

---

# Opportunities and Challenges of Comparative Oncology from a Pharma Perspective

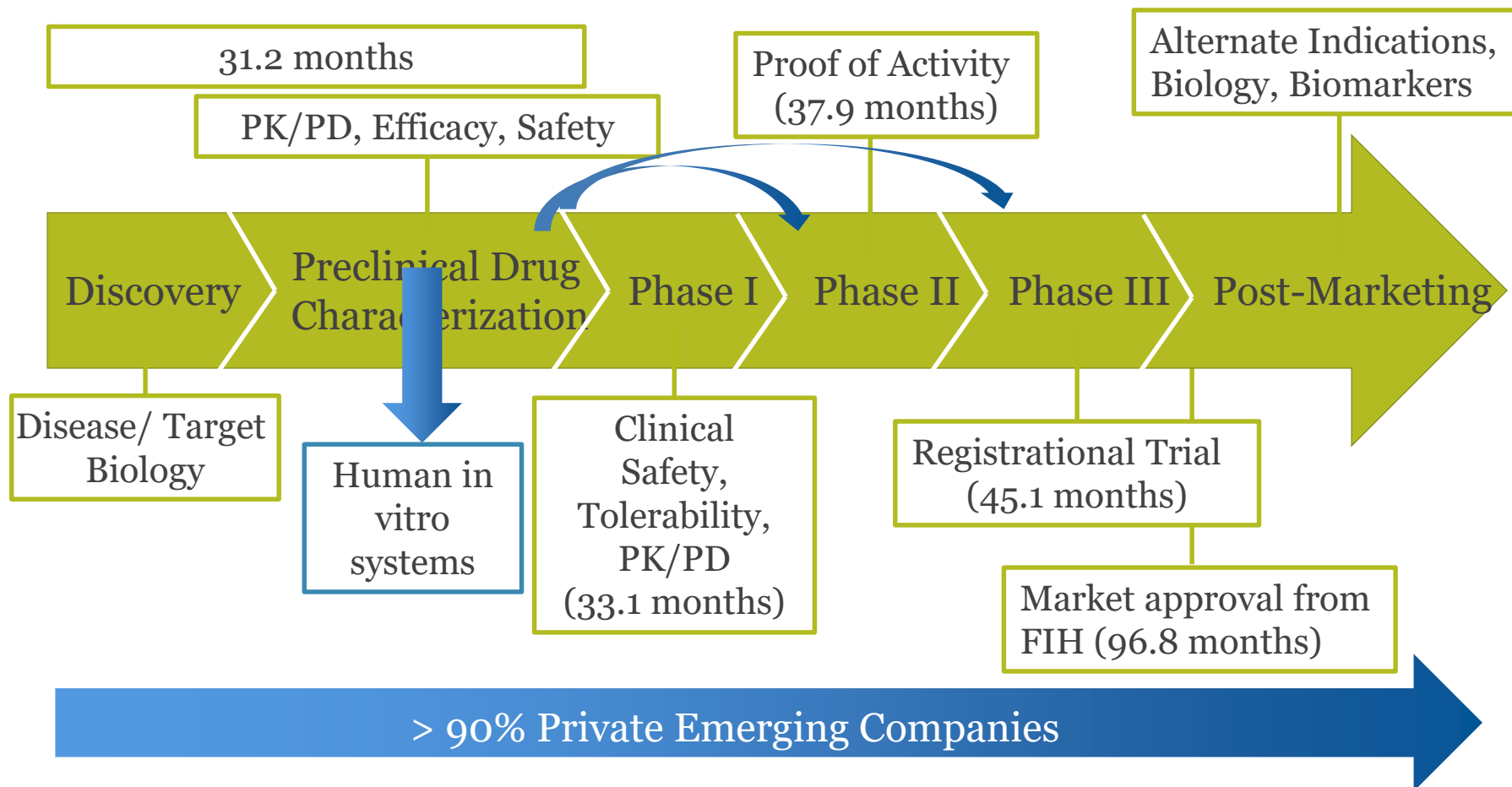
Tanja S. Zabka, DVM, DACVP, DSP

on behalf of the Comparative Oncology Team

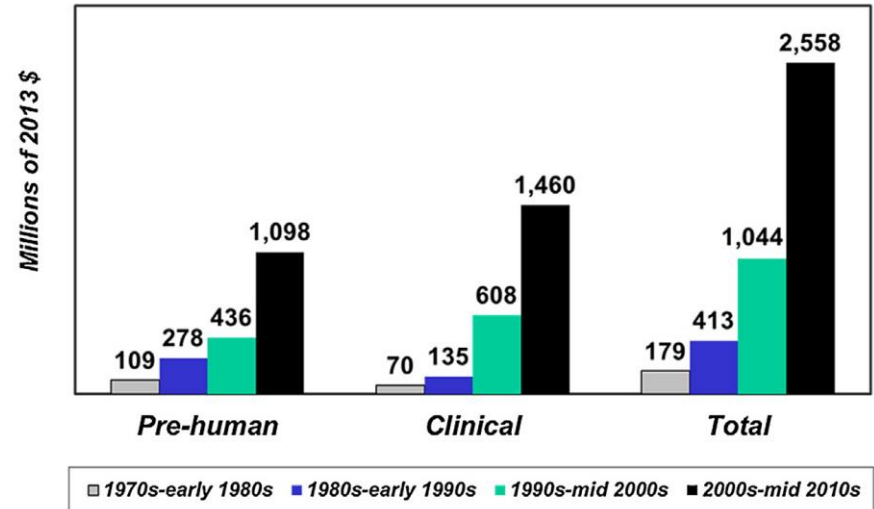
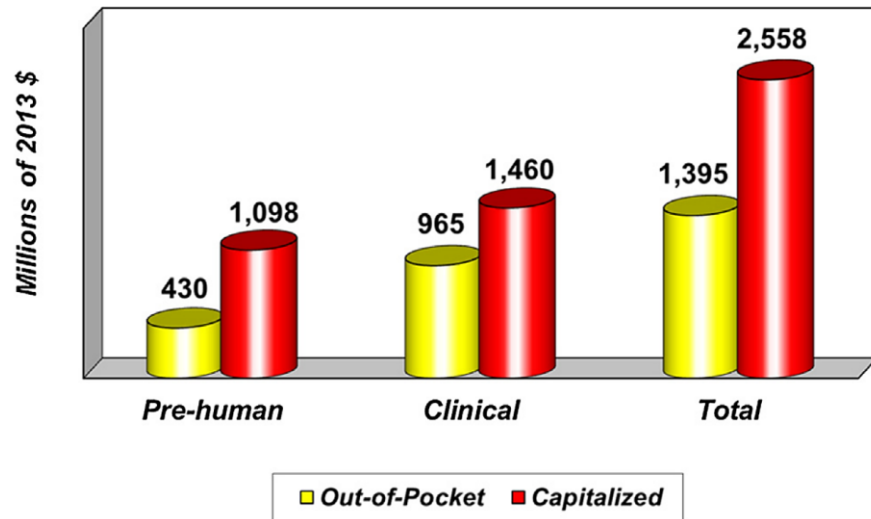
C3O Symposium, Durham NC, 15Feb2019

# The drug development paradigm, today and tomorrow

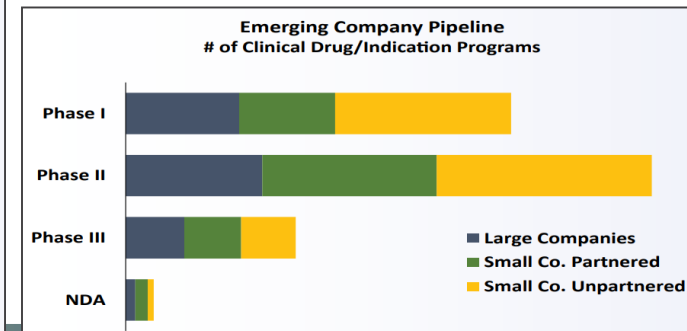
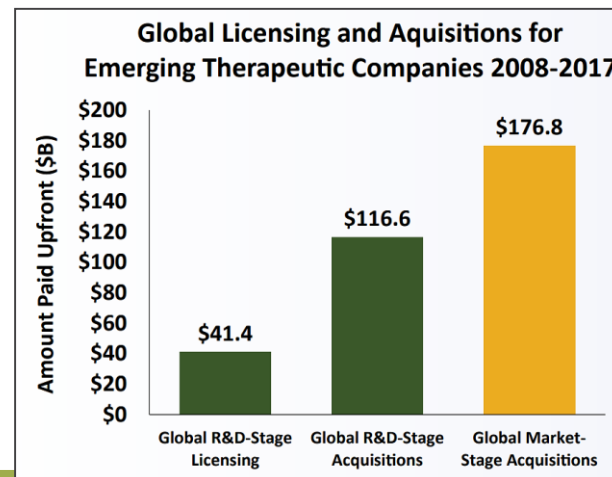
Features growing alliances among firms of all sizes, growth of a small firm sector and consolidation among large firms



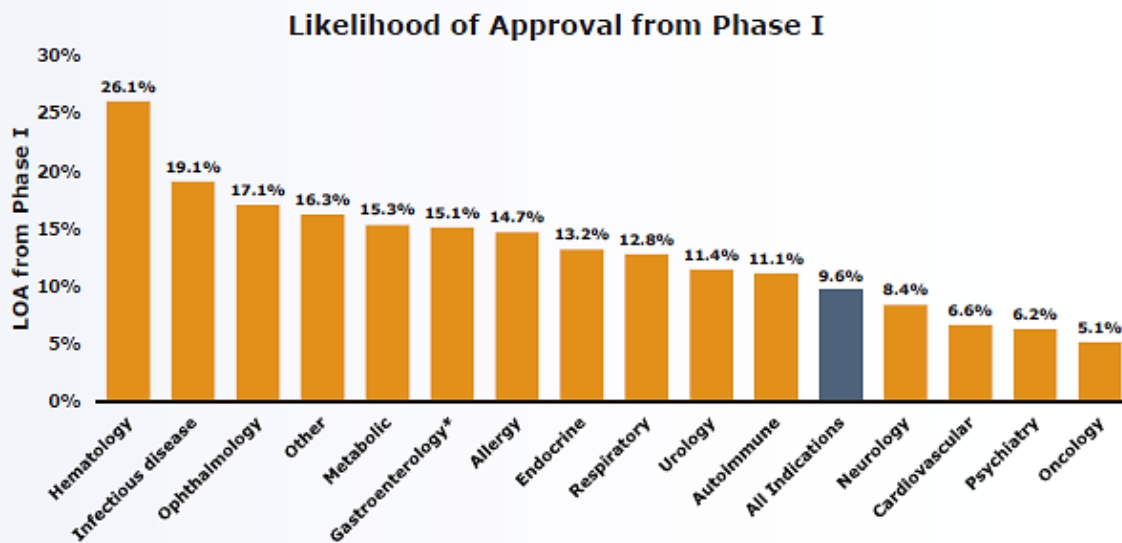
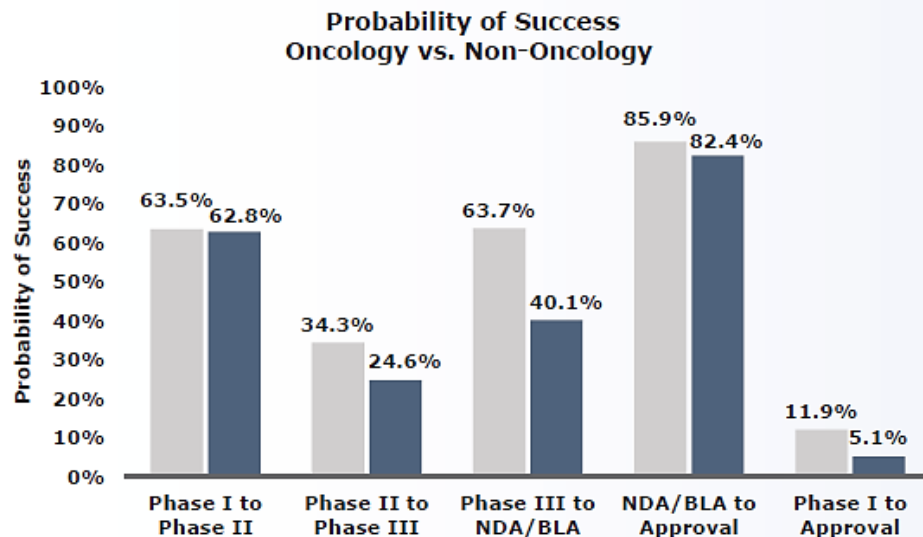
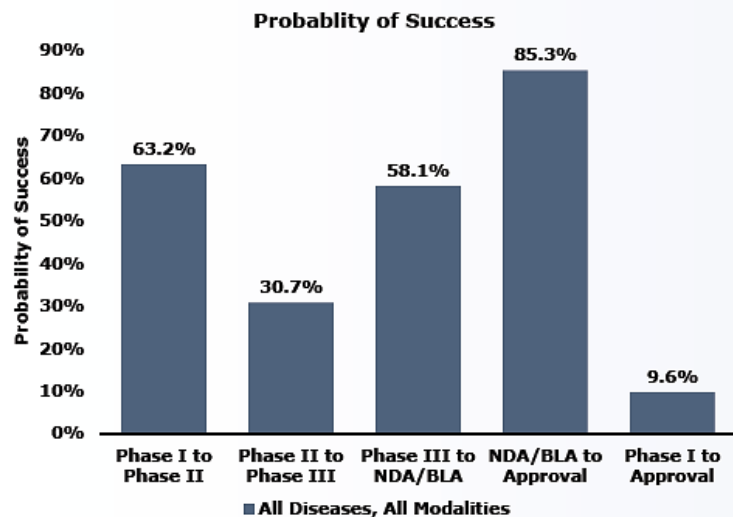
# Average cost of developing a new drug, today and yesterday



In constant dollars

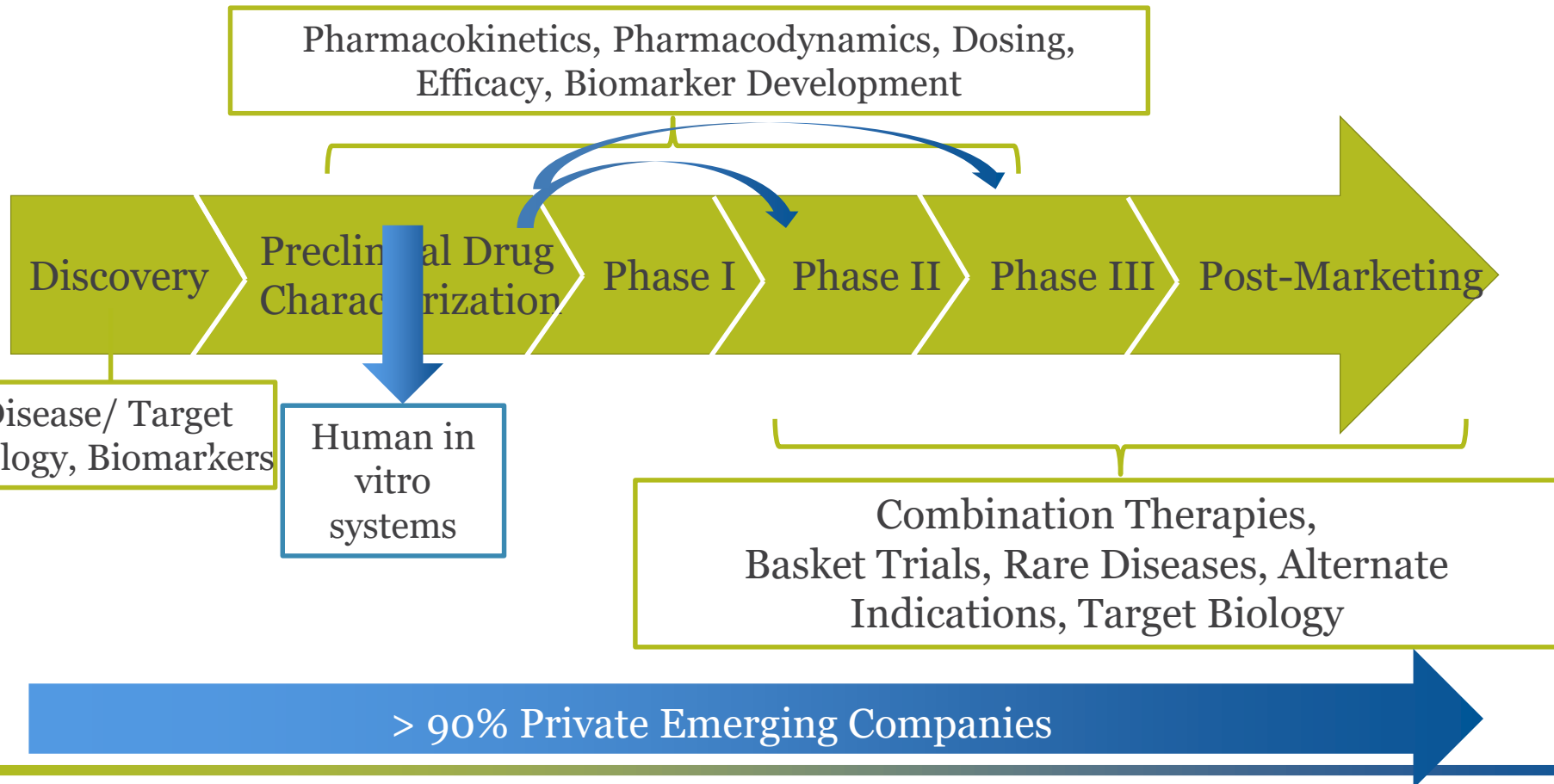


# Attrition in drug development



# Opportunities for comparative oncology

Must demonstrate that the biology of the canine system is superior to mouse in translation to human and that we also can achieve comparable PK/PD profile  
→ ~ 2.5 yrs nonclinical & ≤ 8 yrs clinical time line



# Challenges for comparative oncology

## Understanding target biology in the dog

- Limited publically available genomic and mutational load data
- Needed to use in all drug development stages

## Cross species relevance of large molecules and new therapies

- Veterinary & human drug companies have limited business case
- Personalize health care is increasingly human and individual specific
- Small molecules may be decreasing in focus

## Canine specific tools

## Agility and speed

## Internal and consortia building

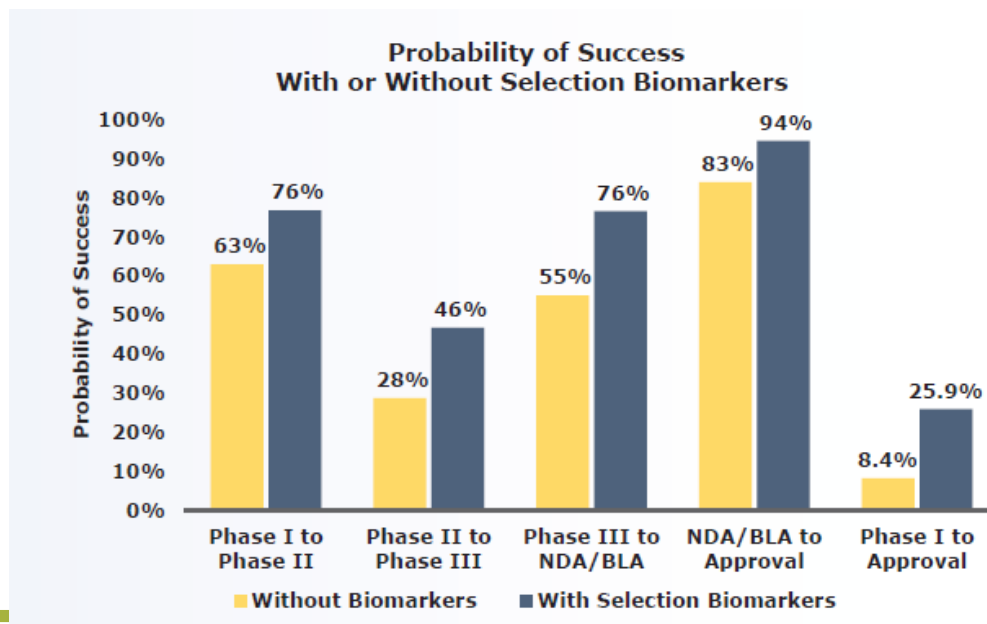
# Targeted therapy

Targeted therapy is a mainstay in drug development

Patient heterogeneity influences drug responses

- e.g. differences in oncogenic drivers, immune status, mutational load

Understanding target expression and roles in disease are critical for studying therapeutic interventions



# Comparative new therapies

## **Large molecules, such as therapeutic antibodies, are a mainstay in oncology**

- Important as single agents and in combination therapies
- Many antibodies are first line therapies

## **Antibodies must have similar affinities and PK profiles across species**

- Target conserved epitopes across species

## **Large molecules are antigenic**

- Requires species-specific backbones
- Anti-therapeutic antibodies limit efficacy
  - Rapid drug clearance

## **Relevance of canine patients for newer therapies**

- Genetherapy, personalized vaccines...



# Canine specific reagents

Access to canine specific reagents and assays is critical for all stages of comparative oncology

- Investigative tools to understand canine biology, genomics, & mutational load
- Pharmacodynamic assessments
- Predictive and pharmacodynamic biomarker development

Increasing availability

- Continues to be dwarfed by mouse and human reagents

Requires independent validation for the dog

- Human and rodent assay may not translate
- Validation requires canine-specific controls

# Agility



Drug development requires rapid decisions to move programs forward

- Continual push to inform next development phase

Requires agility in legal, study design, recruitment, data generation, and data interpretation

- Integrative and big data solutions are critical

Race between preclinical and clinical data

- Data can only be informative if it is timely

# FAQs of comparative oncology team

What is the underlying molecular biology in canine cancer?

How do you account for breed differences in dosing and pharmacokinetics?

What happens if there is a safety finding in a comparative oncology study?

Does the drug engage the canine target ~ human target?

Do you have comparable tools to interrogate pathway modulation and immune system response?

Does this require our internal resources?

What is the intellectual property agreement?

What is the enrollment rate / time to data?

Dogs get cancer?



# Opportunities for consortia

## **Increased industry collaborations and data sharing demonstrate the inability to go it alone**

Open Science & Robust informatics solutions → meaningful data at scale

Shared sense of urgency → impact

Cross-functional → leverage expertise

Creative fiscal solutions → overcome limited budgets

Strategic alignment → advance the field together

Passionate

Practical



# Thank You

## **GNE/Roche Comp Onc Team**

Noel Dybdal  
Joshua Webster  
Lily Ackerman  
Maryellen Allen  
Rochelle Ellenburg  
Stephen Gould  
Bert Lum  
Dale Miles  
Elaine Murray  
Melissa Schutten  
Leah Schutt  
Dietrich Tuerck

## **GNE Collaborators**

Mark Merchant	Mark Davis
Aaron Fullerton	Joanne Adamkewicz
Dawn Coulburn	Jeanne Cheung
Liling Liu	Sophia Chang
Alan Deng	Maryam Tabrizizad
John Moffat	Marc Ragasa
Tony Contreras	Silvia Kimpfler

## **External Collaborators**

Matthew Breen  
Steven Dow  
Will Eward  
Deborah Knapp  
Mark Heffernan  
Brant Inman  
Amy LeBlanc  
Christina Mazcko  
Kristy Richards  
Douglas Thamm  
Wendy Shelton  
Rod Page

*Doing now what patients need next*