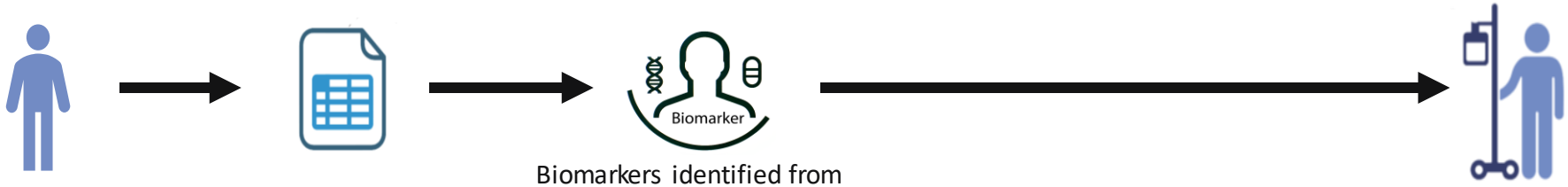
Current state of the art vs. future state with ADAPT

TA1: Therapy Recommendation Techniques

TA2: Evolutionary Clinical Trial

TA3: Treatment & Analysis Platform

Standard biomarker development: Biomarkers are only developed ***one time*** at the start of a clinical trial



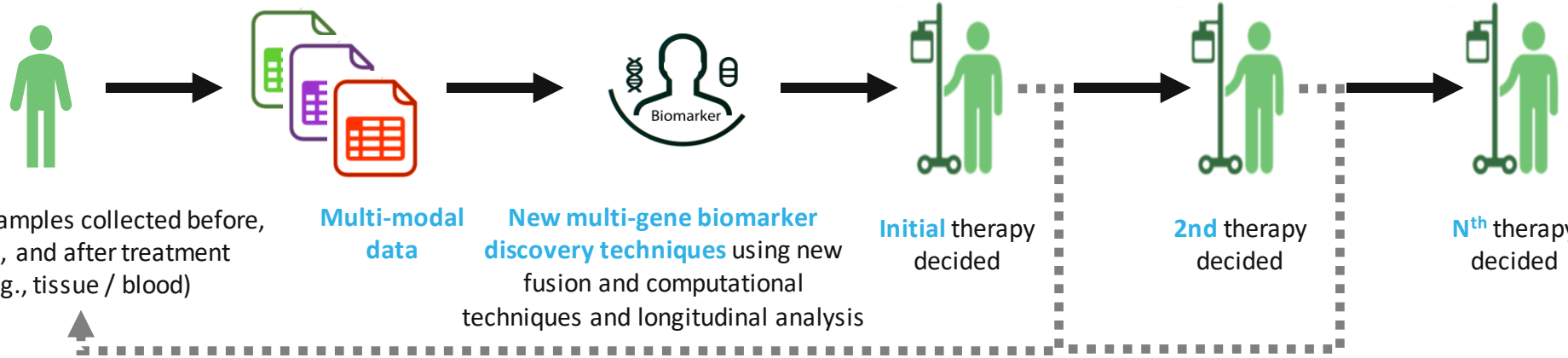
Patient samples collected before treatment (e.g., tissue / blood)

Limited data types

Biomarkers identified from single data type and single genes

Therapy is set for remainder of clinical trial, acquired resistant traits not identified or used for next therapy

ADAPT approach: Biomarkers will ***sequentially*** be ***discovered, tested*** and ***implemented*** in the evolutionary clinical trial to guide therapy selection as the tumor evolves pre- and post-treatments.



Patient samples collected before, during, and after treatment (e.g., tissue / blood)

Multi-modal data

New multi-gene biomarker discovery techniques using new fusion and computational techniques and longitudinal analysis

Initial therapy decided

2nd therapy decided

Nth therapy decided

Repeated identification of resistant tumor traits and associated biomarkers

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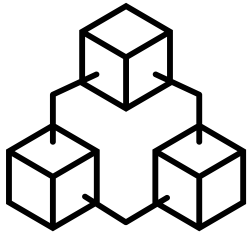
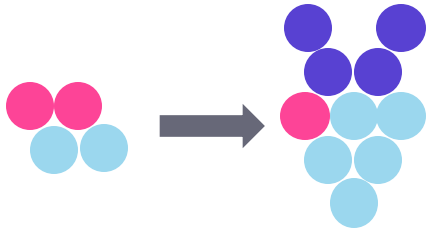
TA1: Therapy Recommendation Techniques

TA1: Therapy Recommendation Techniques

TA2: Evolutionary Clinical Trial

TA3: Treatment & Analysis Platform

Objective: Develop biomarkers that predict optimal treatment based on a tumor's biology

	TA1.1: Multi-Modal Data Fusion	TA1.2: Resistant Trait Modeling	TA1.3: Biomarkers that Predict Drug Response
			
ADAPT Innovation	Extend data fusion methods to combine information from multi-modal data types to create a unified representation that offers a more personalized, robust and accurate understanding than any single data source alone for downstream creation of predictive cancer biomarkers	Scale, extend, and adapt techniques to identify emerging resistance traits in near-real time on 100s of patients during treatment, using multi-modal longitudinal data	Extend biomarker discovery algorithms to leverage multi-modal data, link resistant traits to therapy recommendations, and computationally validate the predictive biomarkers

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TA1 Specifications

TA1.1: Multi-Modal Data Fusion
Early-data fusion, late-data fusion, or both including **fusion of research-omic data and clinical data** from TA2 performers
Integration of biomarkers from individual data modalities into composite biomarkers.
Methods must be **reproducible and transparent**.

TA1.2: Resistant Trait Modeling
Approaches must analyze **multi-modal data**, including research and clinical data from TA2 performers, across multiple time points.
Approaches must identify pathway and gene/protein level traits and drug targets that emerge during treatment.
Approaches must include **dynamical/temporal modeling**, tracking tumor evolution.
Methods must be **reproducible and transparent.**

TA1.3: Biomarkers that Predict Drug Response
Biomarkers developed using **advanced mathematical and/or computational approaches** (e.g., AI, ML, mechanistic models, etc.) for prediction of drug response.
Approaches must use **multi-modal data** types to test drug prediction capabilities through TA2's evolutionary clinical trial.
Biomarkers must predict drug response to a currently used therapy in metastatic cancer treatment.
Biomarkers must use a complexity of data for predictions with a **minimum of 5 mutations, transcripts, or proteins**.
Approaches must integrate into the TA3 platform and be **testable by external reviewers.**

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TA1 Metrics

TA	Metric	Description	Phase I, Stage I (0-6 mo)	Phase I, Stage II (7-36 mo)	Phase II (37-72 mo)
TA1.1	**Data fusion pipeline**	# of data types integrated from TA2	Target set by 6 months	≥ 50%	100%
TA1.2	**Drug resistance models**	# of resistance mechanisms discovered	Set up modeling algorithms	2-5	6-15
TA1.3	**Therapy coverage**	% therapies that have an associated multi-modal biomarker*	5%	≥ 30%	≥ 90%
TA1.3	**Algorithm predictive accuracy**	Accuracy of association between biomarker and whether patient responds to therapy*	20% - 50%	≥ 75%	≥ 90%
TA1.3	**Cancer predictive biomarker development**	# of novel predictive biomarkers discovered*	n/a	≥ 5	≥ 15
TA1.3	**Biomarker processing speed**	Time from availability of tumor measurement data to therapy recommendation	n/a	< 72 h	< 24 h

ARPA H

TA2: Evolutionary Clinical Trial

Current state of the art vs. future state with ADAPT

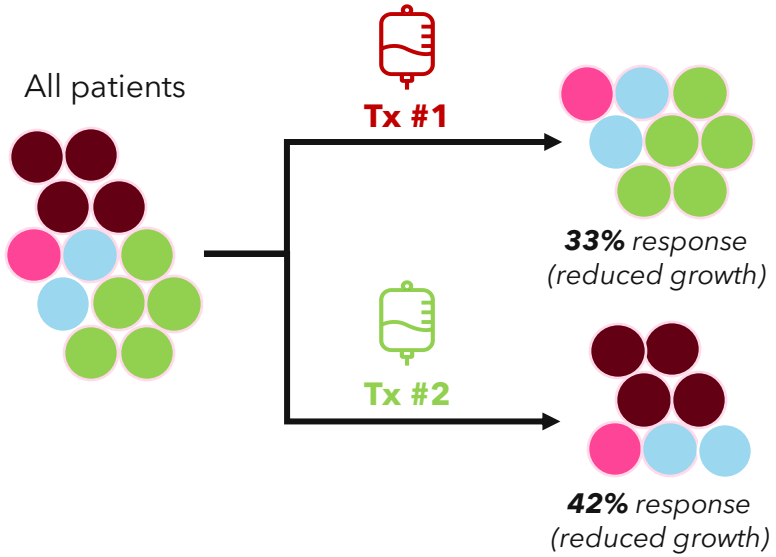
TA1: Therapy Recommendation Techniques

TA2: Evolutionary Clinical Trial

TA3: Treatment & Analysis Platform

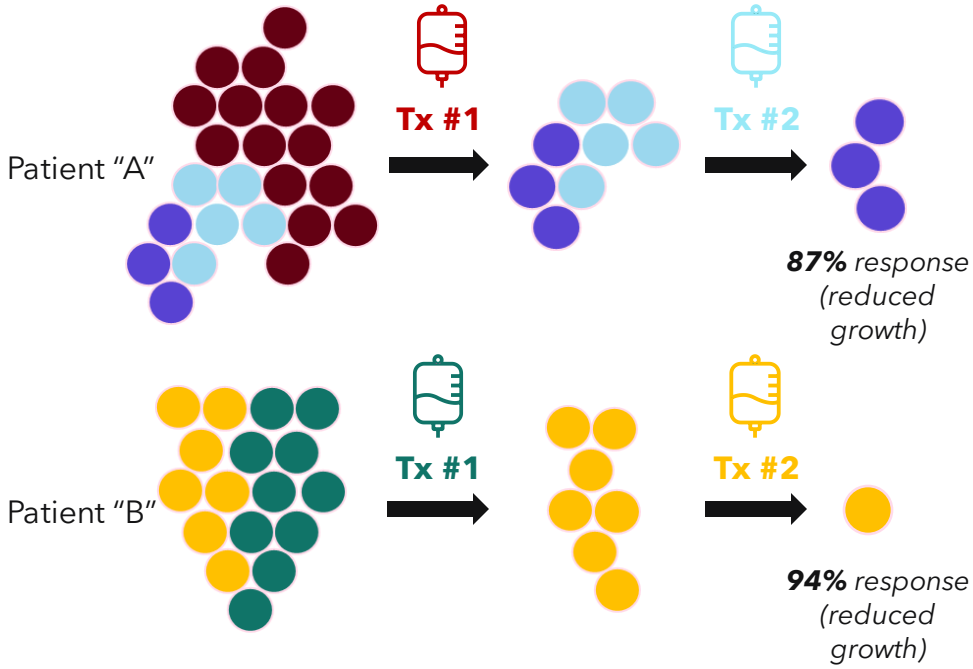
Current state of the art – Clinical trials define the treatment and trial structure *a priori,* then seek patients to fit the trial. Randomized, adaptive, n-of-1, and pragmatic trials are specific types.

- May not conduct multi-modal genetic and molecular analysis of tumors, which restricts its ability to tailor therapies to a specific tumor.
- Therapy is tested at a population level and not at an individual level.
- Often, only one sequence of treatment is tested in a clinical trial, missing out on measuring and targeting evolution of resistance over multiple lines of treatment.



ADAPT Evolutionary Trial – New clinical trial protocol that defines the trial structure and treatment based off patient tumor presentation.

- Assigns patients to a specific treatments based on tumor biology measurements including biomarkers taken pre- and post-therapy
- Trial follows patients as tumors change during multiple treatments
- Individualizes treatment over time, and enables matching of therapy to observed tumor biology/biomarkers
- Potential for higher drug response rates



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TA2: Evolutionary Clinical Trial

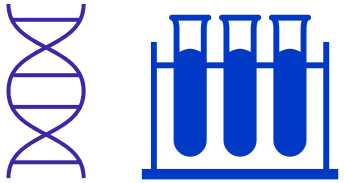
TA1: Therapy Recommendation Techniques

TA2: Evolutionary Clinical Trial

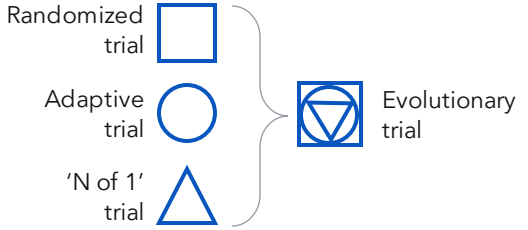
TA3: Treatment & Analysis Platform

Objective: Develop mechanisms to learn from real-time tumor evolution in clinical environments and provide more precise and effective therapies to cancer patients

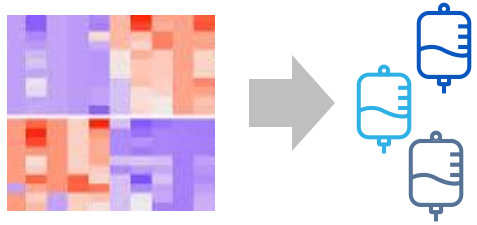
2.1: Tumor Measurement Technologies



2.2: Evolutionary Trial Protocol



2.3: Evaluation of TA1 Biomarkers



ADAPT Innovation

Tumor biology measurement technologies (e.g., blood-based circulating tumor DNA/RNA/methylome, single cell, bulk tumor 'omics and spatial imaging) can be collected serially before, during and after treatment, and combined with clinical data (e.g., EHR, imaging, and pathology data) to inform biomarker development.

Develop new modular trial protocol that integrates existing or new approaches (e.g., adaptive trials, randomized trials, 'N of 1' trials, umbrella trials etc.), that flexibly adapts treatment arms over time for each cancer subtype and drug treatment, and that can be scaled rapidly across sites.

Biomarkers developed by TA1 performers will be integrated into the evolutionary trial for testing and validation, thereby creating a rapid feedback cycle between research and clinical practice.

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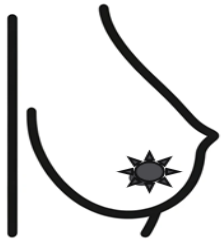
TA2: Evolutionary Clinical Trial

ADAPT will include a diversity of cancer types to build robust biomarkers and generalizable methods across diverse patient populations and treatments.

TA1: Therapy Recommendation Techniques

TA2: Evolutionary Clinical Trial

TA3: Treatment & Analysis Platform

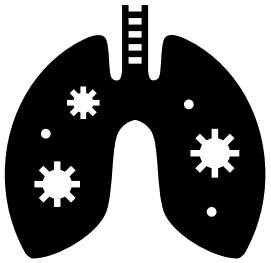


Breast cancer

Breast cancer is the most common cancer in women in the US, except for skin cancer, and the second-leading cause of cancer death in women (after lung cancer)

About 1 in 8 women will get invasive breast cancer in their lifetime.

For metastatic estrogen receptor positive breast cancer, overall response rates for second line targeted and/or chemotherapy are <25% and <1-year median progression-free survival



Lung cancer

Lung cancer is the third most common cancer in the US, and the leading cause of cancer death

About 1 in 16 people will develop lung cancer in their lifetime

For metastatic lung cancer, overall response rates for first- and second-line therapies are ~50 % with <1-year median survival time

Colon cancer

Colorectal cancer is the second most common cancer in the US, and the second leading cause of cancer death

Emergent global epidemic of colon cancer among people younger than 50

African Americans are about 20% more likely to get colorectal cancer and about 40% more likely to die.

For metastatic colon cancer, overall response rate of 47% to first line chemotherapy and <25% to second line chemotherapy with a progression free survival (PFS) of 6.1 months, with no personalized treatments.

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TA2 Specifications

Tumor Measurement Requirements
Tissue or blood samples must be of sufficient mass and quality to support research data extraction (e.g., sequencing).
Diversity of tumor biology data types: bulk and single cell DNA- and RNA-sequencing, blood-based assays such as circulating tumor DNA/RNA/methylome sequencing, and single cell assays e.g., transcriptomics, proteomics, and mutation analysis.
Raw and summarized data from measurements will be made available to and used by performers and researchers.
Analysis of measurements must be feasible **within one month** from collection and processing.

Clinical Trial Requirements
Clinical trial for **metastatic** cancer patients.
Includes multiple lines of therapy under a **single protocol**.
Flexible protocol that enables changes in design (e.g., randomized, adaptive, etc.).
Collect **serial** tumor and blood-based measurements.
Trial protocol includes a treatment line with a Progression Free Survival (PFS) rate of <9 months average.
Trial protocol includes **mechanisms for biomarker evaluation**.
Modular clinical trial design enabling rapid dissemination and protocol uptake by different sites.

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TA2 Metrics

TA	Metric	Description	Phase I, Stage I (0-6 mo)	Phase I, Stage II (7-36 mo)	Phase II (37-72 mo)
TA2.1	**Biological sample collection**	# of sequential samples collected per patient during trial	n/a	≥ 2	≥ 3
TA2.1	**'Omics data collection**	% samples with 'omic data (ex. DNA-, RNA- sequencing) generated, processed, & uploaded	≥ 60%	≥ 80%	≥ 95%
TA2.1	**Imaging data collection**	# of images per patient	n/a	≥ 2	≥ 3
TA2.1	**Collection of clinical trial data for data lake**	% of clinical (ex. EHR, imaging, etc.) data made available to TA3	n/a	≥ 80%	≥ 95%
TA2.2	**Clinical trial enrollment**	# of patients enrolled in evolutionary trial	Approve protocol	200 - ≥500	500 - ≥1000
TA2.2	**Clinical trial sites**	# of new clinical trial sites	≥ 3 sites open	≥ 6 sites open	≥ 8 sites open
TA2.2	**Patient diversity**	% adherence to diversity rate for target population(s)	Demographic targets set by national averages for cancer type	< 10% deviation from population	< 5% deviation from population
TA2.3	**Drug treatments**	# of non-standard of care drug therapies used based on tumor resistance evolution	n/a	≥ 1	≥ 3
TA2.3	**Clinical response**	% improvement in progression free survival (PFS) rate	Measure PFS for standard of care	Measure PFS for biomarker-guided standard of care	≥ 50% for ≥ 1 patient subgroup using resistance targeting therapy

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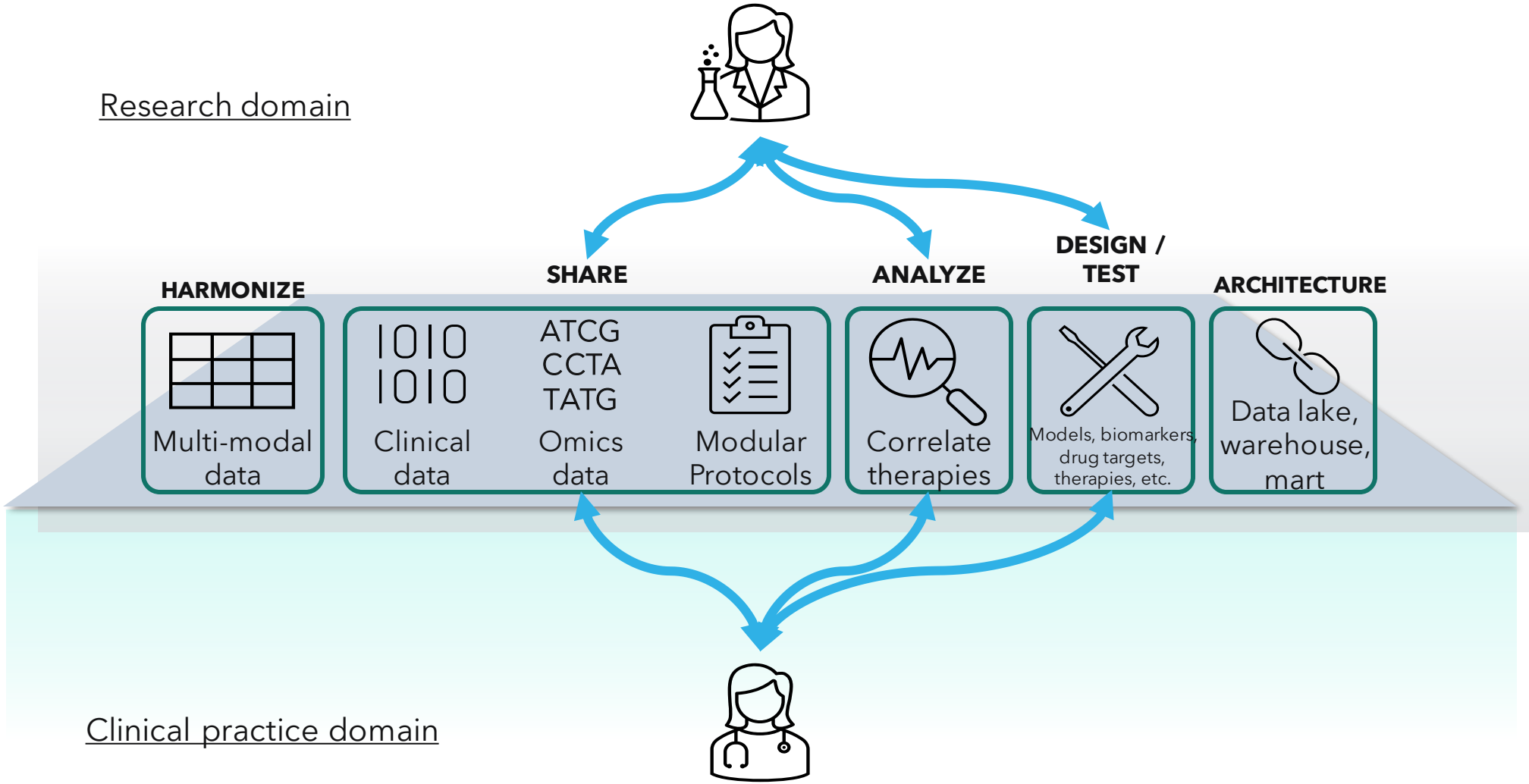
TA3: Treatment & Analysis Platform

ADAPT will provide long-term resources for the entire research and clinical community.

TA1: Therapy Recommendation Techniques

TA2: Evolutionary Clinical Trial

TA3: Treatment & Analysis Platform



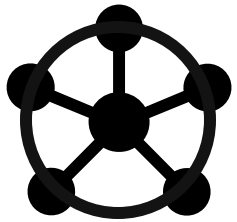
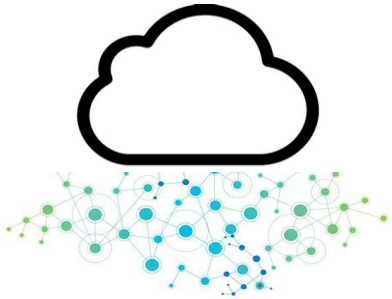
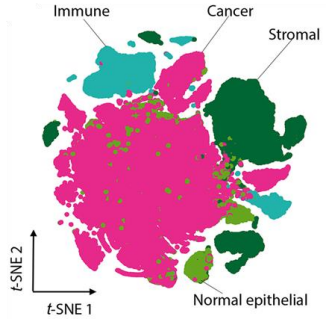
TA3: Treatment & Analysis Platform

TA1: Therapy Recommendation Techniques

TA2: Evolutionary Clinical Trial

TA3: Treatment & Analysis Platform

Objective: Create an open-source collaboration platform for developing, analyzing, and sharing data, models, and trial protocols between research and clinical practice to increase innovation speed

	Cancer Data Linkage	Data architecture	Collaborative Platform & Testing Ground
			
ADAPT Innovation	Improve the volume and insight-richness of cancer data through data annotation, standardization, and harmonization, and ensuring compatibility / consistency across data types and structures.	Prepare architecture for cancer data, algorithms and pipelines through a data lake and accessible data warehouse. Integrated data will be utilized in the platform to enable near-real time data availability, protocol distribution.	Develop open-access platform and toolset (including auto-generation of therapy recommendation test reports) enabling clinicians and researchers to design, analyze, and share innovations from TA1 & TA2 (including biomarkers, tumor genomic profiles, health records, models, treatment strategies, and trial protocols)

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TA3 Specifications

Requirements
A scalable **data management solution** that stores the raw and processed multi-modal data from cancer researchers and the evolutionary clinical trial.
A **computational pipeline** to rapidly process tumor biology measurements, perform quality control (QC) analysis, detect sampling bias, manage data curation, mapping, annotation, and linkage of disparate data types from the same patient.
Implementation plan for **data harmonization** to ensure compatibility and consistency across different data sources.
Development of **open APIs**, a data portal, and other tools for data access, sharing, analysis, querying, and visualization. Whenever possible FHIR HL7 APIs and open data standards (e.g., USCDI+) should be leveraged.

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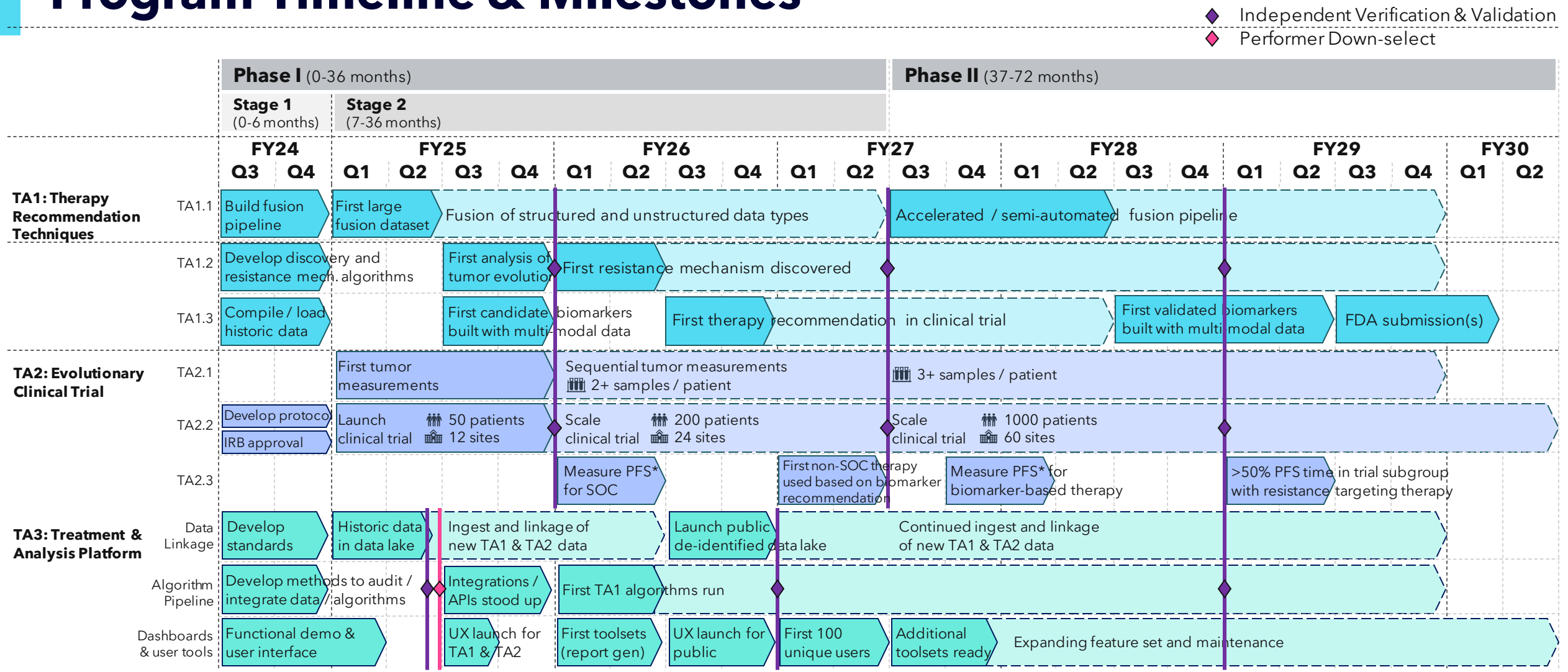
TA3 Metrics

TA	Metric	Description	Phase I, Stage I (0-6 mo)	Phase I, Stage II (7-36 mo)	Phase II (37-72 mo)
TA3	**Data quality assurance**	% of data that has gone through ETL and quality assurance across data types	n/a	≥ 80%	≥ 98%
TA3	**Ingest of clinical trial data to data lake**	% of available data ingested	n/a	≥ 85%	≥ 95%
TA3	**Portal engagement**	# of unique visitors or users per year	n/a	≥ 100	≥ 500
TA3	**User experience with platform**	Likert scale assessment of usability by users	Target set by 6 months	≥ 80% approval	≥ 90% approval
TA3	**Collaboration & support for TA1 & TA2**	Likert scale assessment of satisfaction with support	Target set by 6 months	≥ 80% approval	≥ 90% approval

ARPA-H

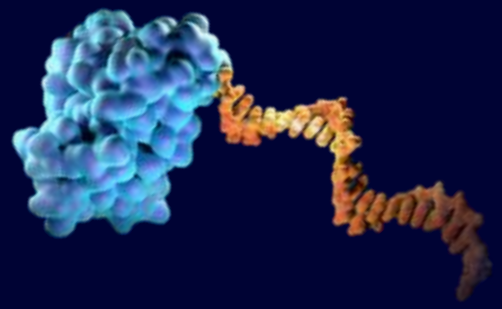
Program Timeline & Milestones



*PFS = Progression free survival
*SOC = Standard of care

Key Outcomes

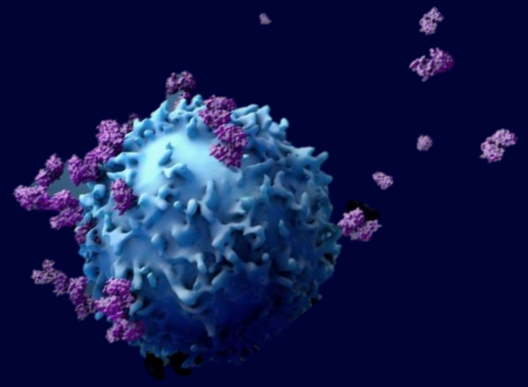
TA1: Therapy Recommendation Techniques



For the first time, a consistent mechanism will exist to build and clinically validate biomarkers for both standard of care and new therapies.

≥ 15 new biomarkers so that ≥ 90% of SOC therapies have an associated biomarker

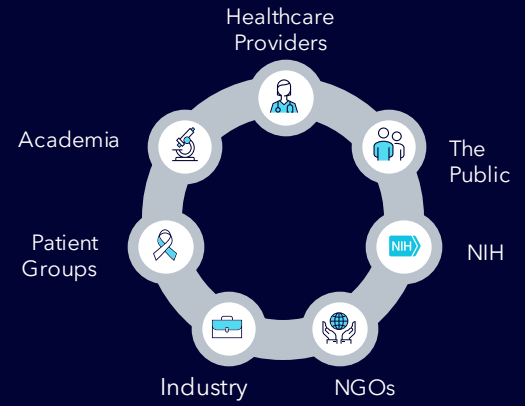
TA2: Evolutionary Clinical Trial



Novel clinical trial design to implement biomarkers and treatment regimens targeting resistance and decrease cancer growth, leading to longer survival time.

> 50% improvement in Progression Free Survival time across multiple treatment arms

TA3: Cancer Treatment & Analysis Platform



Creation of an accessible data library and digital foundry for developing new therapeutic approaches and clinical trials.

95% of relevant clinical trial data available to the research and clinical community.

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Impact of ADAPT

Patients

Benefit from improved care through treatments that are more effective by specifically targeting new traits of the tumor as revealed by biomarkers

Scientists

Benefit from clinical trial infrastructure and deep data that enables translation of research discoveries and ideas for patient benefit and continued care over multiple sequences of drugs

Clinicians

Benefit from better informed treatment decisions and drug selection to treat individual patients

Insurers/Pharma

Benefit from minimized unnecessary side effects, less ineffective treatments, and identification of new cancer targets

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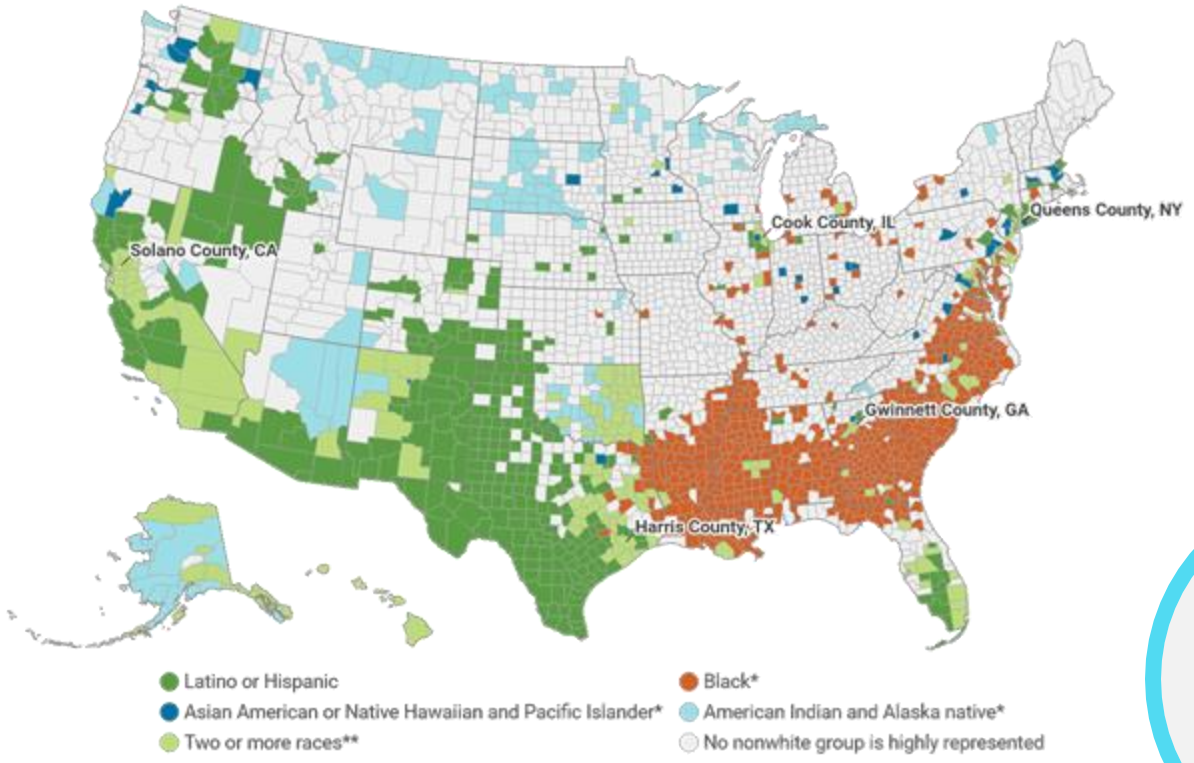
The ADAPT evolutionary clinical trial will ensure equitable access for patients in the U.S. by establishing sites with high diversity



(2020 Census)

A key aspect of equitable access is ensuring that the population participating in clinical trials reflects the diversity of people who live in the United States and serves the patient population impacted by the disease.

Enrollment for the clinical trials will serve as an accurate demonstration of the correlation between race and cancer type in the US. For example, breast cancer incidence is 66% White, 14% Hispanic or Latino, 11% Black or African American, 8% Asian, and 1% American Indian and Alaska Native.

Incorporate patient feedback throughout the trial to ensure the user experience is considered from a variety of perspectives, including comprehensive cancer centers that serve a diversity of cancer patients, clinicians, and scientists.

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Next Steps: Submit a Solution Summary

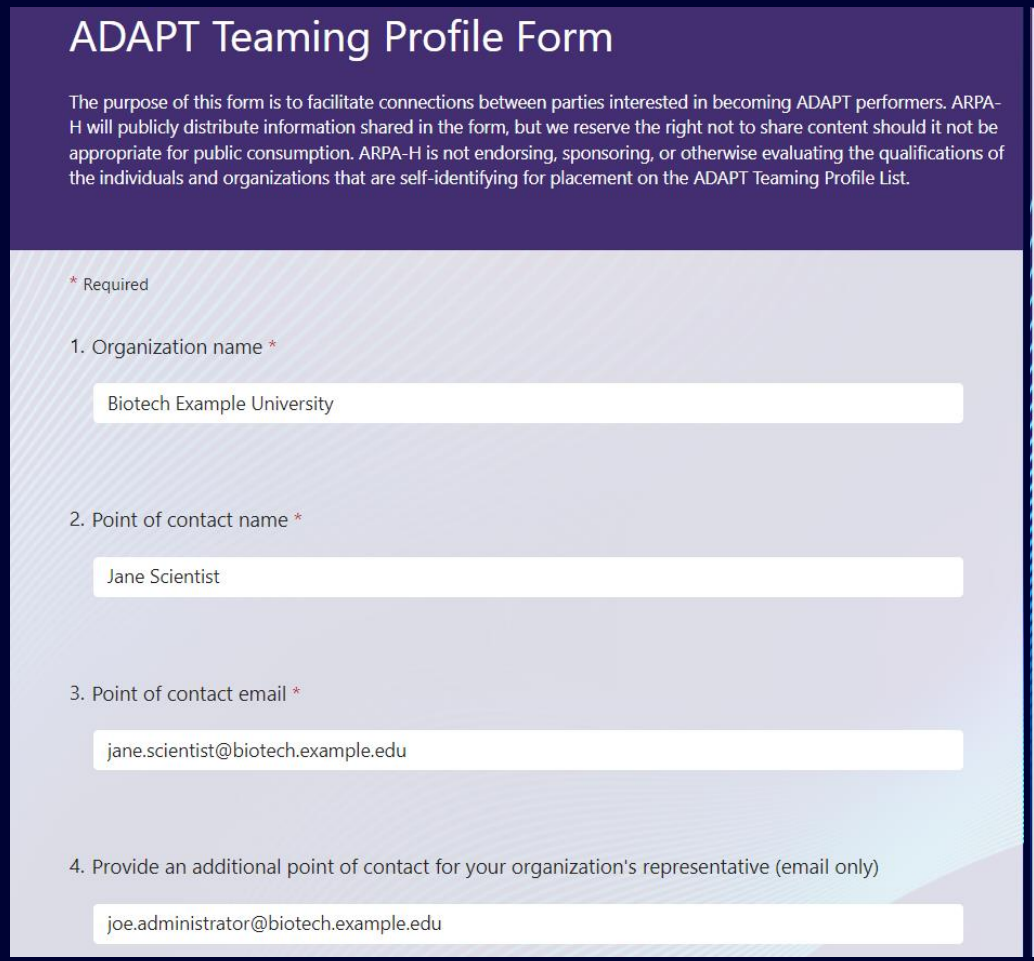
- The ADAPT Program just posted a Special Notice Request for Solution Summaries.
- A solution summary is an abstract submitted to an ARPA-H solicitation. A solution summary is not required to submit a full proposal to the ADAPT solicitation; however, it is **highly recommended** as it is an opportunity to receive "recommend full proposal submission" or "discourage full proposal submission" feedback from the ADAPT Program team.
- Solution summaries are due March 29, 2024, at 10:00 AM ET.

- Use the ARPA-H Solutions Portal at https://solutions.arpa-h.gov to submit your solution summary.

Next Steps: Submit Teaming Profile

- **Teaming is optional.**
- Teaming profile form submissions will be reviewed and posted in a table on the ADAPT program web page.
- The table of team submissions can be searched, for example "TA2" or "lung cancer"

ADAPT Teaming Profile Form



ADAPT Teaming Profile Form

The purpose of this form is to facilitate connections between parties interested in becoming ADAPT performers. ARPA-H will publicly distribute information shared in the form, but we reserve the right not to share content should it not be appropriate for public consumption. ARPA-H is not endorsing, sponsoring, or otherwise evaluating the qualifications of the individuals and organizations that are self-identifying for placement on the ADAPT Teaming Profile List.

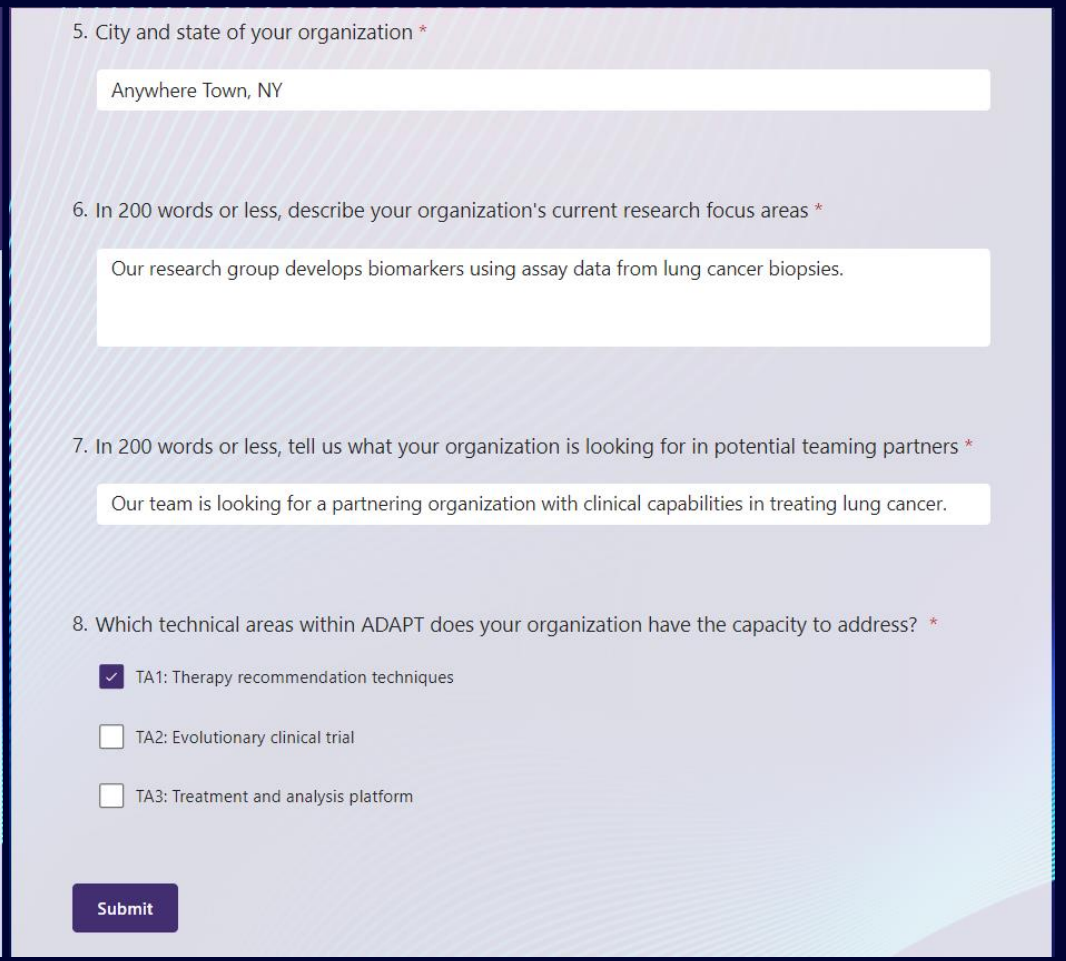
* Required

1. Organization name *
Biotech Example University

2. Point of contact name *
Jane Scientist

3. Point of contact email *
jane.scientist@biotech.example.edu

4. Provide an additional point of contact for your organization's representative (email only)
joe.administrator@biotech.example.edu



5. City and state of your organization *
Anywhere Town, NY

6. In 200 words or less, describe your organization's current research focus areas *
Our research group develops biomarkers using assay data from lung cancer biopsies.

7. In 200 words or less, tell us what your organization is looking for in potential teaming partners *
Our team is looking for a partnering organization with clinical capabilities in treating lung cancer.

8. Which technical areas within ADAPT does your organization have the capacity to address? *
- [x] TA1: Therapy recommendation techniques
- [ ] TA2: Evolutionary clinical trial
- [ ] TA3: Treatment and analysis platform

Submit

https://forms.office.com/g/M0TUL36bPh

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Next Steps: Review ADAPT Resources and Submit Questions

- ADAPT Program Page
  - View teaming profiles from other teams
  - View Proposers' Day recording and slides
  - Link to the program solicitation and special notices

https://arpa-h.gov/research-and-funding/programs/adapt

- Ask A Question
  - Submit program and technical questions

https://solutions.arpa-h.gov/Ask-A-Question

ARPA-H

Acquisition Details

The Submission Process

Caitlin Burns

Business Innovation Division

ARPA-H

ARPA-H ADAPT Solicitation/Funding Opportunity Basics

Master Announcement Instructions (MAI) and APRA-H ADAPT Module Announcement

MAI is your manual and provides detailed instructions

MAI covers high-level instructions that are applicable to each Module Announcement

A Module Announcement provides project/ program specific technical details.

Module Announcement has unique instructions specific to the Module.

The Module Announcement will refer to the MAI; have both documents available while writing proposal responses.

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ARPA-H ADAPT Module Announcement Basics

Notable Dates

- Module Announcement release date: 03/08/2024
- Virtual Proposers' Day: 03/15/2024
- Questions & Answers (Q&A) due date: 03/22/2024
- Questions & Answers (Q&A) release date: 04/01/2024
- Solution Summary Due: 03/29/2024
- Proposal due date: 05/06/2024

Program Schedule

- 6-year effort composed of 2 Phases
- Phase 1 is divided into 2 Stages:
  - 6-month Stage 1
  - 30-month Stage 2
- Phase 2 is 36-months
  - Phase 2 is contingent upon approval by ARPA-H leadership

Open-Source Standards

- Emphasis in creating and leveraging open-source technology and architecture
- IP rights asserted should be aligned with open-source regimes
  - Approaches that don't reflect open-source standards should describe how program objectives can be met with IP rights that are restrictive

Software Component Standards

- Existing Standards
- Existing Standard – only partial functionality
  - Do NOT prohibit or interfere with backward compatibility, and create sufficient documentation
- Include a technical plan to align with applicable standards
- Solutions outside the standards – Proposer must schedule a meeting with ARPA-H representatives to discuss the deviation prior to proposal submission

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APRA-H ADAPT Module Announcement Basics, cont.

Module Categories

- **BIT Module** is ≤ $2,000,000: Volume 1 shall be limited to **10** pages.
- **BYTE Module** is > $2,000,000 ≤ $4,999,999: Volume 1 shall be limited to **15** pages.
- **KILO Module** is > $5,000,000 ≤ $10,000,000: Volume 1 shall be limited to **20** pages.
- **MEGA Module** is > 10,000,000 ≤ $25,000,000; Volume 1 shall be limited to **25** pages.

The following is the Government's estimation of Module category for each TA and TA1 sub-TA.

TA1: Individually proposed sub-TAs are anticipated at the **BYTE level.**
TA1: Combined proposal for **two** (2) sub-TAs is anticipated at the **KILO level**.
TA1: Combined proposal for all **three** (3) sub-TAs is anticipated at the **MEGA level.**
TA2: Proposals must address all sub-TAs therefore proposals are anticipated at the **MEGA level**.
TA3: Proposal are anticipated at the **MEGA level.**

Any proposals that combined TAs (TA1-TA2, TA2-TA3, TA1-TA3, etc.) are anticipated at the MEGA level.

Proposals that simply align a proposed budget to the Module Category ceiling value is strongly discouraged. Thus, if a proposal is selected for Stage 2 submissions and the basis of estimate was simply aligned to the Module Category ceiling value, the Government will require a full cost proposal (i.e., direct and indirect rates, labor hours, equipment, material, other direct costs, etc.) that must be substantiated by salary documentation, indirect rate agreements, material and equipment quotations and a justification for proposed labor categories and hours that correlates directly to the proposed Task Description Document.

APRA-H ADAPT Module Announcement Basics, cont.

Stage Submissions

- Stage 1
  - Technical & Management
  - Basis of Estimate (BOE)
  - Task Description Document
  - Administrative & National Policy Req.

- If selected for potential award, Stage 2 Volume 2 proposal will be requested by the Agreement Officer
  - Price/Cost Proposal
  - Agreement Certification
  - Model Agreement (red-line for negotiation)

Bundles of Attachment for Other Transaction Agreements

- Stage 1 and Stage 2 each have a bundle of attachments that should be used

- Stage 1 Volume 1 bundle of attachments have been posted with the ADAPT Solicitation on SAM.gov

- Stage 2 Volume 2 bundle of attachments will be provided to those proposers who have been selected for potential award

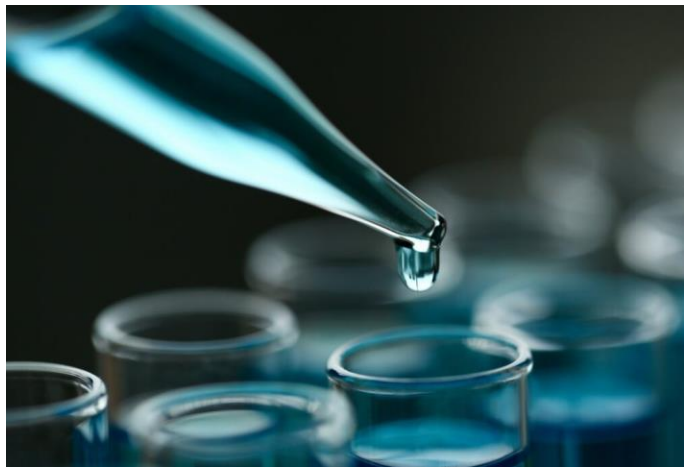
Award Types – Other Transactions (OTs)

What are OTs?

- ARPA-H has authority to award OTs when "*use of such authority is essential to promoting the success of the project*"
- OTs are Agreements (e.g., mutual assent, expressed by a valid offer and acceptance; adequate consideration; capacity; and legality)
- OTs reflect commercial contracting rather than traditional FAR procurement contracts

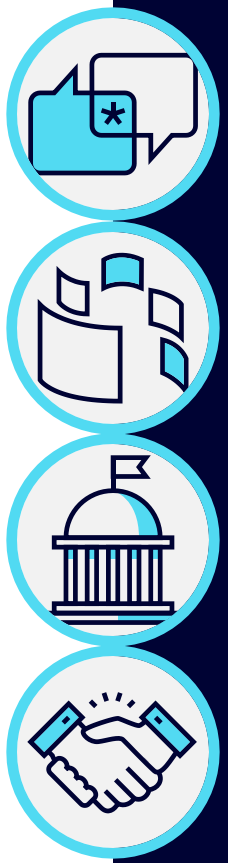
OTs are collaborative

- Increased collaboration and partnership, leading to more effective use of resources and knowledge sharing.
- Free-flowing negotiations and less restrictive than FAR based procurements.



Other Transactions (OTs)

- **Pros:**
  - Many laws/regulations do not apply
    - Competition in Contracting Act; Bayh-Dole; 45 CFR 75; FAR/HHSAR; Cost Accounting Standards; Bid Protests, etc.
  - Invokes commercial practices, allowing for negotiating terms and conditions
    - May negotiate intellectual property (IP), payments, etc.
  - Streamlined award process



- **Cons:**
  - Lack the guardrails performers might desire under financial assistance or FAR contracts
    - Requires careful negotiation by knowledgeable parties
    - Can take longer to negotiate

ARPA-H

Process Overview

Proposers' Day

- Proposers' Day is **NOT** mandatory to attend to submit a proposal
- Material presented today will be made available to the public via the ARPA-H ADAPT website
- The ADAPT Module Announcement is the official solicitation and therefore should be used as the official document to develop your proposals

Solution Summary Submission

- Submission is NOT mandatory
- Length should not exceed three (3) pages
- Should include all sections noted in the template
- Submitted via the ARPA-H Solutions Website

Proposals

•Follow the stage submissions

•Submitted via eCPS

•Do **NOT** select a larger Module category to gain more pages only to reiterate your solution in different ways

•Do **NOT** align your BOE to the Module category level without proper analysis and assumptions

•Do **NOT** include data storage and analysis costs – this will be GFR

Evaluation and Selection

- The Government will review each conforming proposal against criterion 1-3 in descending order of importance.
- Stage 2 submissions will **ONLY** be requested if the technical volume has been selected for potential award.
- Selection for potential award will be made as outlined in the Master Announcement Instructions and ARPA-H ADAPT Module Announcement.

ARPA-H

Evaluation Criteria, Stage 1

1

Overall Scientific and Technical Merit (Stage 1)

- Innovative, feasible, achievable, and complete
- An outcome that achieves the expected goals
- Technical risk(s) identification with a feasible mitigation strategy
- Intellectual Property (IP) rights structure; impact to Gov's ability to transition

2

Proposers' Capabilities and/or Related Experience (Stage 1)

- Team expertise and experience
- Experience in managing similar efforts

3

Potential Contribution and Relevance to the ARPA-H Mission (Stage 1)

- Future application, including unmet needs within biomedicine and to improve health outcomes
- Potential for interdisciplinary approach

Evaluation Criteria, Stage 2

4

Price and Value Analysis/Cost Realism/Reasonableness (Stage 2)

- Price Reasonableness - Ensure the overall price is fair and reasonable (e.g., not too high no too low)
- Do prices reflect the technical goals and objectives of the solicitation and the proposed scope of work
- Value Analysis – what is the value of the research in comparison to the proposed price

Final Guidance

Monitor SAM.gov

- Any/all changes to the MAI or Module Announcement will be made via formal amendments and posted online at SAM.gov
  - No information discussed at Proposers' Day shall be construed as modifying the terms and conditions of the MAI or Module Announcement

Conform to all Requirements

- Thoroughly read the MAI and Module Announcement
- Non-conforming proposals **will not** be evaluated or considered for award

Reminders

- Use the Bundle of Attachments to develop your proposal submissions
- Read the solicitation in total before you develop your proposal
- Do not align BOE's to the Module category level(s) without proper thought and assumptions

Dates and Deadlines

- Solution Summaries Due Date: March 29th, 2024 at 10:00 AM ET
  - Submit to ARPA-H Solutions
- Proposal Due Date: May 6th, 2024, 1:00 PM ET
  - Submit to eCPS

Questions

- Submit questions to ARPA-H Solutions

Important Reminders: Proposal Submission

Remember: The ADAPT program solicitation is your ultimate reference.

- Submission of multiple proposals from a single institution:
  - PIs from the same institution can each submit their own separate proposals.
- Number of proposals a single PI can submit:
  - A PI may submit only one prime proposal but is not limited to the number of subawards given that the level of effort meets the needs of each subaward.
- Budget limits for total cost:
  - Budget limits for BIT/BYTE/KILO/MEGA modules are for total cost (direct + indirect costs).
- Proposal submission from international entities:
  - Pursuant to 42 U.S.C. 290c(n)(1), ARPA-H will prioritize awards to entities (organization and/or individuals) that will conduct funded work in the United States. Non-US entities are encouraged to collaborate with domestic U.S. entities.

Ask a Question!

https://solutions.arpa-h.gov/Ask-A-Question

ARPA-H

Important Reminders: Proposers' Day

- Proposers' Day Recording:
  - A recording will be posted to the ADAPT program webpage in the coming days, at https://arpa-h.gov/research-and-funding/programs/adapt

- Proposers' Day attendance:
  - You do not need to have attended Proposers' Day in order to submit a proposal.

Ask a Question!

https://solutions.arpa-h.gov/Ask-A-Question

Important Reminders: Technical Requirements

- Cancer types addressed by ADAPT:
  - Proposals responsive to ADAPT will address metastatic breast, lung, or colon cancers.
  - Proposers with an innovative solution for other cancer types may consider submitting a proposal to the ARPA-H Office-Wide Innovative Solutions Opening. See SAM.gov for more information. https://sam.gov/opp/0f71794fda5b47b68ee28139c2468fdb/view
- Previously developed biomarkers:
  - Existing biomarkers previously applied to patient data and have demonstrated significant predictive capability are welcomed. However, TA1.3 proposals must also address the development of mathematical, statistical, or computational ***methods*** for evolutionary cancer analysis and biomarker development for implementation into the broader program and a diversity of different therapies.
- FDA involvement:
  - The ADAPT team is working closely with the FDA. Performers who are selected for the program will subsequently work with our ARPA-H team and an FDA team for insights into the regulatory science supporting the evaluation of the new technologies.

Ask a Question!

https://solutions.arpa-h.gov/Ask-A-Question

Important Reminders: Technical Requirements

- Capabilities of proposers and teaming:
  - Proposals to TA2 need not address biomarker development capabilities as long as the clinical trial includes treatments that would benefit from the development of drug response biomarkers.
  - Teams with clinical capabilities who wish to team with biomarker developers may use the ADAPT teaming page at https://arpa-h.gov/research-and-funding/programs/adapt/teaming
  - Proposals to TA1 need not address clinical capabilities. TA1.3 applicants develop computational pipelines for efficient biomarker development across different therapies with multi-modal data.
  - Biomarker development teams who wish to team with clinical trial applicants may do so through the ADAPT teaming page at https://arpa-h.gov/research-and-funding/programs/adapt/teaming and together submit a single proposal addressing multiple TAs.
- Contract Research Organizations (CROs):
  - The ADAPT team will select a CRO to manage centralized clinical trial components and data collection. TA2 proposals should not include CRO costs in their budgets, nor should they include data storage and analysis costs, as these will be covered by the ADAPT program. CROs should not apply to ADAPT.

Ask a Question!

https://solutions.arpa-h.gov/Ask-A-Question

Thank you for attending ADAPT Proposers' Day!

Reminders:

- Submit your teaming request form (optional): https://forms.office.com/g/M0TUL36bPh

Teaming Link

- Submit a solution summary (optional, but highly recommended): due March 29, 2024, 10:00 AM ET.
- Submit a full proposal: due May 6th, 2024, 1:00 PM ET.

Ask a Question!

Questions Due: 3/22/24

https://solutions.arpa-h.gov/Ask-A-Question

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