

# Drug Development Challenges

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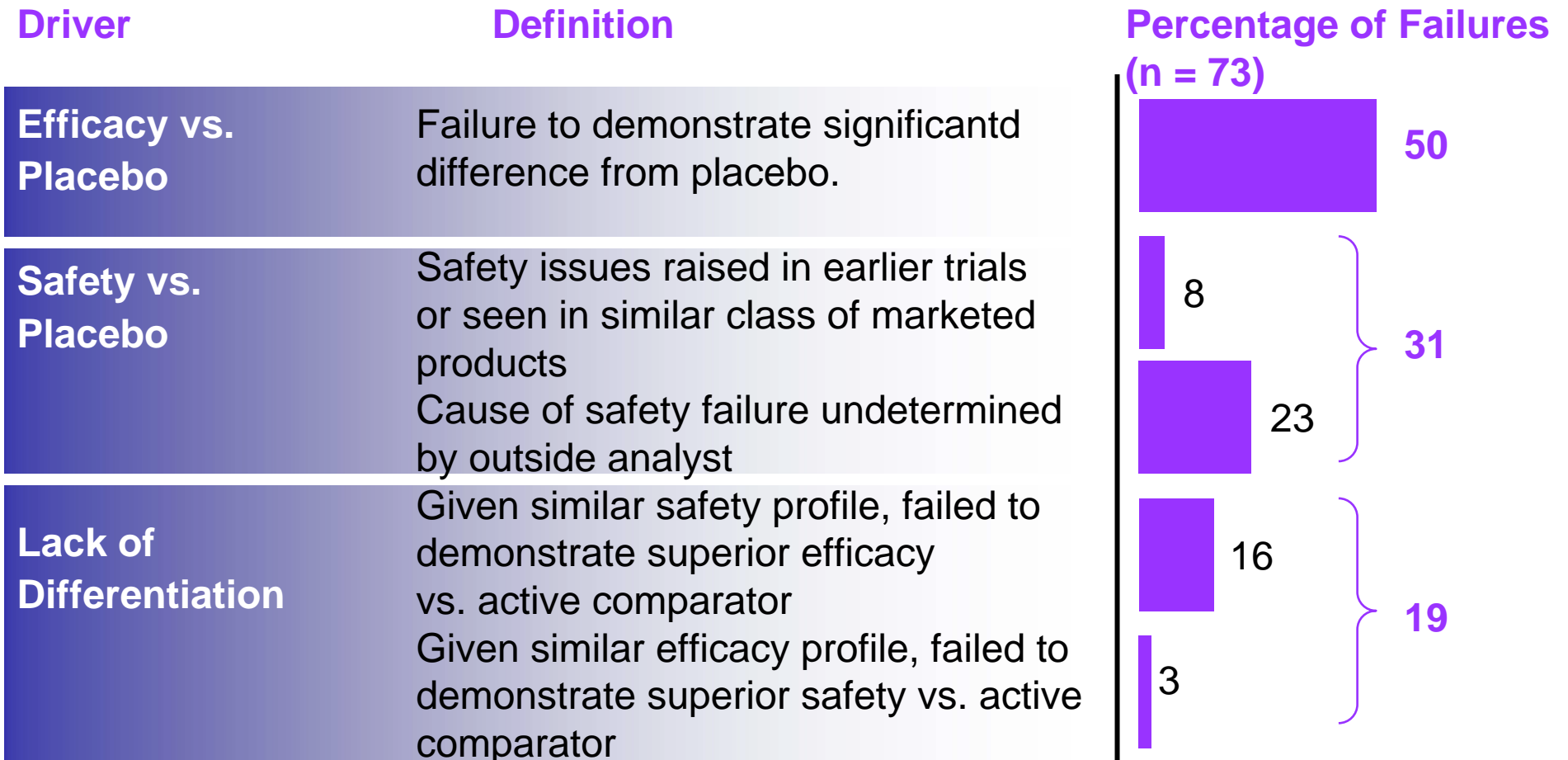
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# Major challenge: Portfolio attrition in Phase III

## *More than 50% cannot show superiority to placebo*

Many compounds enter Phase III without having first shown proof of efficacy established in Phase II



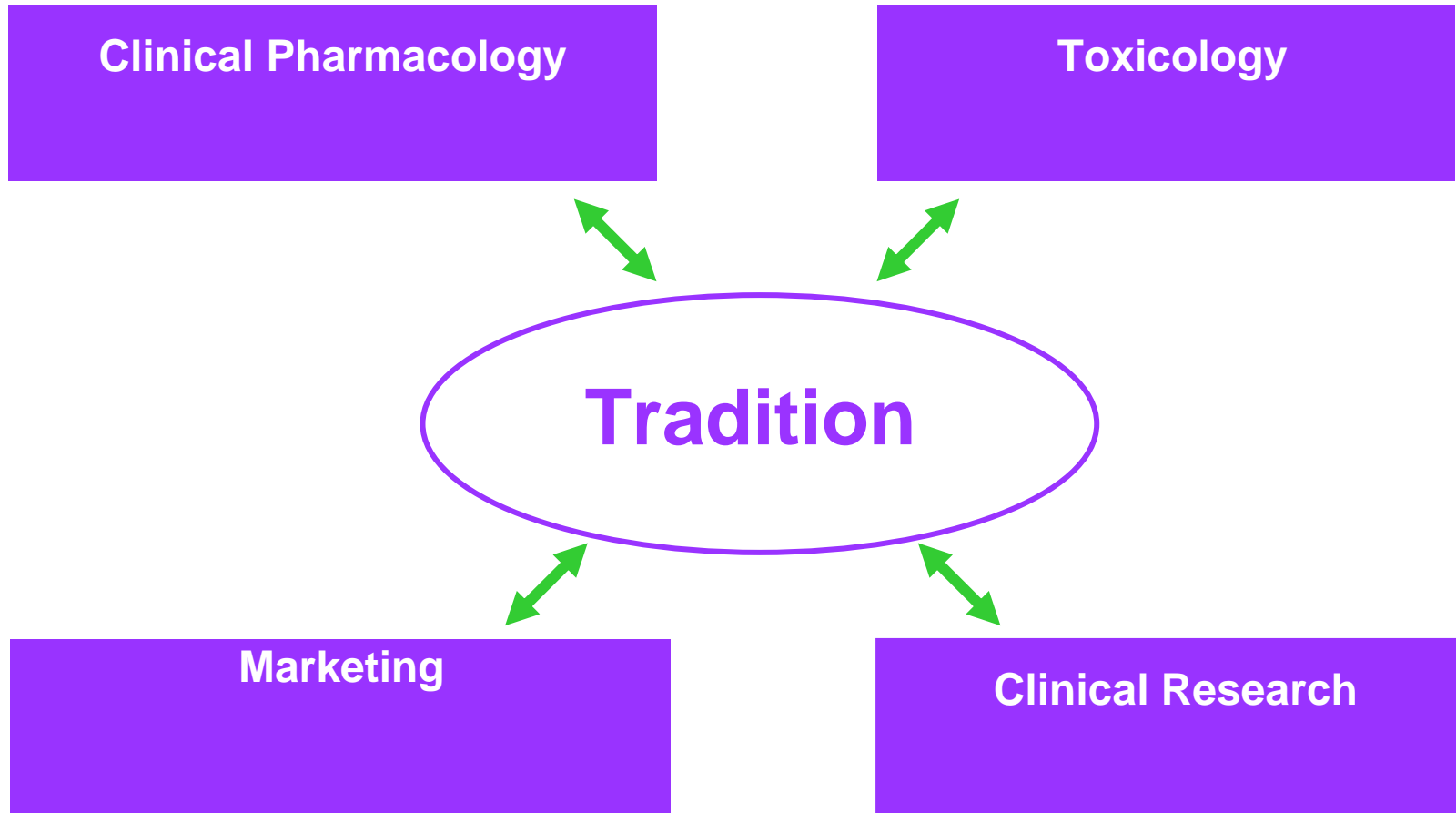
# Addressing portfolio attrition

## *Actions to consider*

- Stop non-competitive compounds early — Phase 0 or I
- Better profile compounds early
  - Deeper knowledge of biology
  - Listen to the product not to the “oracles”
- Enhance clinical trial design — e.g. aligned, objective end points between Proof of Concept, Phase II and Phase III
- Better and actively manage portfolio risk
- Develop sharper decision tools
- Encourage bottom-up input by creating “Information Markets” through which internal as well as external colleagues can offer their view regarding portfolio decisions

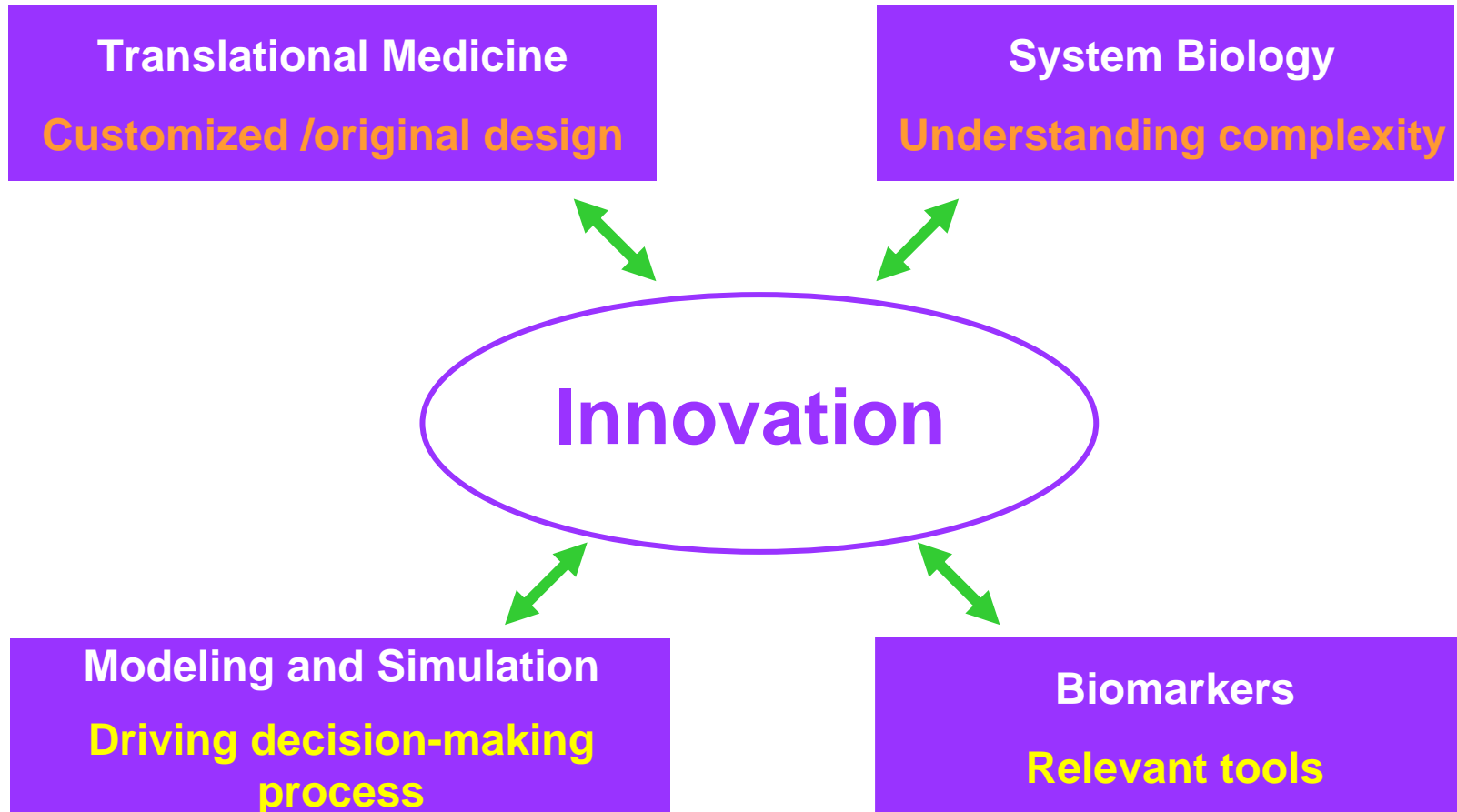
## Older R&D model

*Do not change anything at its core, so far it has worked so well for us!*



# New R&D model

## *Innovation truly at its core*



# New Roche R&D Model

## *Major shift in Roche R&D focus*

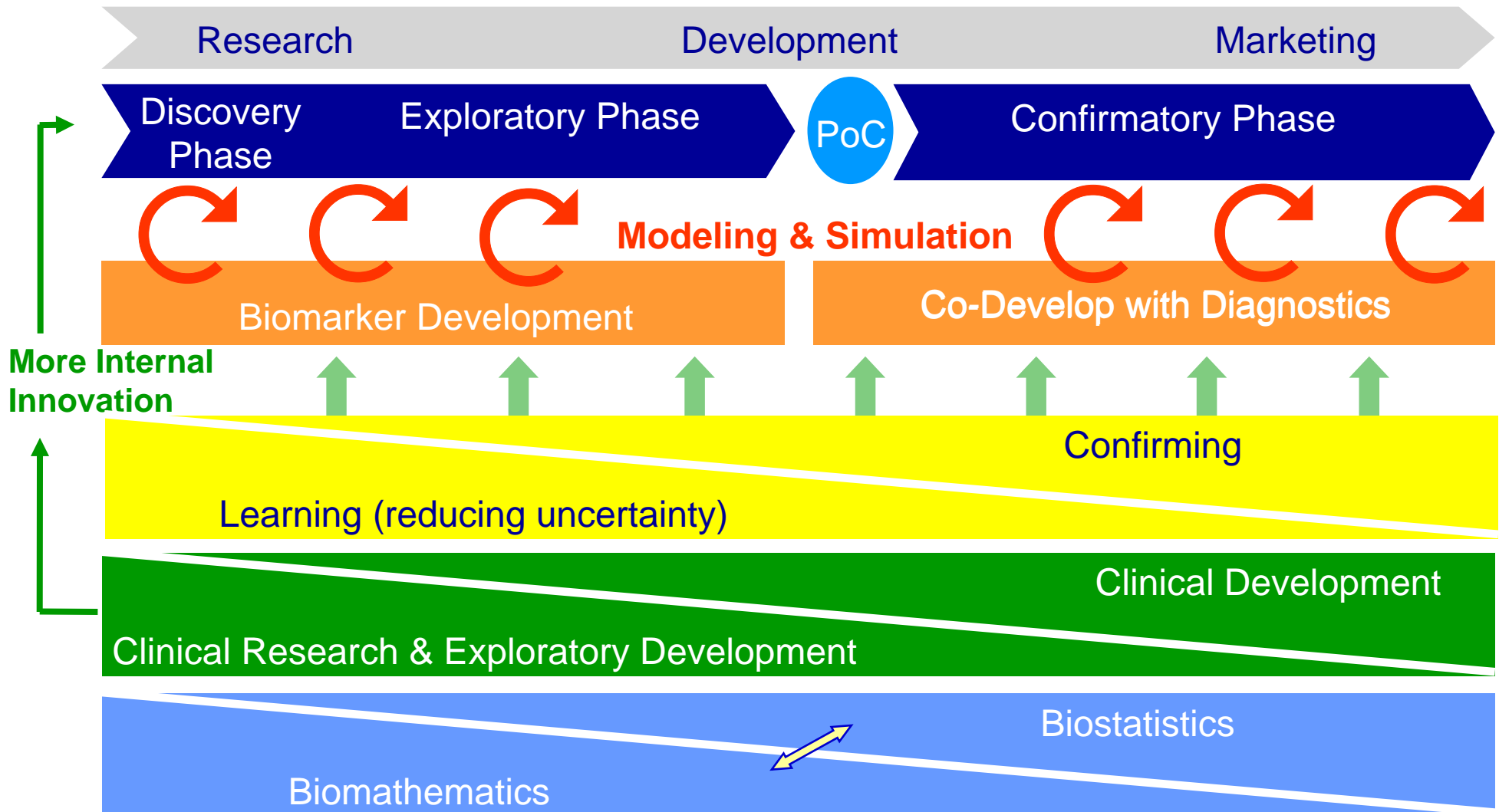
### Current Focus

### Future Focus

1	Sequential, step-wise decision-making model based on milestones	Continuous, parallel process with ongoing decision-making capability
2	Problem-solving approach based on functions	Fully integrated, collaborative, and multi-disciplinary approach
3	Model driven by guidelines, using new technologies and methodologies mainly as afterthoughts or “rescue therapy”	Model centered on system biology, biomarkers, modeling, and simulation
4	“One-size-fits-all” model	Customization according to state-of-art knowledge in target and disease biology

# Key to Future Innovation

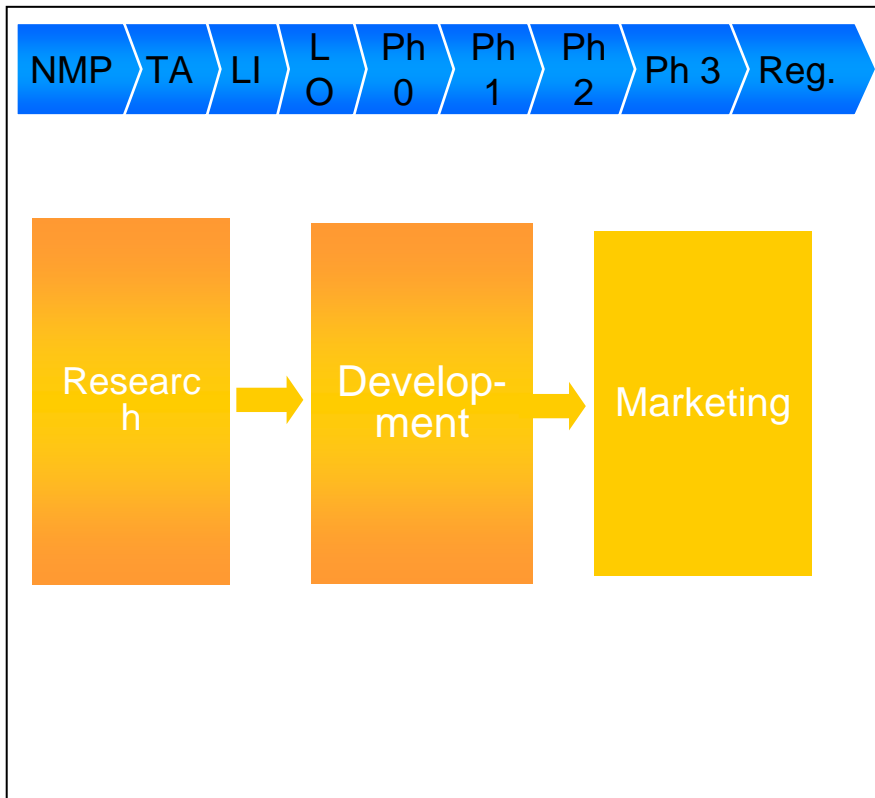
## *Integration of biomarkers across development*



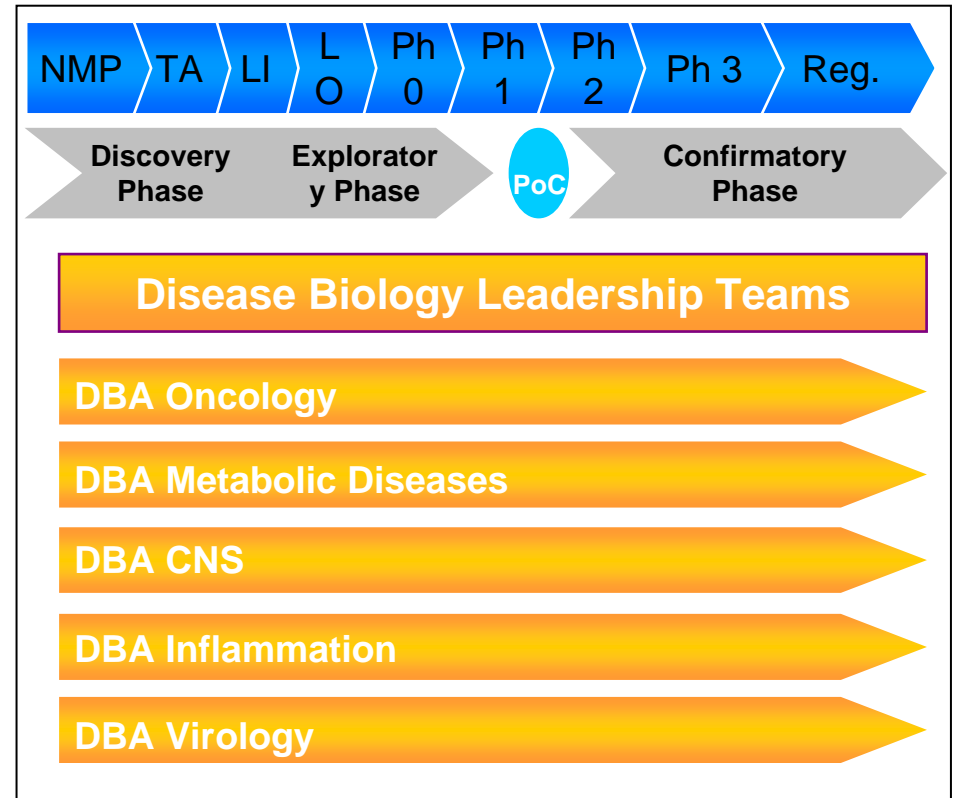
# New Roche R&D Model

## Five Disease Biology Areas (DBAs)

### Old (functional) model



### New Disease Biology Area model



# Role of the Biomarker function in CRED

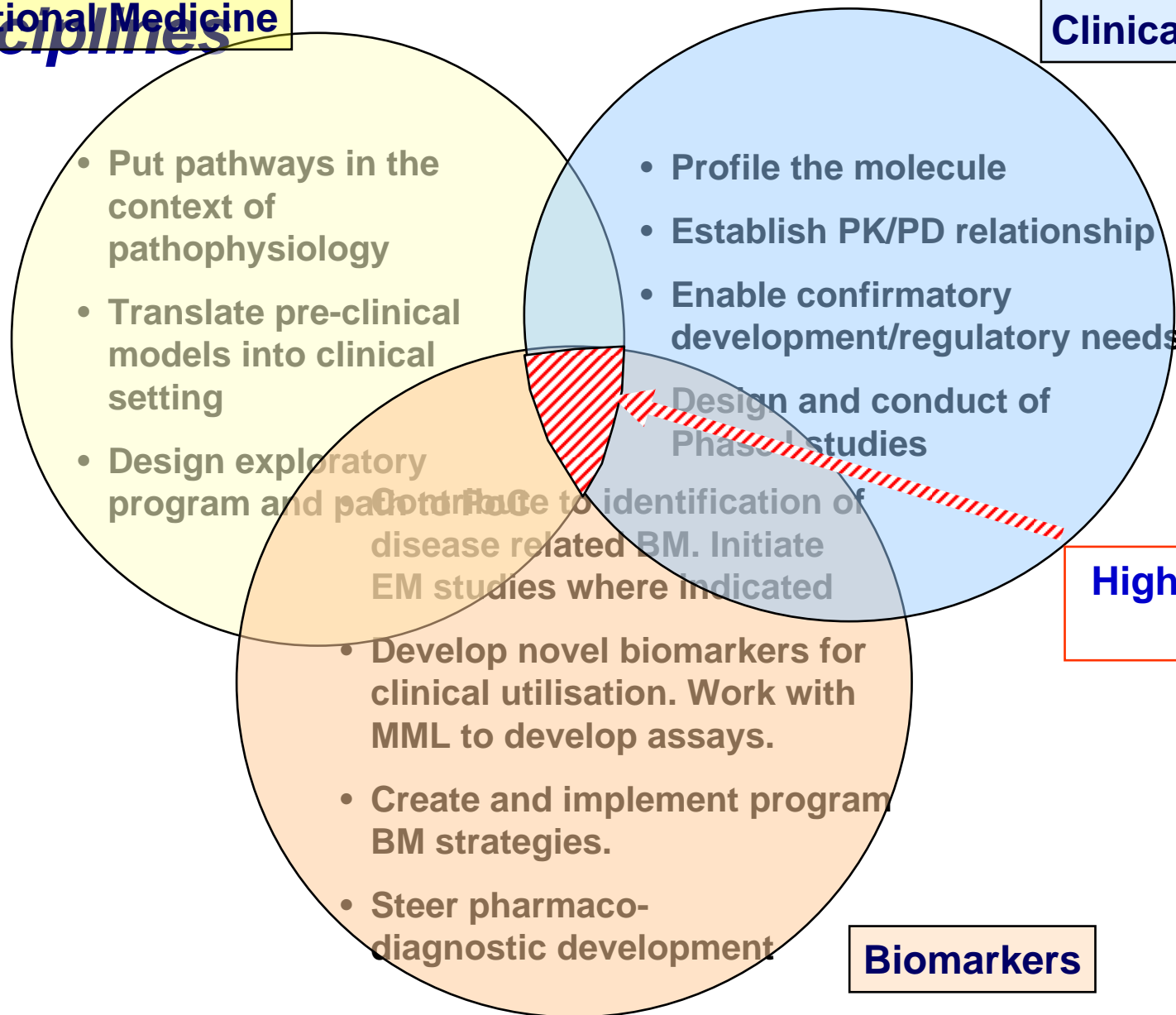


## *Innovation occurs at the interfaces between*

**Translational Medicine**

*disciplines*

**Clinical Pharmacology**



**High Opportunity Zone Innovation**

**Biomarkers**

# The new Exploratory Development model is centered around translational medicine approaches and biomarkers

- Biomarkers become a central element throughout the lifecycle of a medicine
- Earlier interactions between clinicians and researchers to discuss targets and related biomarker strategies
- Invest more effort in understanding pathways and mechanisms to allow a more rational approach to personalized health care
- Include exploratory biomarkers within the decision making process

**This will enable us to improve our ability to progress a greater number of better profiled molecules into late stage development**

# Introduction of novel concepts is an multi and inter-disciplinary effort

## ***Novel concepts come from little literature & no compounds***

**Examples of necessary tools and approaches for exploration:**

- Proteomics/genomics
- Molecular biology
- Antibody and assay development
- In vivo experiments (shRNA, viral overexpression, conditional expression)
- Small molecule & protein chemistry
- Experimental medicine approaches
- Acquisition of clinical sample collections
- Imaging
- Statistics

**Expect 2-3 novel targets, 2-3 novel biomarkers in next 12 months**

# A Great Biomarker Strategy Enables Translational Medicine and Target Discovery



## Conclusion:

- It is ok not to rely on established frames of references
  - Actually it is very healthy!
- Innovation is born out of new disciplines and interfaces
  - Not out of established disciplines
- Biomarkers are not a side dish in drug development
  - But are the central course
- It drives the decision making process with its 3 other partners:
  - Modeling and simulation
  - System biology
  - Translational medicine



*We Innovate Healthcare*