

## Industry – Academia collaboration in the AHSC

Frank S Walsh



# Pharma R&D is being squeezed from both ends

## Increasing expectations

Wall street wants double digit growth

The patient wants better medicines

The regulator wants safer medicines

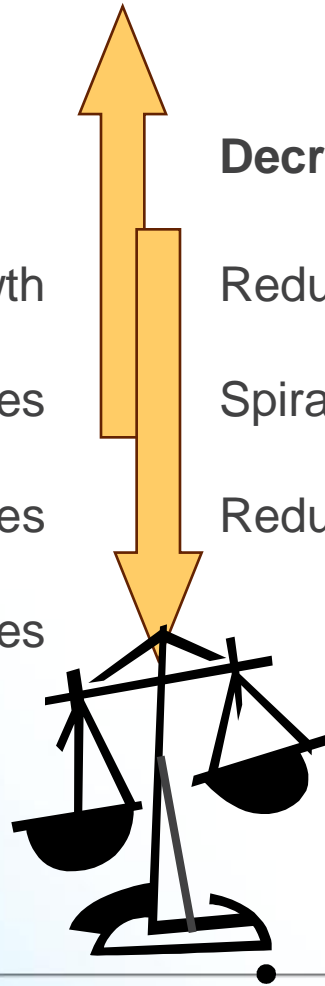
The govnt, wants cheaper medicines

## Decreasing productivity

Reduction in NCE approvals

Spiraling R&D costs (\$900MM/NCE)\*

Reduced return on marketing spend\*

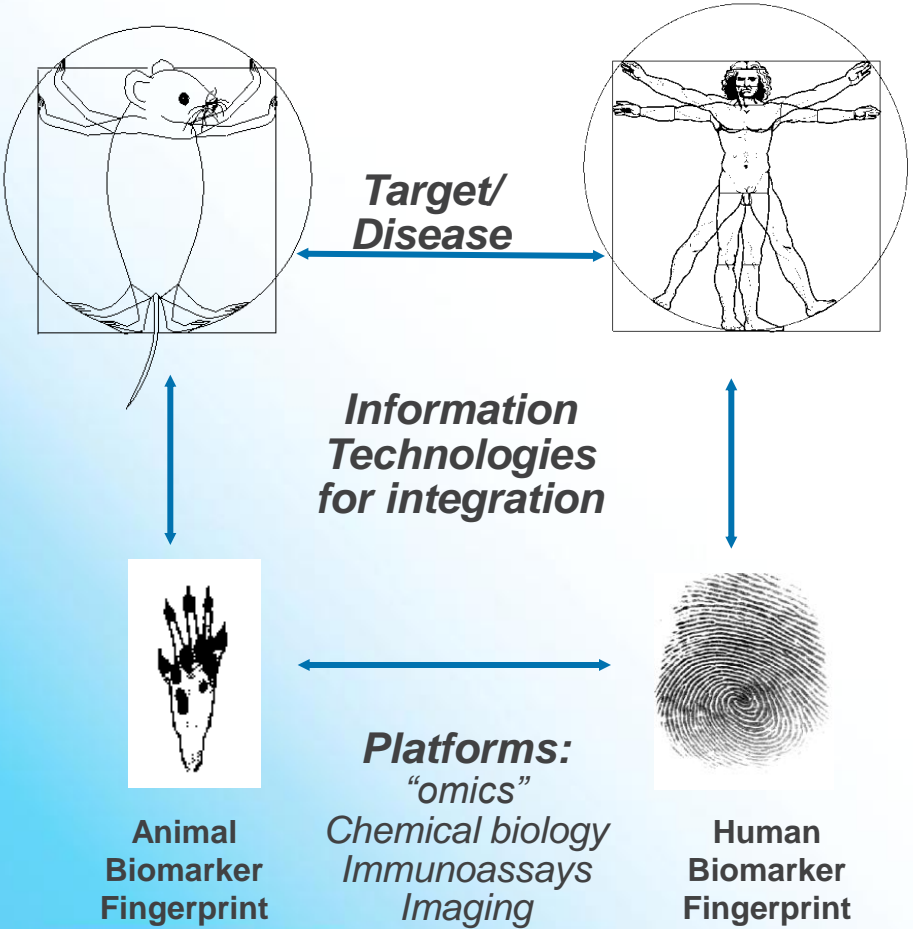


# Lack of efficacy and safety issues are the major causes of Phase 2 attrition



Both the proportion & absolute number of compounds that prove safe & effective in humans is declining, despite an increasing number that are safe and effective in animal models

# So how can the most promising drug candidates be identified earlier in development?

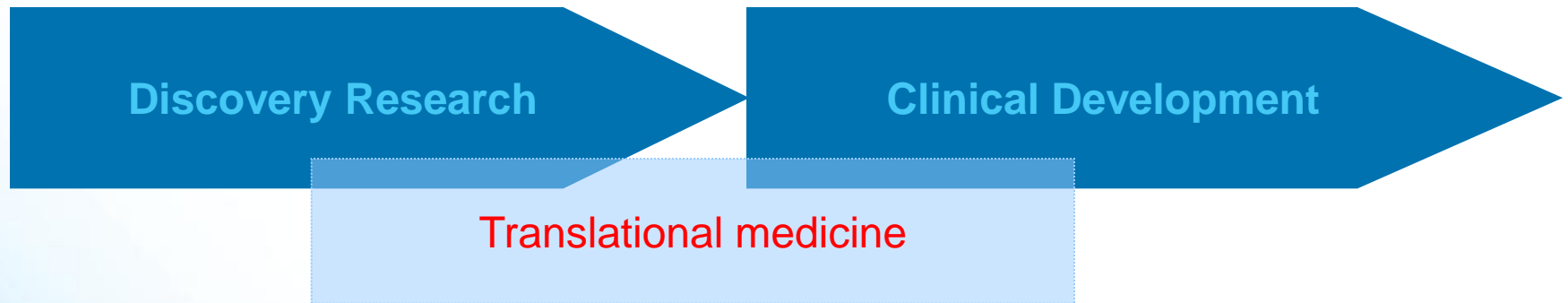


## Translational Medicine

- ✓ Animal models do not accurately predict the effects of drugs in man
- ✓ Discover and develop biomarkers to measure the effects of a drug in humans
- ✓ Better predict drug safety and efficacy in man

# Translational Medicine bridges the gap between pre-clinical and clinical studies

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- ✓ A scientific discipline that bridge the gap between preclinical and clinical studies
- ✓ Allows us to understand the likely behavior of experimental medicines in humans
- ✓ Enables cost-effective determination of efficacy & safety through use of biomarkers

# Academia and Pharma differ in their views of Translational Medicine

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## *Academic view...*

- ✓ Discovering new drug targets
- ✓ Developing HTP capacity
- ✓ Developing drugs for orphan diseases
- ✓ Any clinical academic research and not generally linked to drug studies.

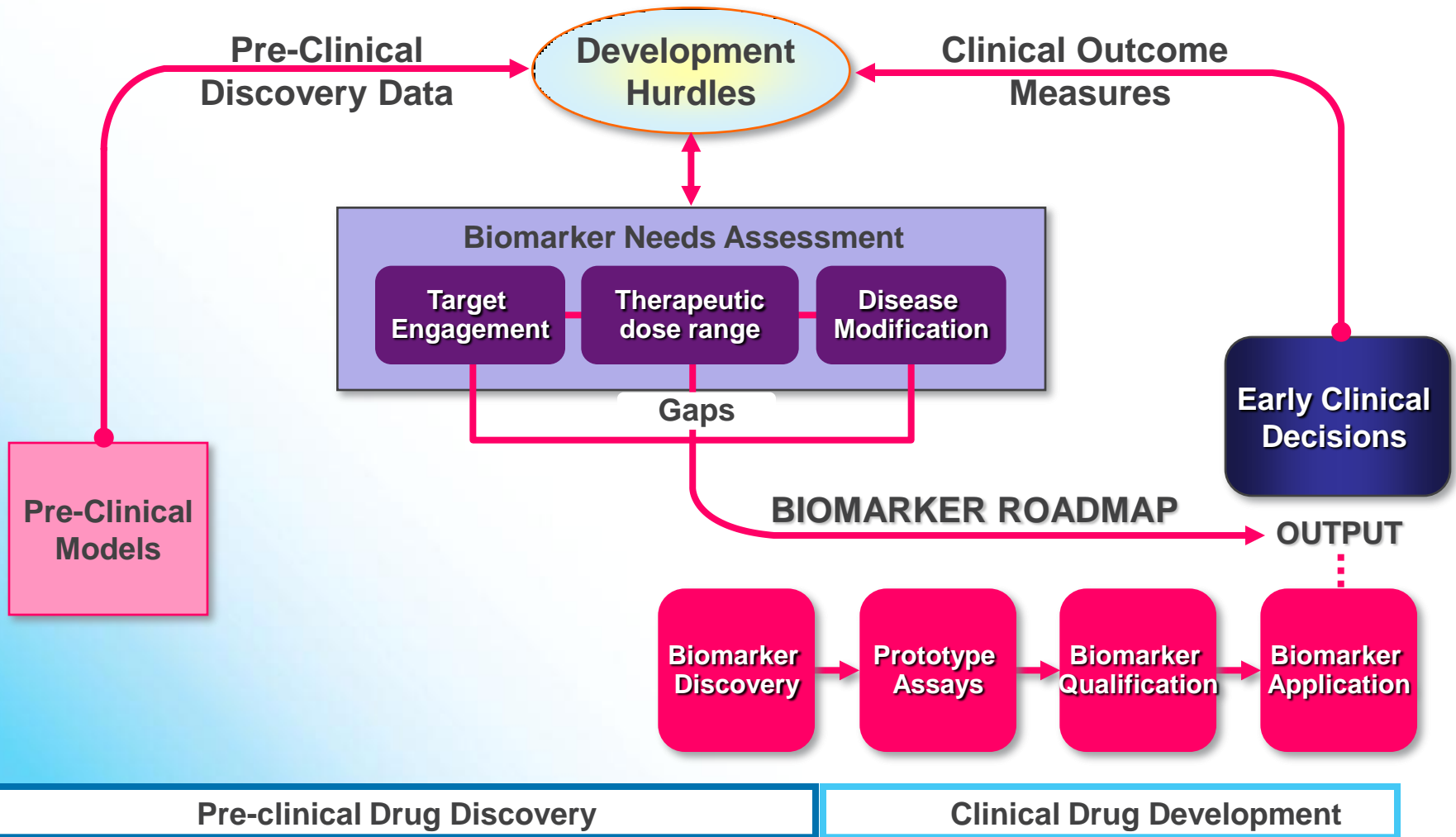
## *Pharma view...*

- ✓ About Biomarkers not Drug Discovery
- ✓ Enriched patient populations for enriched POC
- ✓ Much can be done by contract research.
- ✓ Biomarker needs to be validated for decision making POC

**Both need to modify their positions and develop mutual understanding built on trust and respect.**

# Translational Medicine

*From a Drug Development perspective*



# Biomarkers are the key to success, and serve a number of purposes

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**Biomarker is a quantifiable biological measure that correlates with a physiological, pathological or clinical observation**

- ✓ Interaction between compound and target
- ✓ Relationships between target and disease
- ✓ Mechanism based toxicities
- ✓ Patient response to compound

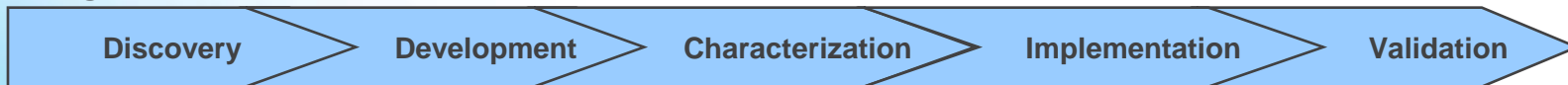
# To impact on phase 2 (POC), studies must begin as early as possible.

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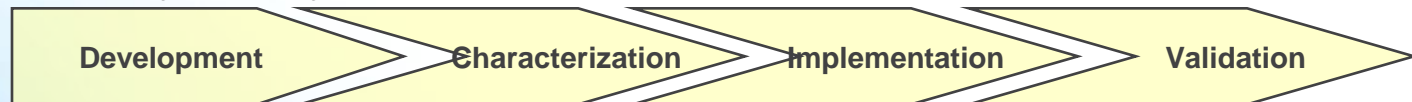
## Drug Discovery & Development Stages



## Target & disease biomarkers



## Efficacy, safety & patient selection biomarkers

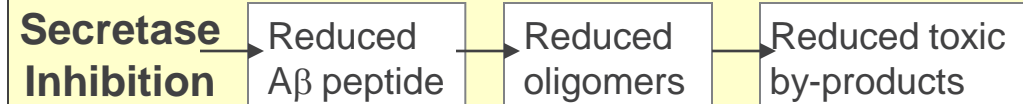


*The time and resource involved in the successful use of biomarkers is greatly under-estimated*

# Case Study 1: Biomarker roadmap for a $\gamma$ -secretase inhibitor for Alzheimer's disease

Phase 2 POC: ADAS-cog insensitive, studies are long, costly, and patients on placebo continue to decline

## 1. Plasma and CSF biomarkers

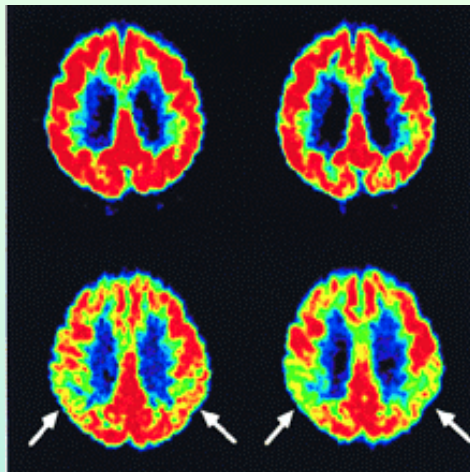


## 2. Mouse and human FDG-PET

Enhanced glucose uptake (neuronal activity)

Normal Memory  
No APOE-4

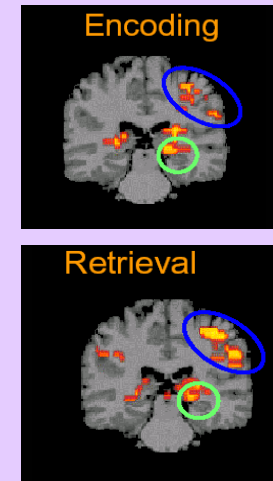
Normal Memory  
(APOE-4)



Small et al., 2000

## 3. Spatial memory with fMRI

Improved cognition and hippocampal activity

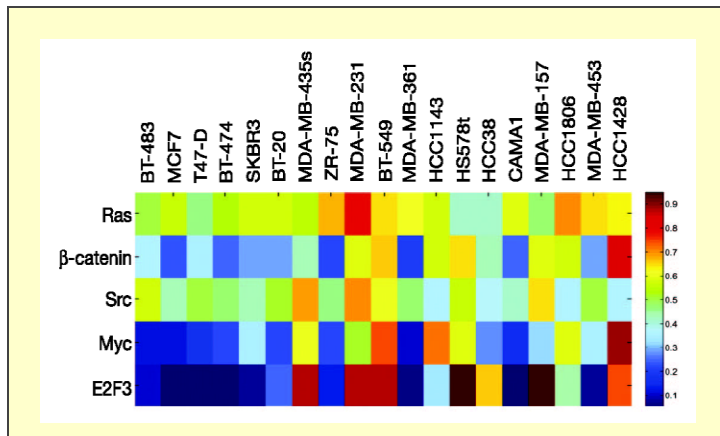


(Parslow et al, 2004)

# Case Study 2: Predicting sensitivity to targeted therapy in patients cancer

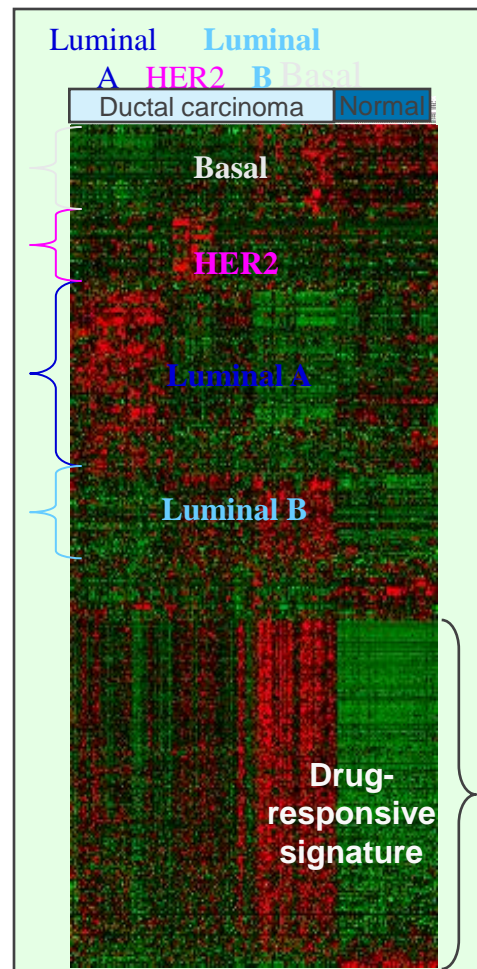
Phase 2 POC: Cancer is heterogenous and driven by different oncogenes, difficulty identifying responders

## 1. Identify drug response signatures in appropriate cell line

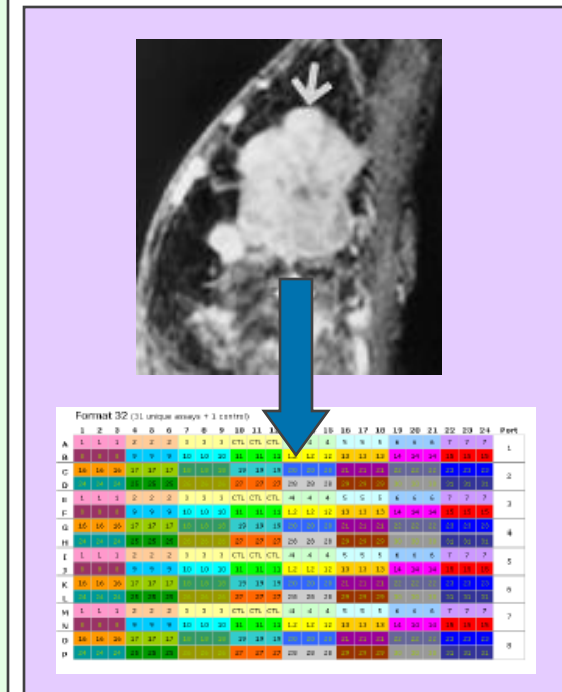


Sorlie et al, 2003; Bild et al, 2006

## 2. Identify tumor subtypes expressing drug-response signatures



## 3. Profile tumors on low density array to identify potential responders



# Academic/industrial collaboration is key to the success of drug development

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**No single pharmaceutical company or university has the necessary breadth and depth of expertise & resource**

NATURE REVIEWS | DRUG DISCOVERY VOLUME 4 | NOVEMBER 2005 | 891

## Finding improved medicines: the role of academic–industrial collaboration

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*Jaye Chin-Dusting, Jacques Mizrahi, Garry Jennings and Desmond Fitzgerald*

NATURE REVIEWS | DRUG DISCOVERY VOLUME 4 | OCTOBER 2005

## Anticipating change in drug development: the emerging era of translational medicine and therapeutics

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*Garret A. FitzGerald*

N Engl J Med 353;15 October 13, 2005

## Translational and Clinical Science — Time for a New Vision

Elias A. Zerhouni, M.D.

# **AHSCs can benefit enormously from Pharma.**

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**World class expertise in many areas of science ( big science)**

**Access to cutting edge technology and platforms.**

**Access to tool compounds and drugs that will give new clinical insights**

**Excellent in vitro and in vivo Pharmacology**

**A culture of teamwork.**

**Ability to set realistic goals and drive projects to conclusions on time and on budget.**

# **Pharma can benefit enormously from AHSCs**

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**Pharma views clinical development as a process not a science.**

**Pharma physicians generally have limited specialist medical training.**

**Regulatory and marketing considerations (the Target Product Profile) drive clinical programmes not science.**

## **A new collaborative model is needed**

**Builds on AHSCs access to well characterised patient populations.**

**Availability of outstanding academic physicians.**

**Access to Experimental Medicine capabilities.**

# In 2006 I sponsored a unique collaboration – the TMRC based on the AHSC concept.

A pan-Scotland research collaboration devoted to translational science and biomarker development



Translational  
Medicine  
Research  
Collaboration

**Wyeth**  
Research



**NHS**  
SCOTLAND

# The TMRC/AHSC works on projects sponsored by both Wyeth and Academia



**Wyeth**  
Research



## Study Sponsorship

- ✓ Studies split between Wyeth & Academia
- ✓ Wyeth is sole corporate partner – will channel TMed studies to TMRC
- ✓ Governance bodies will include Academic / Clinical partners, NHS, Scottish Enterprise and Wyeth

## TMRC Study Distribution

Majority ~ Non-drug

Minority ~ Drug

## Study Type

- ✓ Majority of programs are studies focused on Biomarker ID
- ✓ Exploratory studies with Wyeth compounds will also be pursued

# This is not a funding body grant scheme – it is more structured and governed

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## Grant

## Collaboration

## Contract

Idea originated by investigator

Research plan peer-reviewed

Full project costs covered by funding body

Research plan modified at investigators discretion

IP and data owned by investigator

Results published at investigator's discretion

# Nor is it as rigid as a fee for service contract

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Grant

Collaboration

Contract

Idea originated by company  
Research plan approved by company  
Full project costs paid by company  
Research plan modified by permission  
IP and data owned by company  
Results published with company approval

# This is a true collaboration with peer-review and management from all partners

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Grant

Collaboration

Contract

**Ideas derived jointly and individually**

**Research plan peer-reviewed**

**Project costs paid by company with government infrastructure support**

**Research plan modified by mutual agreement**

**Background IP protected with shared ownership of joint IP and data**

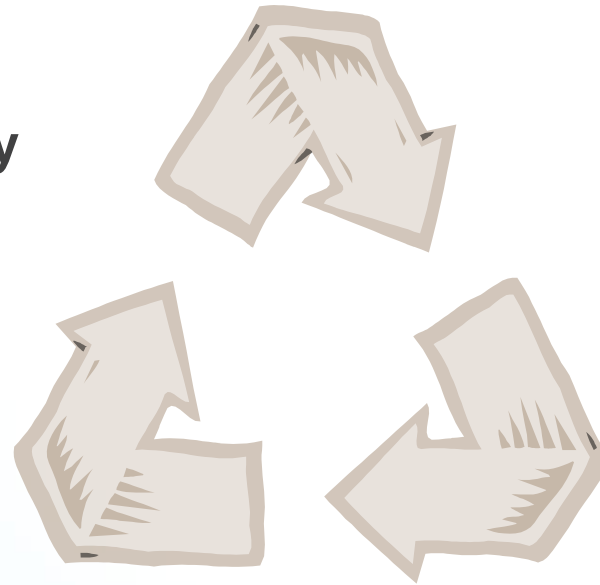
**Results published with TMRC approval**

# The scientific program utilizes three approaches

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## Human exploratory clinical studies

Disease patients  
Normal populations  
Drug, non-drug cohorts



## Biomarker research and Discovery

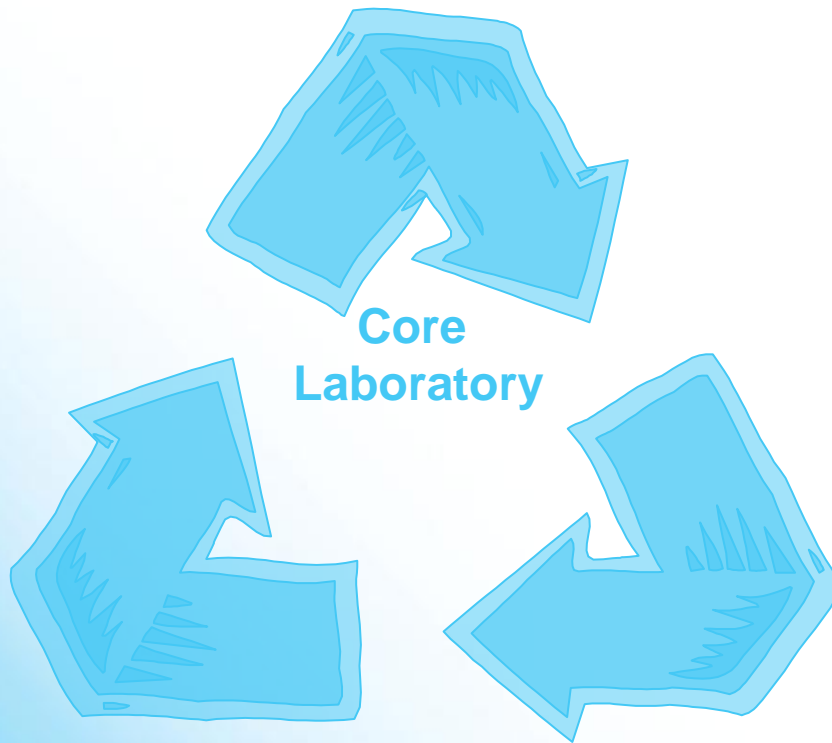
Clinical & preclinical samples  
Efficacy, toxicity & disease stratification

## Biomarker validation and clinical assay development

↕  
Diagnostic development

# The core laboratory acts as a centralized facility for standardization and industrialization

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**Biomarker assays**

**Develop standard procedures**

**Validate analytical methods**

**Extensive QC standards**

**Data repositories and integrity**

**Collaboration-wide**

# The TMRC/AHSC can help overcome major impediments to new biomarker development

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## Universities

Diffuse research activity  
Competing individual interest  
Inadequate resource

## Wyeth

Diffuse research activity  
Secondary to core business  
Inadequate resource

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## Diagnostics

Slow start up  
High cost of discovery/development  
Difficulty in predicting winners

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## TMRC/ AHSC Model

- ✓ Correct expertise & resource
- ✓ Time & cost savings
- ✓ Focused, collaborative activity

# The collaboration allows all parties to participate in this emerging discipline of T Med.

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“Personalized  
medicine”

“Biomarkers”

“Proof of  
mechanism”

“Individualized  
medicine”

“Surrogate  
endpoints”

“Pre-clinical to  
clinical”

## ***For industry...***

Better translation of therapeutic approaches into humans  
Earlier readouts of POC and decreased cycle times.

## ***For academia...***

Better understand human disease  
Unlock power of collaborating across Universities

## ***For NHS***

Maximise value of clinical infrastructure.  
Faster translation to patients

# A number of factors made Scotland an attractive base for this type of collaboration

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- ✓ **Stable and static population**
- ✓ **A single healthcare provider**
- ✓ **University / NHS network**
- ✓ **Health informatics – patient identifiers, disease data registries etc**
- ✓ **Established tissue banks**
- ✓ **World-class pre-clinical and clinical research base**
- ✓ **Shared IP and one stop shop agreements**

# Success from the partnership is anticipated in a number of ways

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## ***Research...***

- ✓ Identification/validation of novel biomarkers
- ✓ New animal and human experimental models
- ✓ A better understanding of human pathobiology
- ✓ Generation of peer-reviewed publications
- ✓ Increased funding opportunities

## ***Commercial...***

- ✓ Shared collection of ideas & IP
- ✓ Economic growth in the life sciences industry
- ✓ New diagnostic tools
- ✓ Increased number of novel and successful therapies
- ✓ Better patient care

# The TMRC/AHSC model has proven to be mutually beneficial

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- ✓ **Significant and long term funding**
- ✓ **Research projects impact on drug discovery and development decision making**
- ✓ **True cross institutional collaboration**
- ✓ **Government backing and nationwide support**
- ✓ **Outstanding experts from both Industry/Academia working together**
- ✓ **Significant training opportunities in evolving discipline.**

# TMRC/AHSC assists in addressing challenges facing drug discovery and development

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- ✓ Translational medicine will help to address the phase 2 attrition issue
  - ✓ *understand the likely behavior of experimental medicines*
  - ✓ *determine efficacy through biomarkers*
  - ✓ *determine safety through biomarkers*
- ✓ Partnerships will help us deliver new medicines to the clinic
  - ✓ *Mitigate risk through partnerships*
  - ✓ *Access knowledge and specific expertise not available in house*
  - ✓ *Form networks to access IP, research, patients etc*
  - ✓ *Allows AHSC to punch above weight & increase competitiveness*