The Role of Tissue/Circulating Based Biomarkers in Clinical Trials: Regulatory Perspective

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Disclosure Information

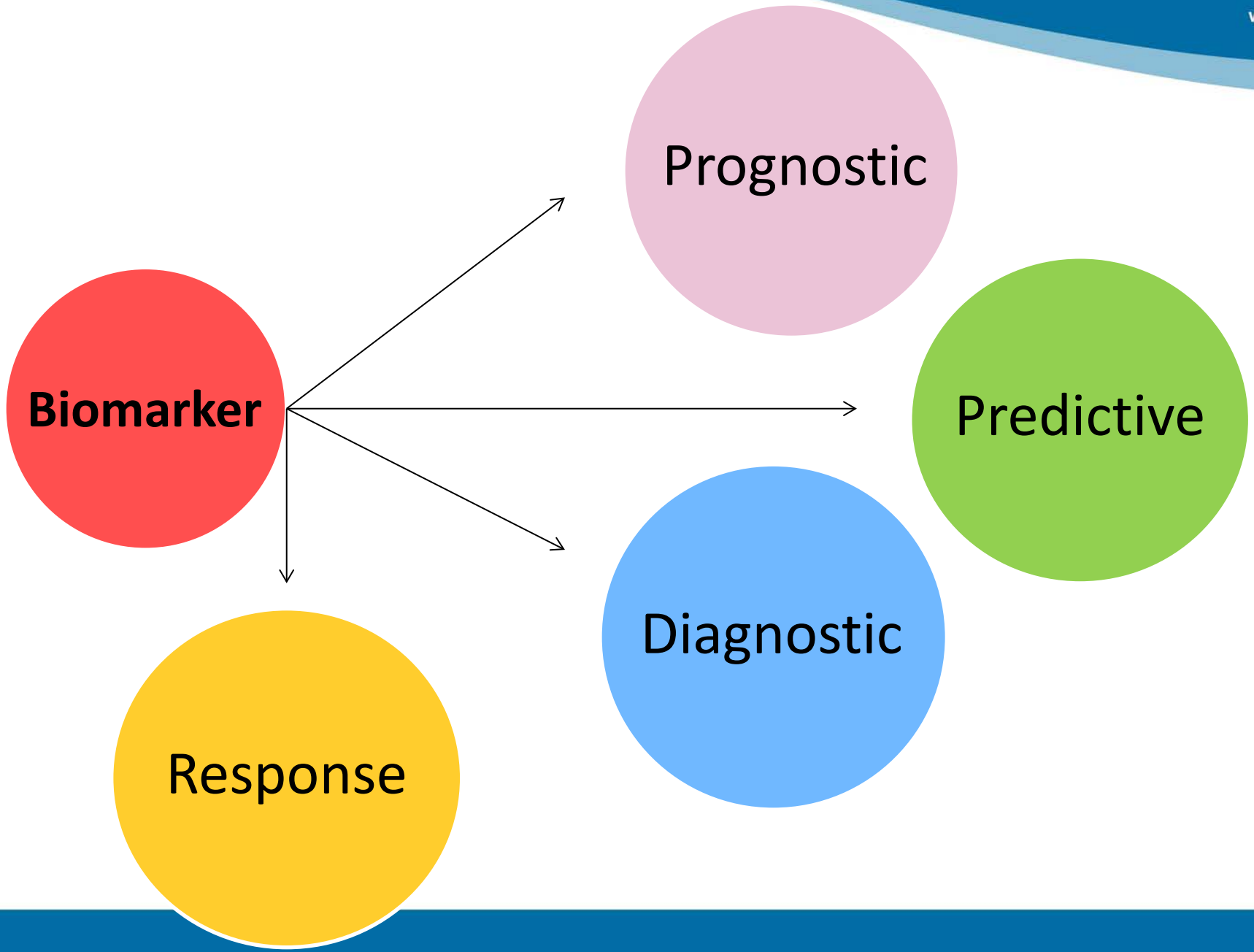
I have no financial relationships to disclose

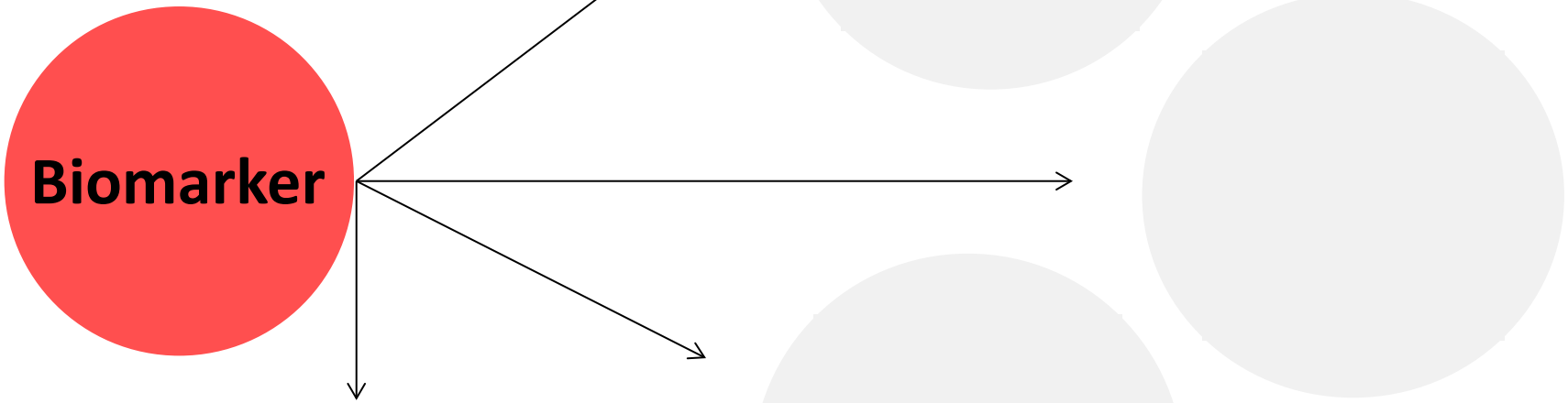
And

I will not discuss off label use and/or investigational use in my presentation

Outline

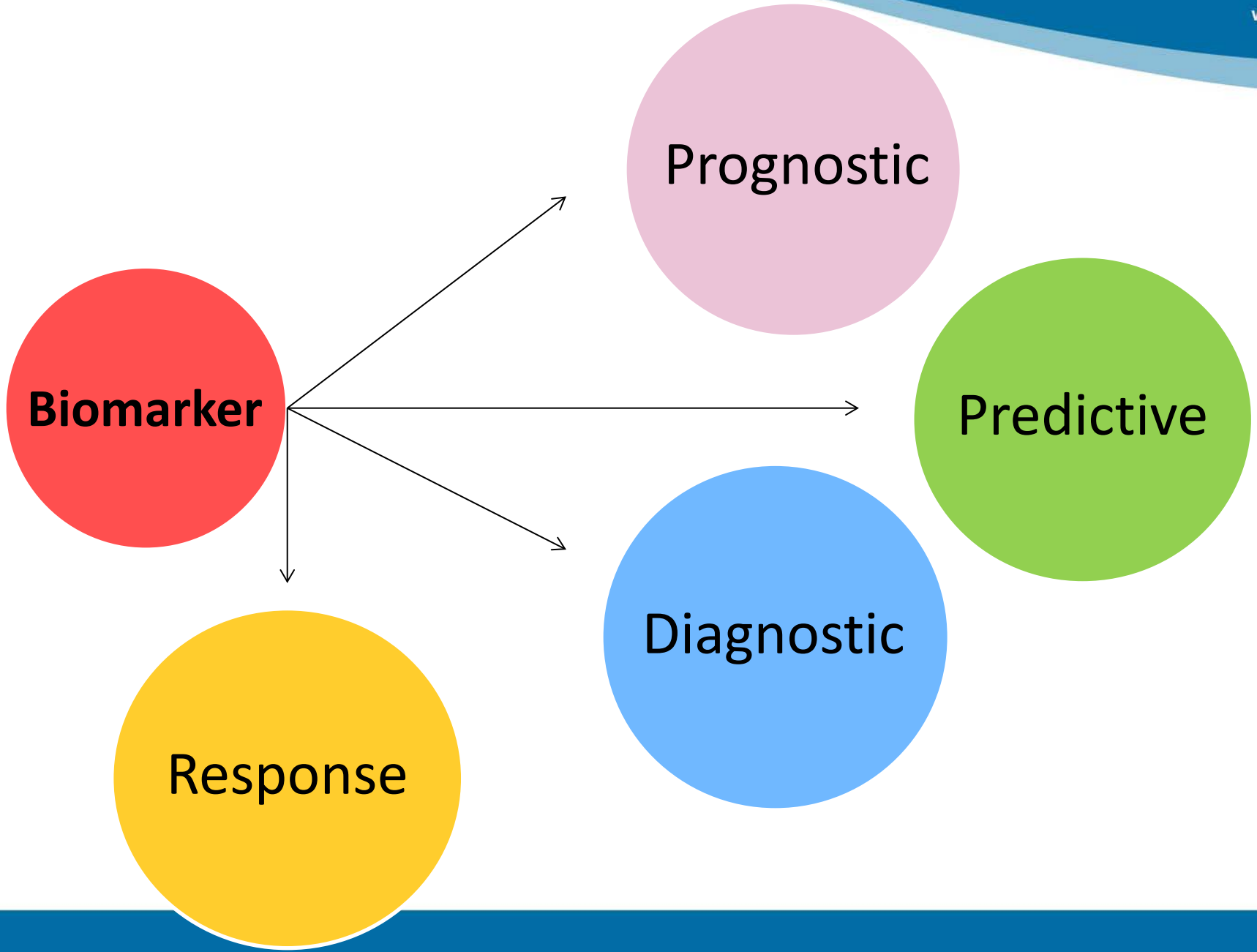
- Biomarker Background
- Options for Clinical Trials
- Regulatory Pathways
- Conclusions


Prognostic
Biomarker
Predictive
Diagnostic
Response



Response

Safety
Pharmacodynamic
Efficacy-Response
Surrogate Endpoint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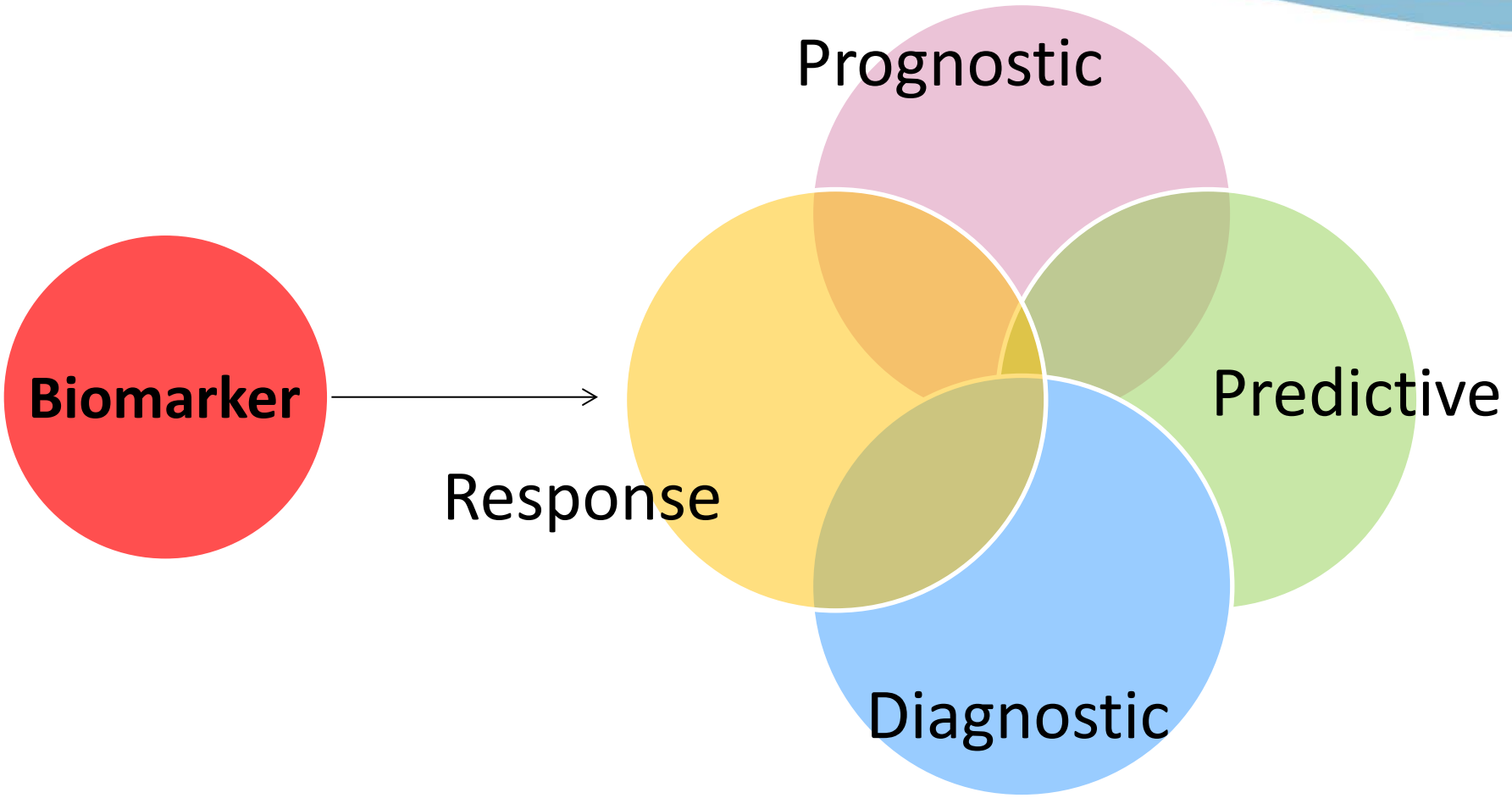
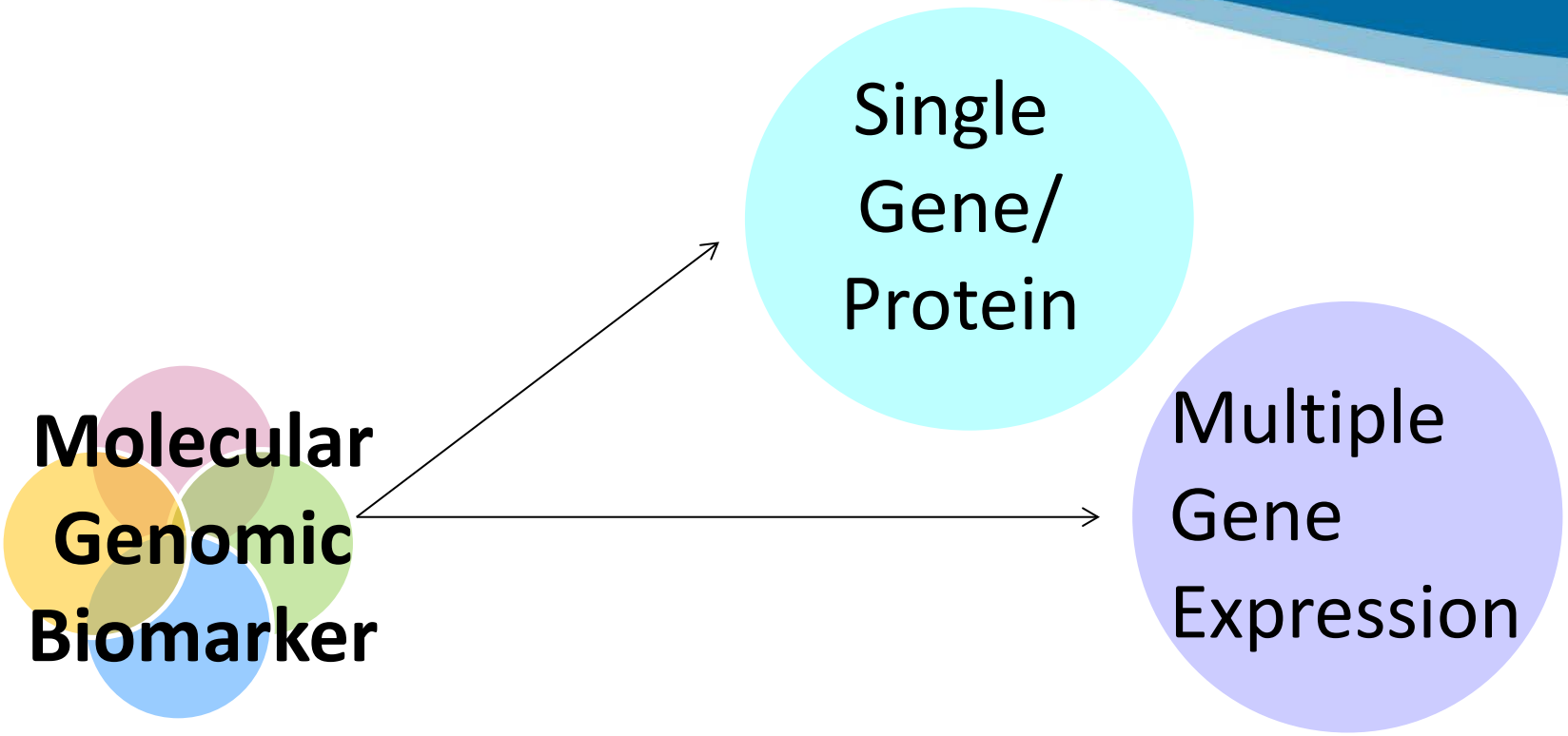
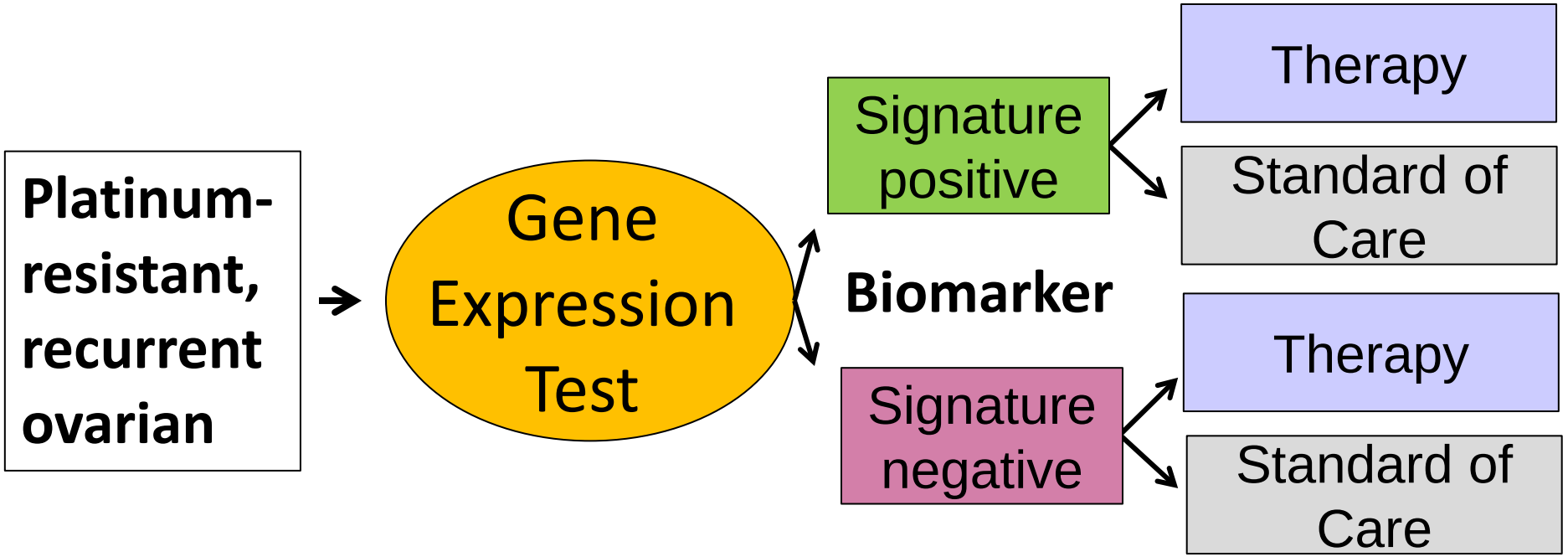

Biomarker
Response
Prognostic
Predictive
Diagnostic



Tissue or
Liquid (e.g. CTCs, circulating cell-free tumor DNA)

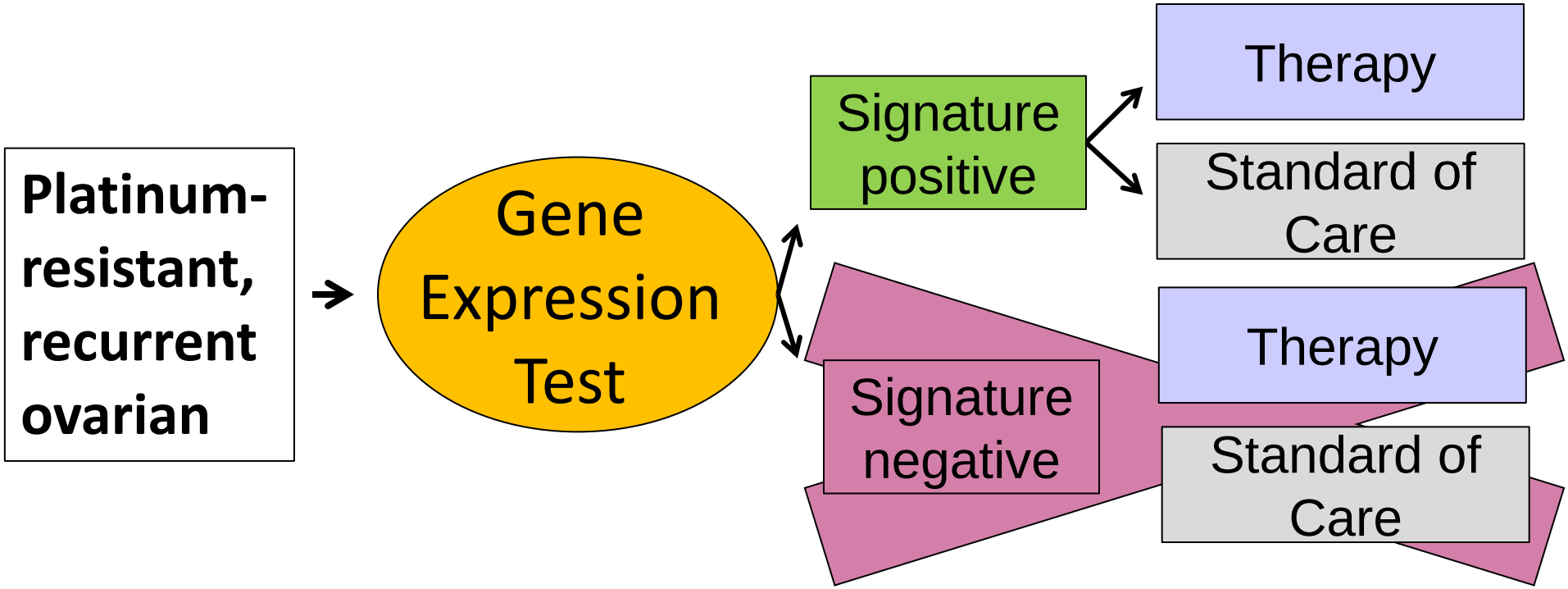
Ovarian Cancer Biomarker Clinical Trials

- Stratification

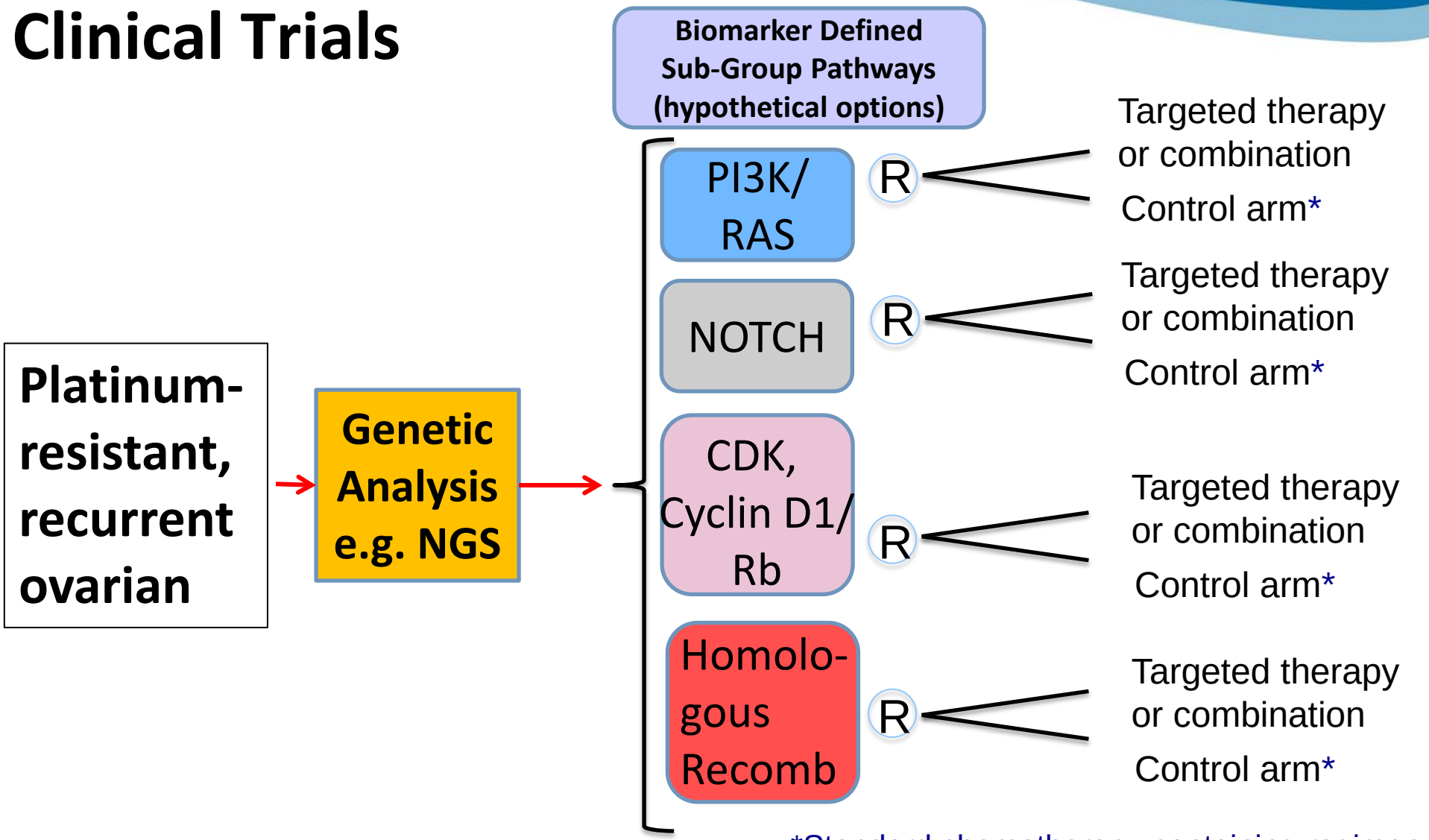


Ovarian Cancer Biomarker Clinical Trials

- Enrichment



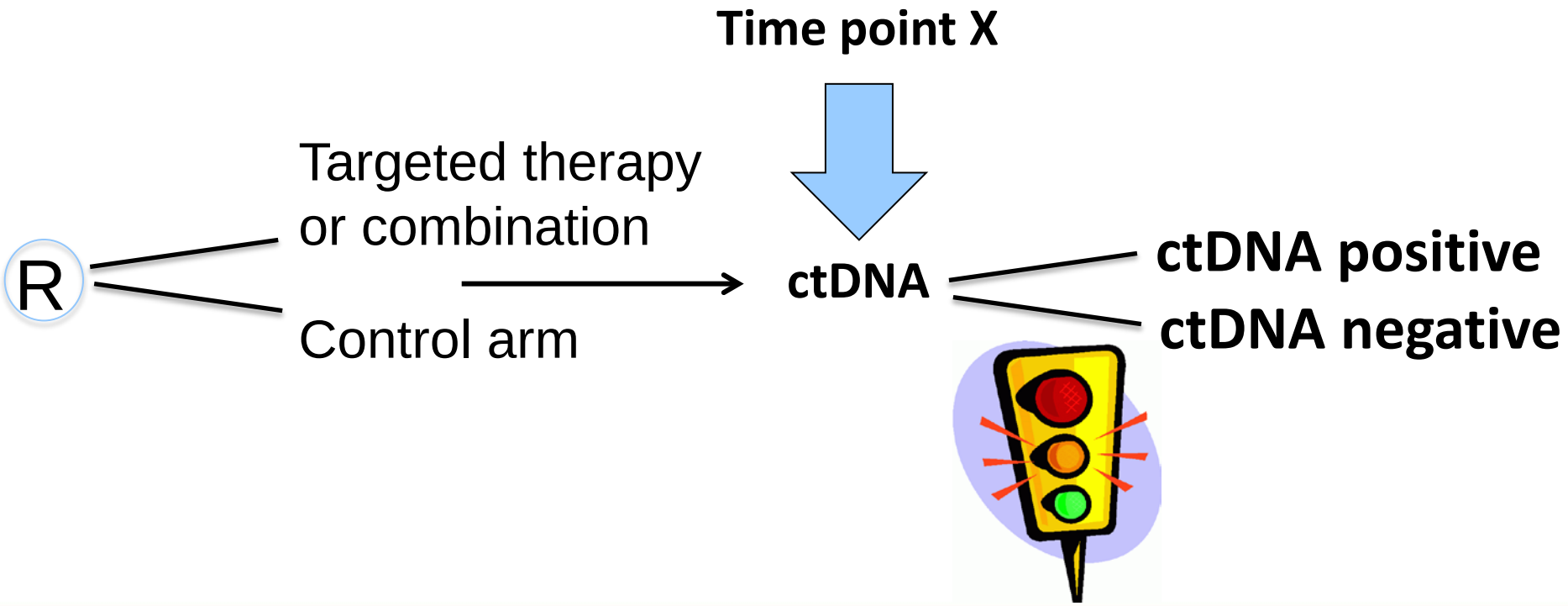
Ovarian Cancer Biomarker Clinical Trials



*Standard chemotherapy-containing regimen

Ovarian Cancer Biomarker Clinical Trials

- Marker of response
  - Go/No Go decision

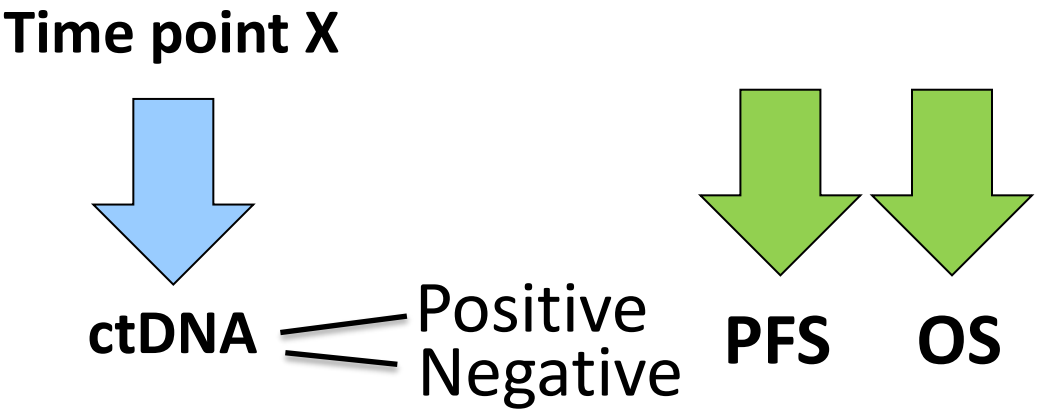


Ovarian Cancer Biomarker Clinical Trials

- Marker of response
  - Prognostic indicator
  - Predictive indicator of early decision to switch therapy

Ovarian Cancer Biomarker Clinical Trials

- Marker of response
  - Surrogate Endpoint



Ovarian Cancer Biomarker Clinical Applications

- Patient Selection for specific treatment
  - e.g. gBRCA and olaparib
- Prognosis
- Need to switch therapy
- Need to treat
- Early diagnosis

Regulatory Options for Biomarker Development

- IND- Therapeutic product (Drug/ Biologic)

- Biomarker Qualification Program

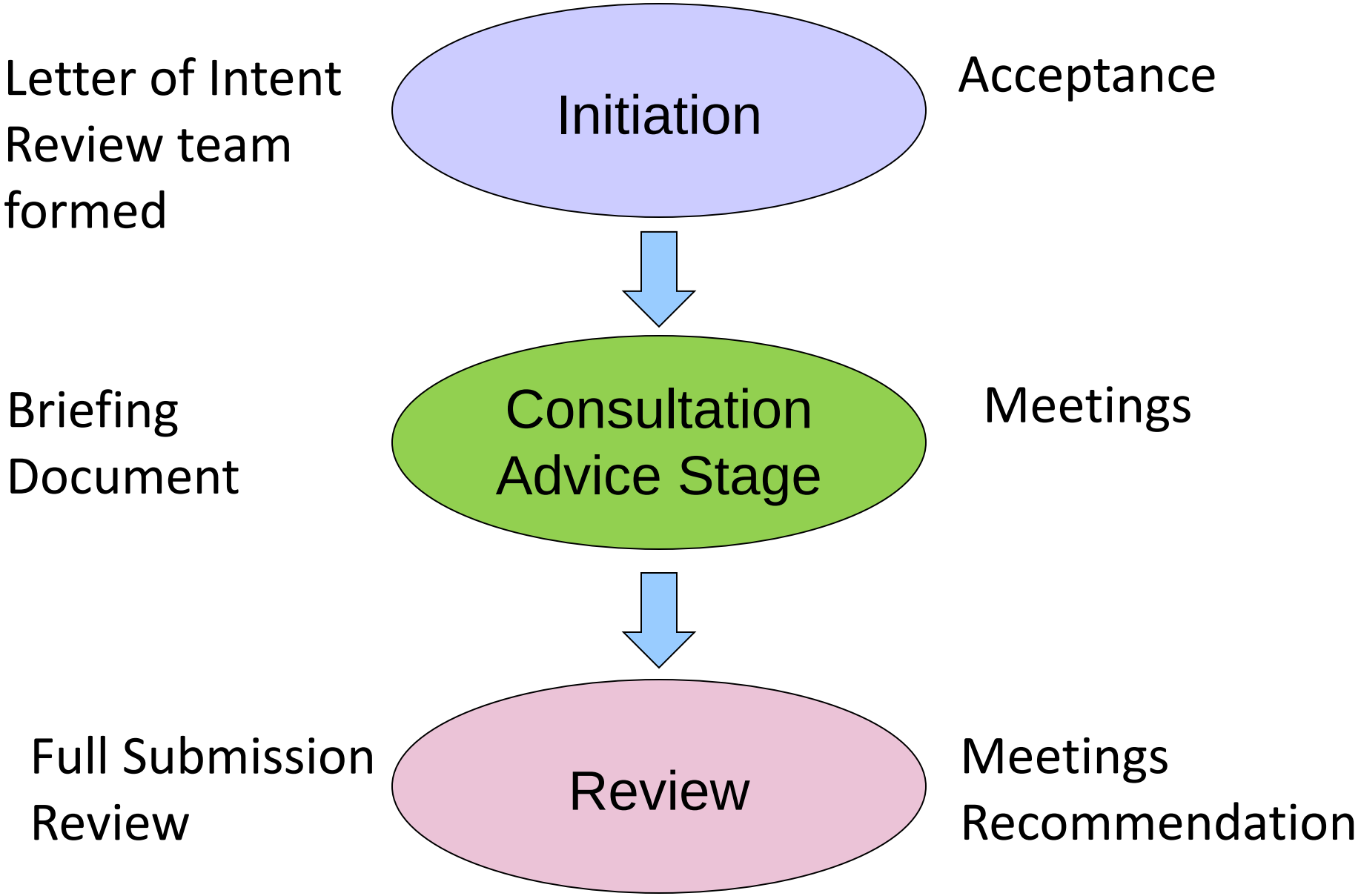
Biomarker Development
Context of Drug/Biologic: **Clinical Trial(s)**

- CDRH- Companion Diagnostic Development
  - Investigational Device Exemption (IDE)
    - Exempt- No IDE
    - Non-significant Risk- abbreviated IDE
    - Significant Risk- IDE application
- CDER
  - Biomarker development plan
  - Clinical Trial design

Biomarker Development
Context of Drug/Biologic: **Submission/Approval**

- CDRH: premarket submission/application
  - Companion Diagnostic: Essential for safe and effective use of therapeutic product
  - Premarket review
- CDER: (s)NDA/(s)BLA
  - Multidisciplinary Review
  - Incorporate biomarker/FDA-approved device into label

Biomarker Qualification Program



Qualified Biomarkers

- Interpretation and application in drug development/clinical trials
- No reconfirmation of acceptance **within context of use**
- Prognostic- COPD/Polycystic Kidney Disease
- Diagnostic- Fungal Infection
- Safety/Response- Nonclinical

Conclusions

- Consider biomarkers throughout drug development
- Communicate early and often with FDA
  - Biomarker Trial design
  - Endpoints
  - Companion Diagnostic
  - Biomarker Qualification

References

- DDT Qualification Guidance http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm230597.pdf
- IVD Companion Diagnostic Guidance http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm262327.pdf
- Biomarker Qualification: Toward a Multiple Stakeholder Framework for Biomarker Development, Regulatory Acceptance, and Utilization. Amur et al. Clin Pharmacol Ther. July 2015

Acknowledgments

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- Reena Philip
- Richard Pazdur