

From Biology to Bedside to Health Systems Implementation

Making Precision Neuroscience Real

National Academy of Medicine Workshop
Precision Medicine in Neuroscience

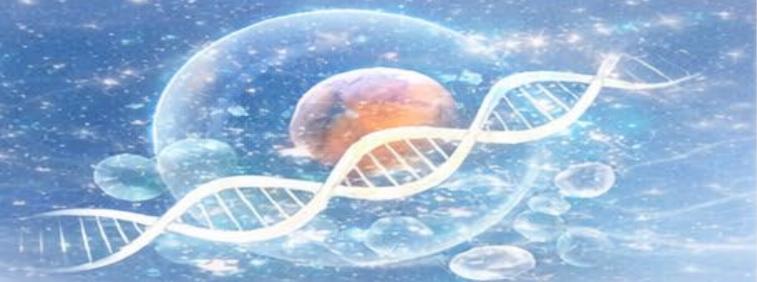
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AI Is Enabling Deeper Biological Insight at Scale

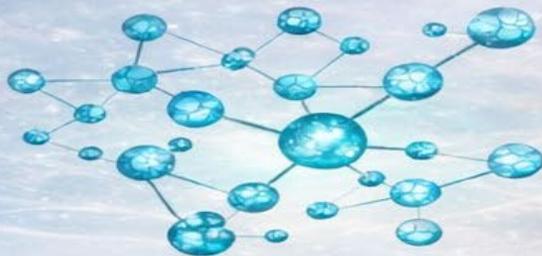
From cells to behavior — resolution is increasing across modalities



>15M cells
profiled

One of the largest
single-cell brain **Atlases**
across four CNS disorders

100K compounds
screened



>90K samples
analyzed

Mechanism-aligned
subtype stratification

Four CNS disorders
Defined by biological
signal, not symptoms



Five brain-behavior
dimensions identified

Psychosis deconvoluted
into measurable axes

Longitudinal biomarker change informs treatment adjustment
— and predicts progression.

Above data from Gayle Wittenberg, Bill Martin and Johnson & Johnson

Hope for the Future: High-dimensional human data define precision subtypes and inform novel endpoints — **BUT...**

MULTI-OMICS

Integration of multi-omics data using network models

PHENOTYPES

Real-world and digital phenotypes

MOLECULAR/FLUID BIOMARKERS

Quantitative, sensitive, reproducible biosignatures



IMAGING/FUNCTIONAL BIOMARKERS

Circuit dysfunction biosignatures



CLINICAL SYMPTOMS



PRECISION SUBTYPES

Patient subtypes most likely to respond to a given mechanism



PRECISION ENDPOINTS

Novel digital measures, biosignatures, surrogate endpoints

High-dimensional integration enables biological definition — **TRANSLATION REQUIRES VALIDATION.**

From Precision Promise to Translational Tension

Discovery is progressing. Validation and delivery pathways are still maturing.

PRECISION PROMISE



Multi-omics integration



Quantitative, reproducible biomarkers



Precision subtypes aligned to mechanism



Novel digital and biological endpoints

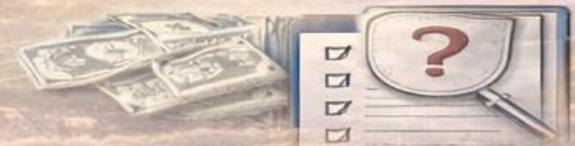
ADVANCE

VALLEY OF UNCERTAINTY
Translational Gap

MATURE

TRANSLATIONAL TENSION

- Few fully validated surrogate endpoints
- Limited consensus diagnostic thresholds
- Unclear reimbursement pathways
- Fragmented implementation infrastructure



VALLEY OF UNCERTAINTY
Translational Gap

**Our disorders share a common problem:
We still cannot routinely measure disease activity in living patients.**

Discovery is advancing faster than validation and system design.

From Bedside Discovery to Health-System Responsibility

ESTABLISHING the “Bedside → Health Systems” Mandate HEALTHCARE CONFIDENCE

MOLECULES

- Genomics
- Multi-omics
- Circuits



MOLECULES

PATIENT

- Diagnosis
- Stratification
- Prediction



PATIENT

CLINIC

- Treatment Selection
- Monitoring



CLINIC

HEALTH SYSTEM

- Workflow
- Reimbursement
- Workforce



HEALTH SYSTEM

POPULATION

- Outcomes
- Prevention
- Equity



POPULATION

Precision Medicine Responsibility

Ethical governance and data privacy guardrails

Biomarkers & Endpoints Mature With Therapeutic Confidence

SCIENTIFIC CONFIDENCE → REGULATORY CONFIDENCE → HEALTHCARE CONFIDENCE

Phase IIa — Signal Detection

- **Mechanistic biomarkers**
- Pharmacodynamic readouts
- **High sensitivity → practicality**
- Predict future clinical benefit

Scientists believe

Phase IIb / Early III — Clinical Meaning

- **Scalable** across sites
- Symptom & function endpoints
- **Translate biology → patient experience**
- Regulatory acceptance

Regulators believe

Phase III → Market — Healthcare Adoption

- **Relapse & hospitalization reduction**
- Functional recovery
- **Low clinical burden**
- Demonstrates economic value

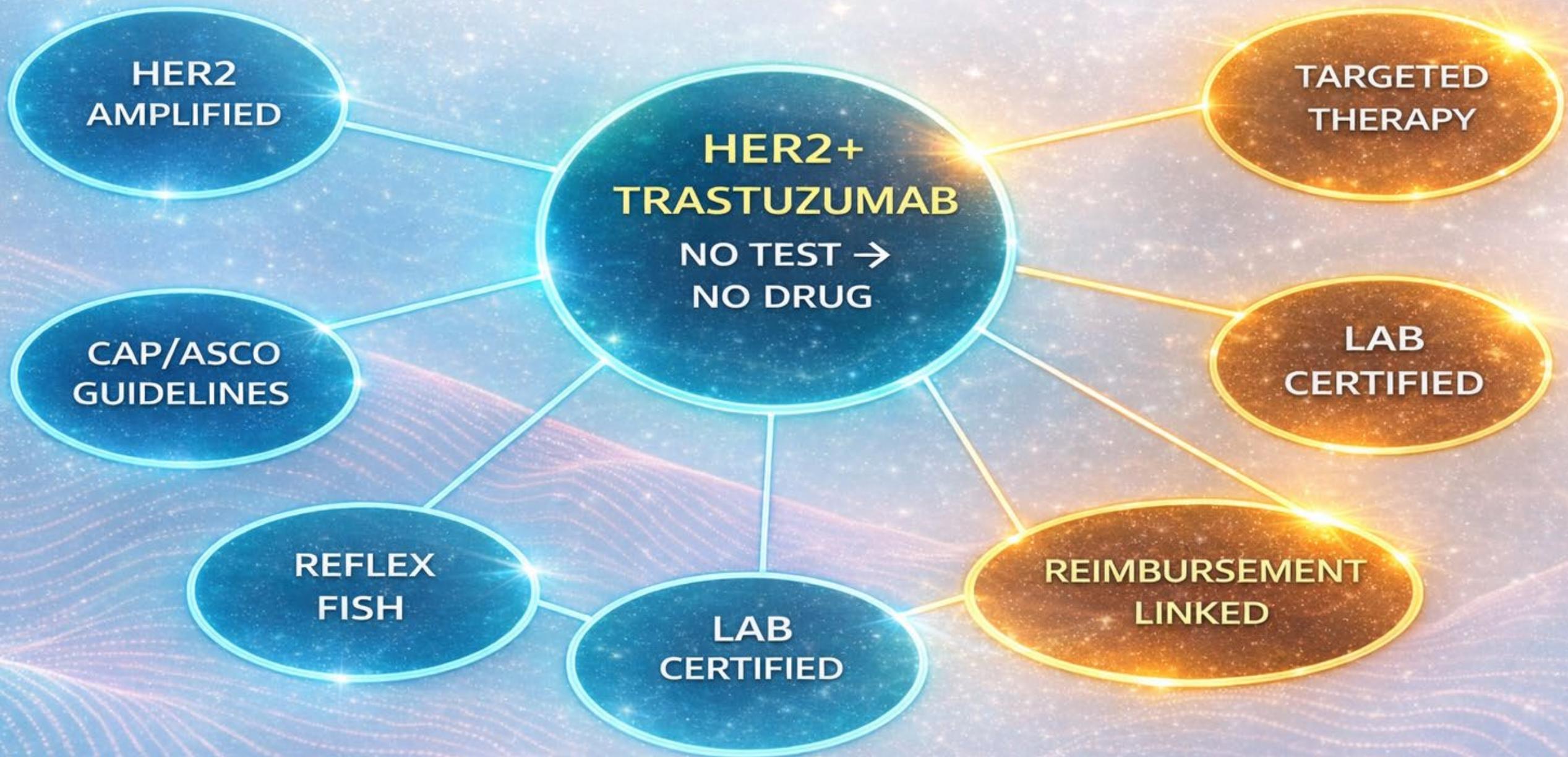
Clinicians believe

Payers believe

A discovery that does not change care delivery has not yet translated

Precision medicine in brain disorders succeeds only when it functions *inside* real systems.

HER2 — DIAGNOSTIC REGULATION ENABLED TRUST



From Discovery to Adoption: The Oncology Model

The system architecture behind routine precision care

- 1. Standardized Testing**
Biological measurement became routine
- 2. Guideline Integration**
Biomarkers embedded into care pathways
- 3. Reimbursement Alignment**
Payment reinforced testing and targeted therapy
- 4. Infrastructure & Workflow Integration**
Hospitals operationalized precision

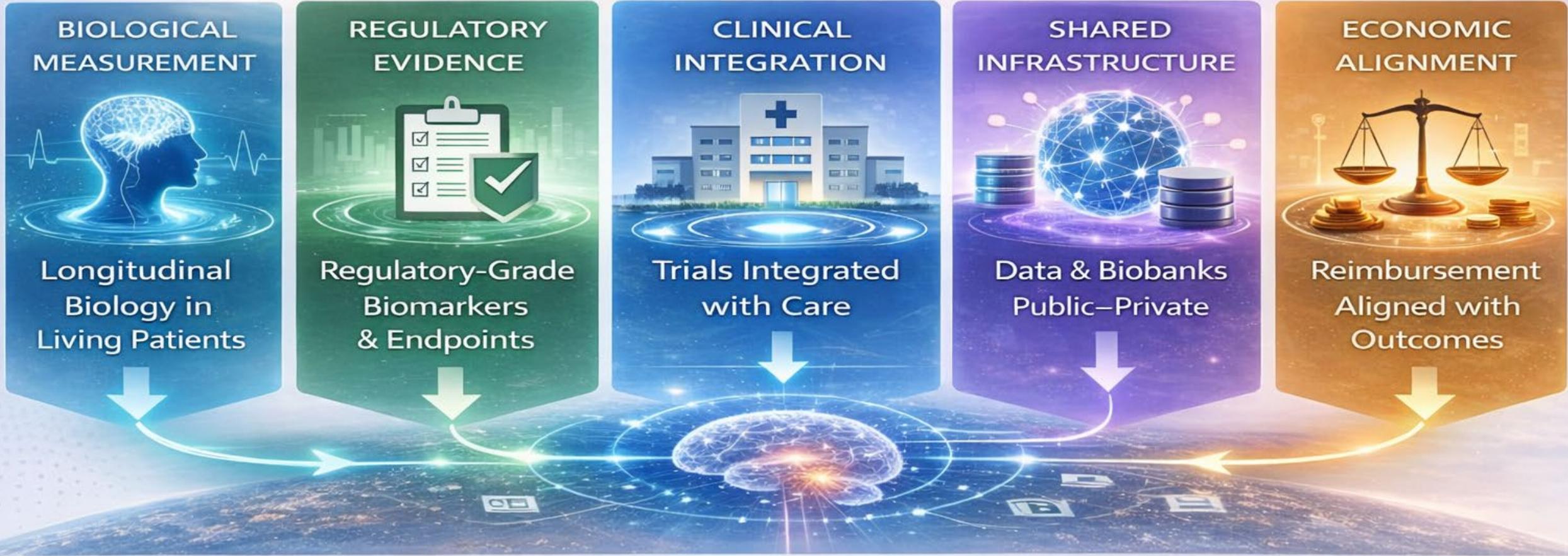


Precision oncology became routine after biology was embedded into systems.

Making Precision Neuroscience Routine Care

What the Field Must Build to realize the promise

What the Field Must Build to realize the promise



Precision Neuroscience → Routine Clinical Reality

The science is advancing. The infrastructure must keep pace.