



# Welcome

## CTTI's Disease Progression Modeling Recommendations & Tool Launch

Thank you for joining us!

This meeting is being recorded.

All participants are muted upon entry.

The presentation and slides will be posted on the CTTI website.

# Agenda

Time (EST)	Content	Presenter
12:00 PM	Welcome Remarks and Introduction to CTTI	Sara Calvert (CTTI)
12:05 PM	Disease Progression Modeling Impact in Medical Product Development	CJ Musante (Pfizer)
12:15 PM	Disease Progression Modeling Project and Recommendations Overview	Lindsay Kehoe (CTTI)
12:30 PM	Partner Perspectives	Karthik Venkatakrishnan (EMD Serono) Tiffany Westrich-Robertson (AiArthritis) Theo Zanos (Northwell Health) Efthymios Manolis (EMA)
12:55 PM	Closing Comments	Lindsay Kehoe (CTTI)
1:00 PM	Adjourn	

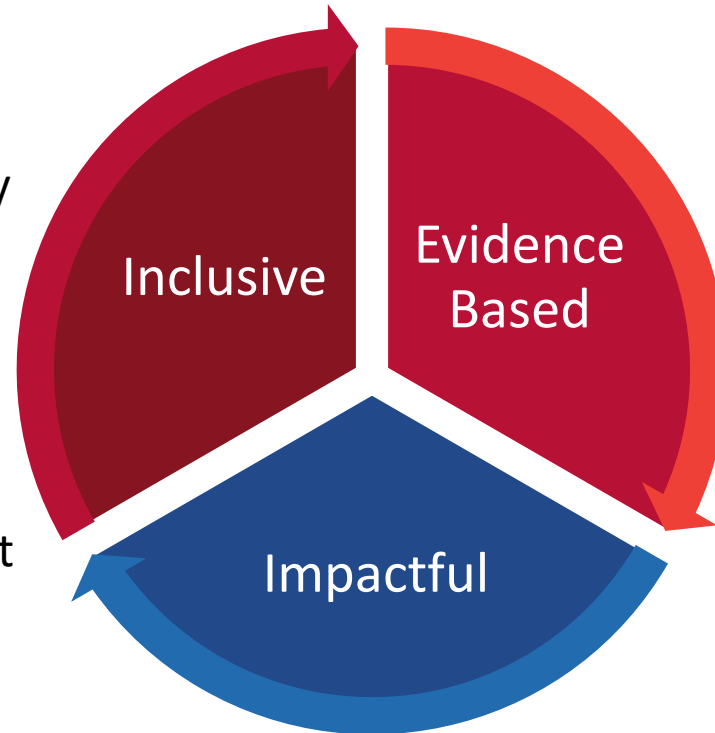
# The Clinical Trials Transformation Initiative (CTTI)

## MISSION

To develop and drive adoption of practices that will increase the quality and efficiency of clinical trials.

## VISION

A high-quality clinical trial system that is patient-centered and efficient, enabling reliable and timely access to evidence-based therapeutic prevention and treatment options.



## PUBLIC-PRIVATE PARTNERSHIP

- Co-founded in 2007 by FDA and Duke University
- Active collaboration with +500 individuals and groups
- All materials are freely available

## SCOPE

Focus on clinical trials of FDA-regulated medical products, recognizing that clinical trials are international and acting as a collaborative global citizen.

# What We Do

➤ Provide **leadership** across the Clinical Trials Enterprise through vision-setting, collaborating, convening, measurement



**Topic-focused convenings**  
**FDA public meetings**  
**State of Clinical Trials**

➤ Produce evidence-supported, consensus **recommendations and tools** to improve quality and efficiency of clinical trials



**30+ Recommendations**  
**80+ Implementation Tools**  
**50+ Case Studies**

➤ Drive innovation through **strategic communication and engagement** efforts that support organizational and overall system transformation



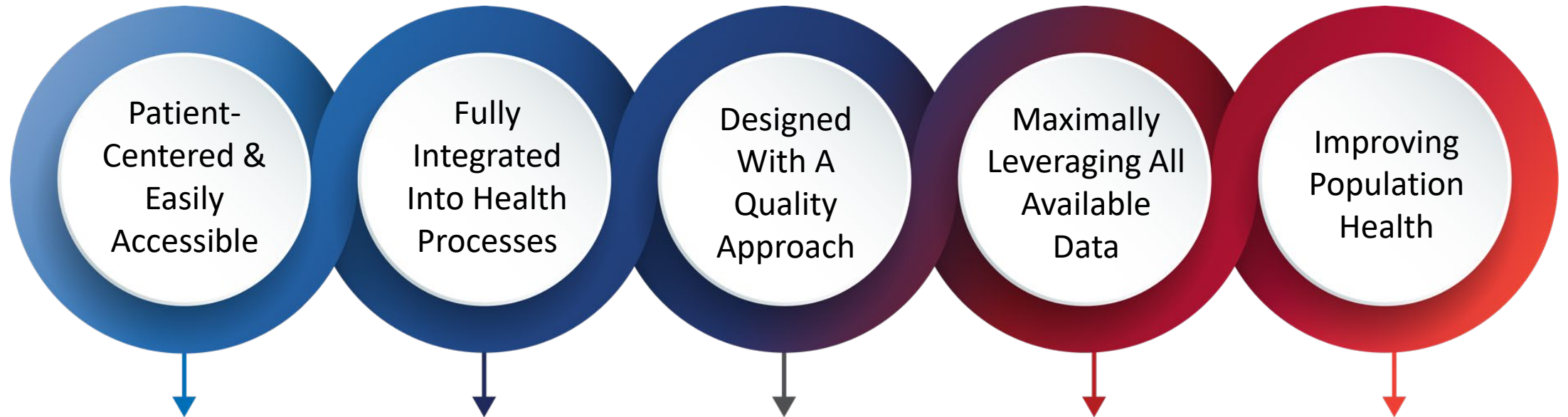
**30,000+ downloads per year**  
**40,000+ media impressions / yr**  
**550+ presentations & workshops**  
**130+ articles & publications**

# CTTI Membership



# Transforming Trials 2030

By 2030, clinical trials need to be:



A critical part of the Evidence Generating System

**CJ Musante**

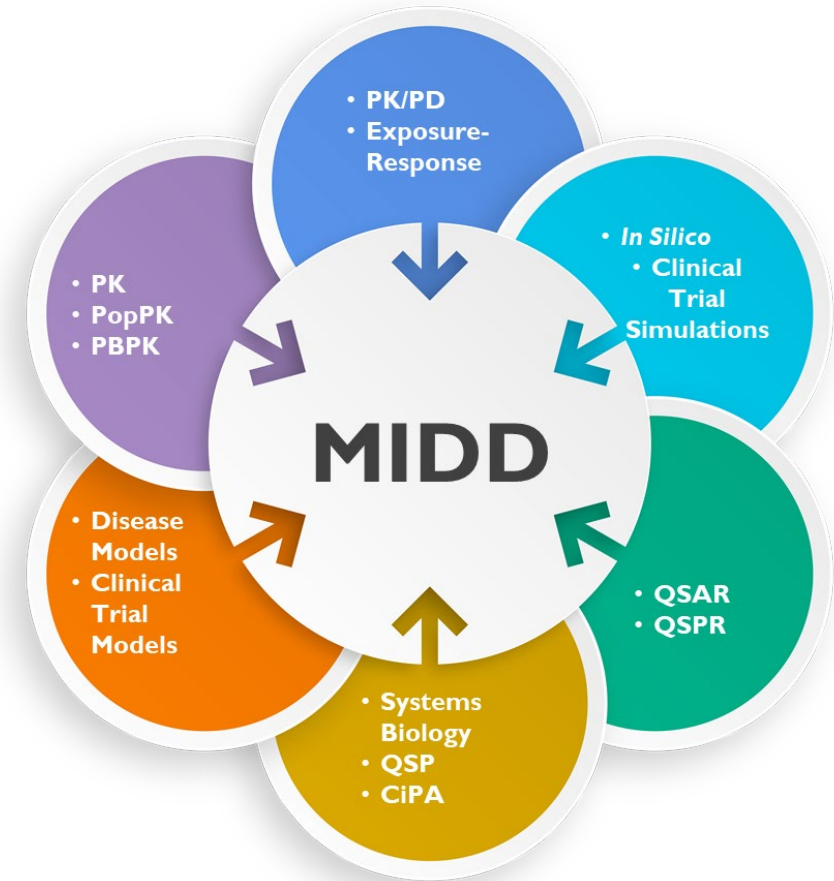
VP Scientific Research

Pfizer



# The Issue

- Many model and simulation forms contribute to Model Informed Drug Development (MIDD)
- The use of some model forms (e.g. PKPD) have matured more than others
- ***The value of disease progression modeling (DPM) to impact medical product development has yet to be fully realized***
- ***DPM: A mathematical model that quantitatively describes the time course or trajectory of a disease***

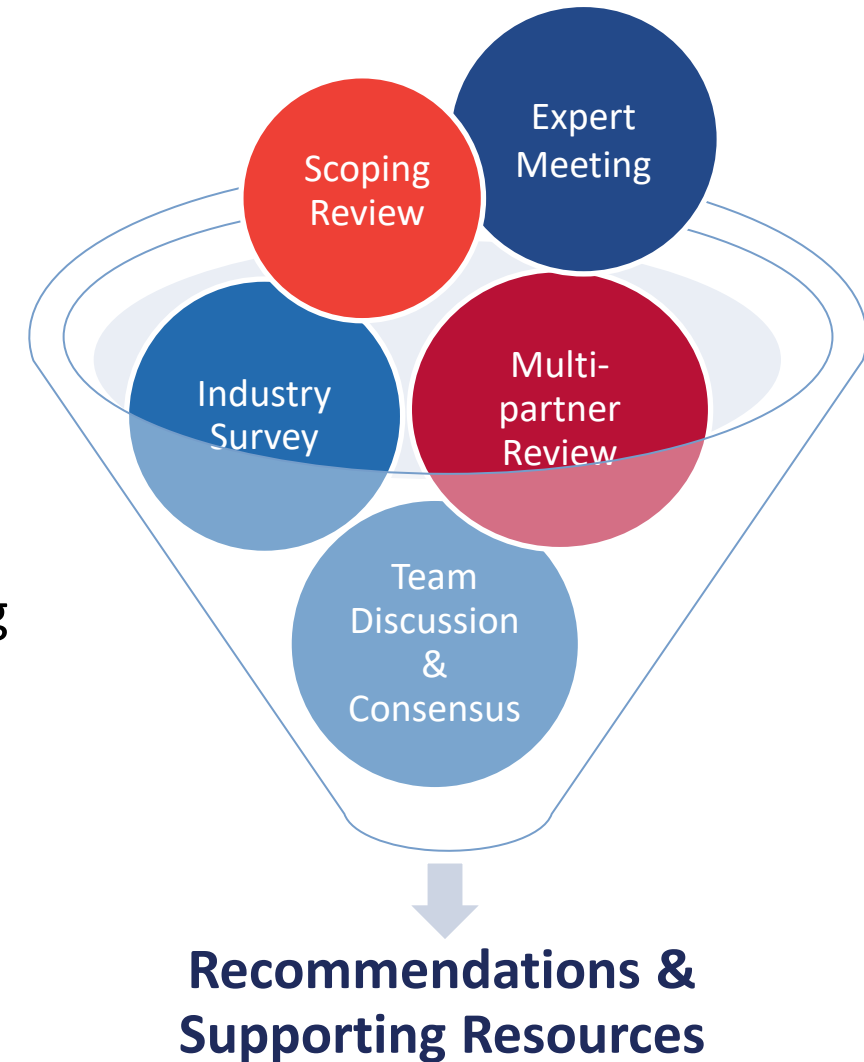


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# CTTI's Disease Progression Modeling (DPM) Project

## Overview

- **Purpose:** Clarify how DPM can advance decision making\* throughout the medical product development lifecycle
- **Objectives:**
  - Describe DPM and its current applications/ contexts of use (COUs)
  - Highlight examples of where DPM is valuable in advancing decision making
  - Develop and disseminate recommendations that address the unique value of DPM and best practices for implementation



\*decision making includes trial design, regulatory, development, and business decision making

# Multi-Partner Project Team

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## Team Leads

Bruce Burnett (NIH)  
Phil Green (Patient Advocate)  
Raj Madabushi (FDA)  
Karthik Venkatakrishnan (EMD Serono)

## Executive Committee Champion

Theodore Lystig (BridgeBio)

## Project Manager

Lindsay Kehoe (CTTI)

## Social Science Team

Summer Starling (CTTI)

## Team Members

Steve Berman (BIO)  
Jenny Chien (Eli Lilly and Company)  
Tony Jiang (Biogen)  
Jiang Liu (FDA)  
Qi Liu (FDA)  
Mark Palmer (Ansys)  
Efthymios Manolis (EMA)

## Communications Lead

Hannah Faulkner (CTTI)

## Acknowledgements:

Malidi Ahamadi (Amgen), Scott Kollins (Holmusk), John Roberts (CSL Behring), Zifang Guo (Merck), Matus Hajduk (Mind Medicine), Lin Lin (Biogen), and Diana Jones (Duke), Brian Perry (Duke)

Herb Pang (Genentech)  
Etienne Pigeolet (Novartis)  
Tiffany Westrich-Robertson (AiArthritis)  
Reem Yunis (RAYS Partners Consulting)  
Theo Zanos (Northwell Health)

## Event Planner

Susan Morris (CTTI)

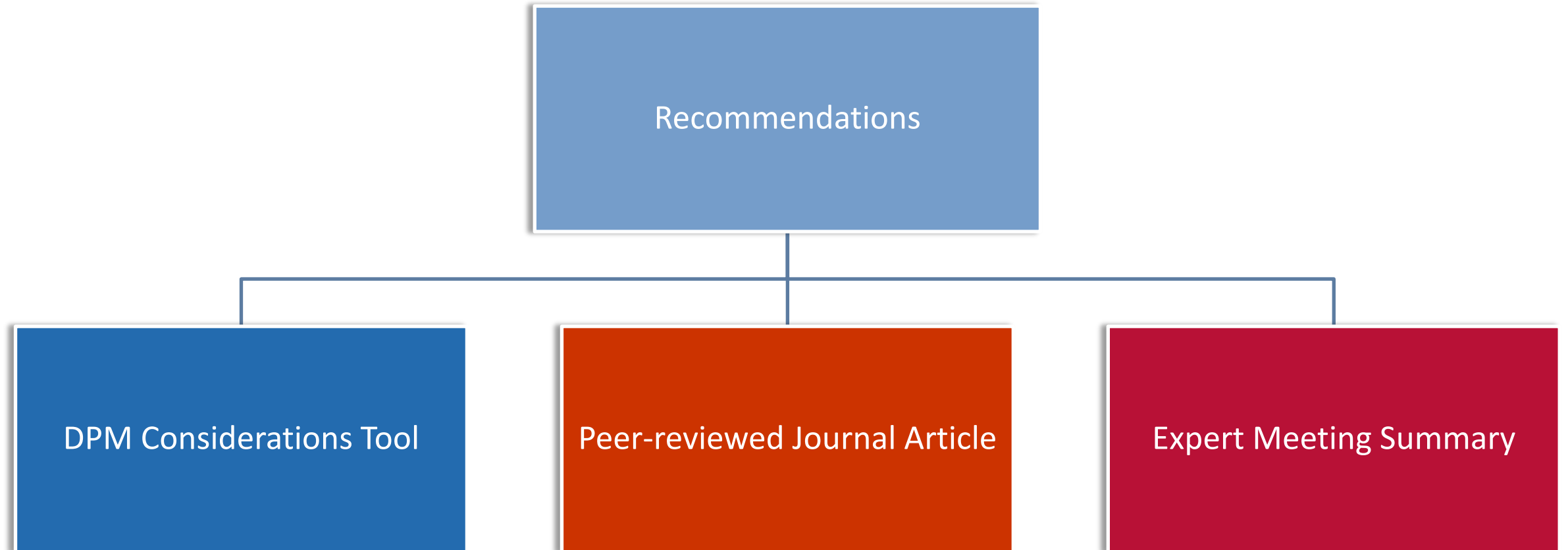
## Recommendations Advisory Committee

Rich Dima (Northwell Health)  
Brian Hare (Vertex)  
Ala Elhelali (Johns Hopkins)  
Belinda Cowling (Ionis)  
Shu Chin Ma (Critical Path)  
Jeffry Florian (FDA)  
Fang-Shu Ou (Mayo)  
Aaron Mann (CRDSA)  
Jin Jin (Genentech)  
Ted Rieger (Pfizer)

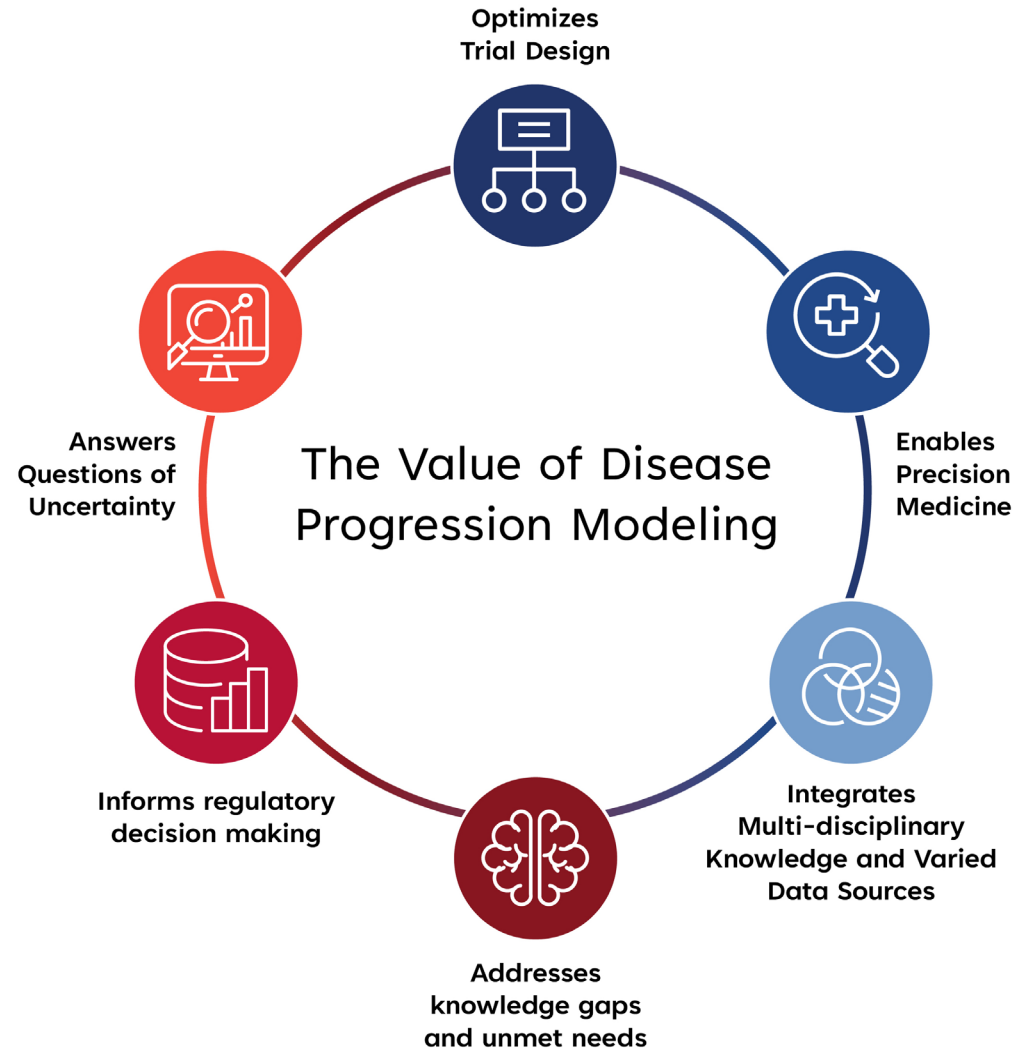
## Writer and Design

Sav Miller (Duke)  
Jonathan Cook (Duke)

# Project Deliverables



# The Value of Disease Progression Modeling



# DPM Recommendations

- **Who: Decision makers** in medical product development
  - e.g., CMOs, heads of innovation or translational medicine, project team leads, regulatory affairs
- **Why: Decision makers need development strategy questions answered** (internal resources, evidence prioritization, ROI, etc.)
- **What: Provides unique benefits of using DPM** in medical product development, when it should be considered over other tools or approaches, & considerations for **how to incorporate it**.

## CTTI Disease Progression Modeling Recommendations

**Introduction:**

The following recommendations aim to highlight the unique benefits of using disease progression modeling in medical product development, when it should be considered over other tools or approaches, and provide considerations for what is needed and how to incorporate it.

These recommendations are intended for decision makers in medical product development, including chief medical officers, heads of innovation or translational medicine, leadership roles in therapeutic areas, project team leads, and regulatory affairs. Cross functional leaders often encounter similar questions around internal resources, evidence prioritization, and return of investment when making medical product development decisions. These recommendations will help decision makers ask the right questions of modeling experts and other subject matter experts to recognize the value of DPM and inform decisions about its implementation.

**What is disease progression modeling?**

A disease progression model (DPM) is a mathematical model that quantitatively describes the time course or trajectory of a disease.<sup>2</sup>

Disease progression modeling can link disease progress, treatment effect, and/or patient behavior to clinical trial outcomes and inform decision making throughout the medical product development process.<sup>2,3</sup>

**The Value of Disease Progression Modeling**

 Optimizes Trial Design	 Addresses knowledge gaps and unmet needs
 Enables Precision Medicine	 Informs regulatory decision making
 Integrates Multi-disciplinary Knowledge and Varied Data Sources	 Answers Questions of Uncertainty

While some modeling and simulation approaches such as pharmacokinetic/pharmacodynamic (PK/PD) and physiologically based pharmacokinetic (PBPK) modeling are well recognized as enabling clinical trials and model-informed drug development, the potential of disease progression modeling to improve the quality and efficiency of medical product development has yet to be fully realized.

**How can disease progression modeling impact medical product development?**

The use of a DPM integrates multi-disciplinary knowledge and data from different sources, including translational, clinical trial, and real-world data to:

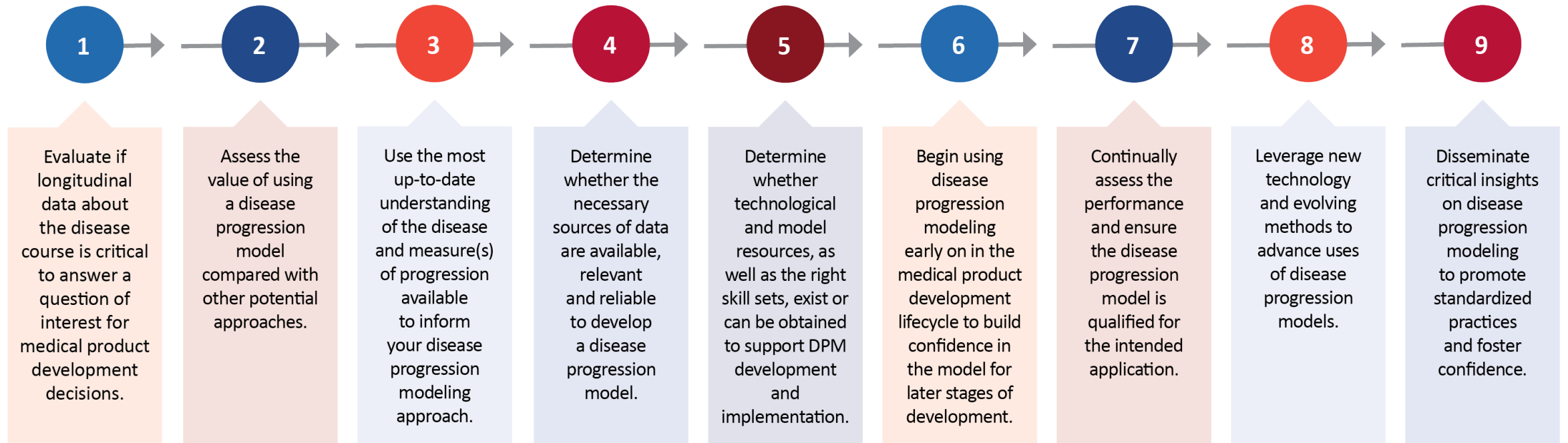
- **Impact trial efficiency**, especially for trials with diseases that progress over a long duration of time, for which running a clinical trial during that period of time is costly and burdensome.
- **Answer questions of uncertainty**. It can account for and provide clarity around heterogeneity across patients and at an individual level.
- **Tailor trials towards precision medicine**. Recognizing that diseases progress differently, across populations and in different stages within a patient, DPM can address individual factors or covariates affecting progression to **enable trial design optimization** and tailor trials towards precision medicine (e.g. stratify populations or adapt treatment plans).
- **Address unmet needs and knowledge gaps**, including supplementing for a small population size with digital twins in rare disease trials, or stratifying a population for patient enrichment for diseases with heterogeneous phenotypes (e.g. autoimmune and neurodegenerative diseases), or supporting a limited understanding of the disease by modeling disease course for endpoint selection.
- **Inform regulatory decision making**. DPM contributes to the totality of understanding of a medical product's benefits and risks, helping to advance its development and support regulatory decision-making both in premarket product review and post-market product assessment.

CTTI further describes the value of DPM, its current applications, and opportunities for uptake in the following article published in Clinical Pharmacology & Therapeutics called [The Potential of Disease Progression Modeling to Advance Clinical Development and Decision Making](#).

 CLINICAL TRIALS TRANSFORMATION INITIATIVE

CTTI Disease Progression Modeling Recommendations | 1

# Recommendations Summary

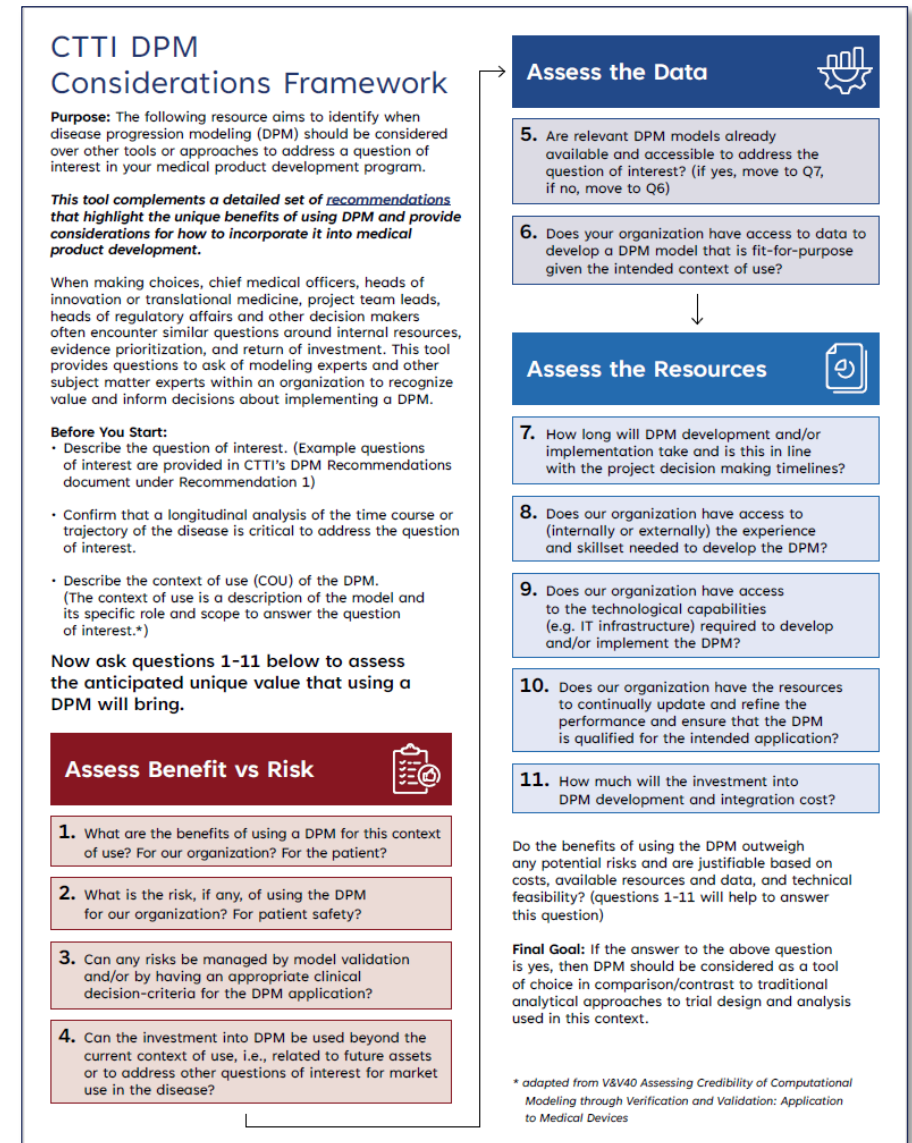


# DPM Considerations Tool

## Overview

- Complements the recommendations
- Identifies when DPM should be considered over other tools or approaches
- Provides questions to ask of modeling and other subject matter experts to inform decisions about implementation

Note:



# Partner Perspectives



**Efthymios  
Manolis**  
EMA



**Karthik  
Venkatakrisnan**  
EMD Serono



**Tiffany Westrich-  
Robertson**  
AiArthritis



**Theo Zanos**  
Northwell  
Health

Moderator: **Lindsay Kehoe, CTTI**

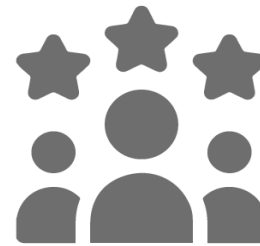
# Thank You



Project Team



Survey Participants

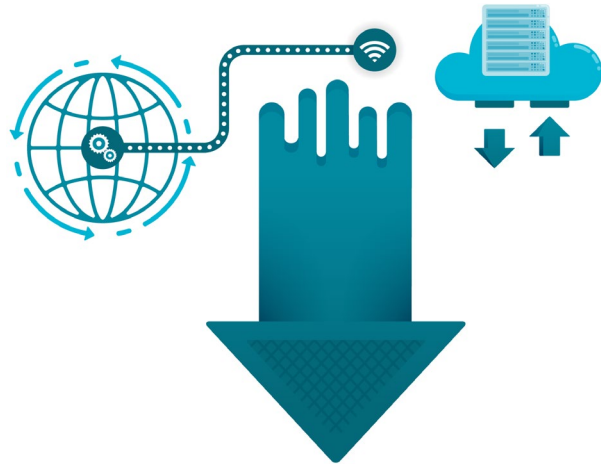


Expert Meeting  
Attendees



Recommendation  
Advisory Committee

## Download the Recommendations & Tool



Available Now on the CTTI website:

<https://ctti-clinicaltrials.org/our-work/novel-clinical-trial-designs/disease-progression-modeling/>

## Share and Learn How Others Implement CTTI Resources



Available Now through the CTTI website:

[https://connects.ctti-clinicaltrials.org/case\\_study\\_exchange](https://connects.ctti-clinicaltrials.org/case_study_exchange)



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TRIALS  
TRANSFORMATION  
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@CTTI\_Trials

Lindsay Kehoe

Senior Project Manager, Lead Emerging Programs

# THANK YOU

[www.ctti-clinicaltrials.org](http://www.ctti-clinicaltrials.org)