

Challenges in project management in front-loading key activities for rapid drug development (Session 399p)

Panel of Speakers

- **Session Chair:** Michael Wang, Ph.D., MBA, Global Project Manager, Roche Pharmaceuticals, Palo Alto, CA, United States
- **Preclinical Aspects of Front-loading:** Jeremy Freeman, Ph.D., Senior Scientist, Preclinical Development, ZymoGenetics, Seattle, WA, United States
- **CMC: To Spend or Not to Spend, That Is the Question:** John David Cornpropst, Director of Global Project Management, Facet Biotech, Redwood City, CA, United States
- **Clinical Aspects of Front-loading:** Julie G Bukar, MBA, Managing Director, JGB BioPharma Consulting Inc., United States



Definition of Front-loading

- Merriam-Webster Dictionary defined front-loading as to assign costs or benefits to the early stages of (as a project, contract, or a time period)
- We define front-loading as activating resources (to enable activities) at risk prior to Go/No-go decisions to ensure rapid drug development in case of a possible Go decision.



Front-loading Considerations:

- When to start?
- What to front-load?

Pre-Ph 1

- Business decisions
- Invest scientific decisions

CTA Filed

Ph 1

Ph 2

EOP2

Ph 3

NDA/BLA

Fast-to-Market
Proof-of-Concept
Proof-of-Developability



Front Loading CMC Activities: To Spend or Not To Spend, that is the question....

John David Cornpropst

Director of Project Management

Facet Biotech, Redwood City CA, United States

David.Cornpropst@facetbiotech.com





The World of Drug Development



Front Loading CMC Activities: To Spend or Not To Spend....

- Scope of Discussion- Monoclonal antibody focused, but many principles will apply to small molecule development as well
- Presentation Outline
 - Corporate strategy and its impact on CMC planning
 - Platform technologies and relevance to CMC
 - Pre-phase 1 through Phase 1 considerations
 - Phase 2 considerations
 - Phase 3 considerations
 - Summary



Corporate Strategy and It's Impact on CMC

- Therapeutic Area/Indication Focus
- Core capabilities: internal vs. external sourcing of CMC work
- Platform Technologies



Therapeutic Area/Indication Focus

- Target Product Profile (TPP)
 - Route of administration
 - IV
 - Subcutaneous
 - Person administering
 - Self administration
 - Healthcare professional
- Commercial presentation of drug product
 - Formulation concentration
 - Container closure
 - Use of delivery devices
 - COGs (Cost Of Goods)



Core capabilities: Internal vs. External Sourcing of CMC Work

- Methods
 - Development
 - Release/stability
- Formulation development
- Manufacturing
 - Process development
 - Drug substance
 - Drug product

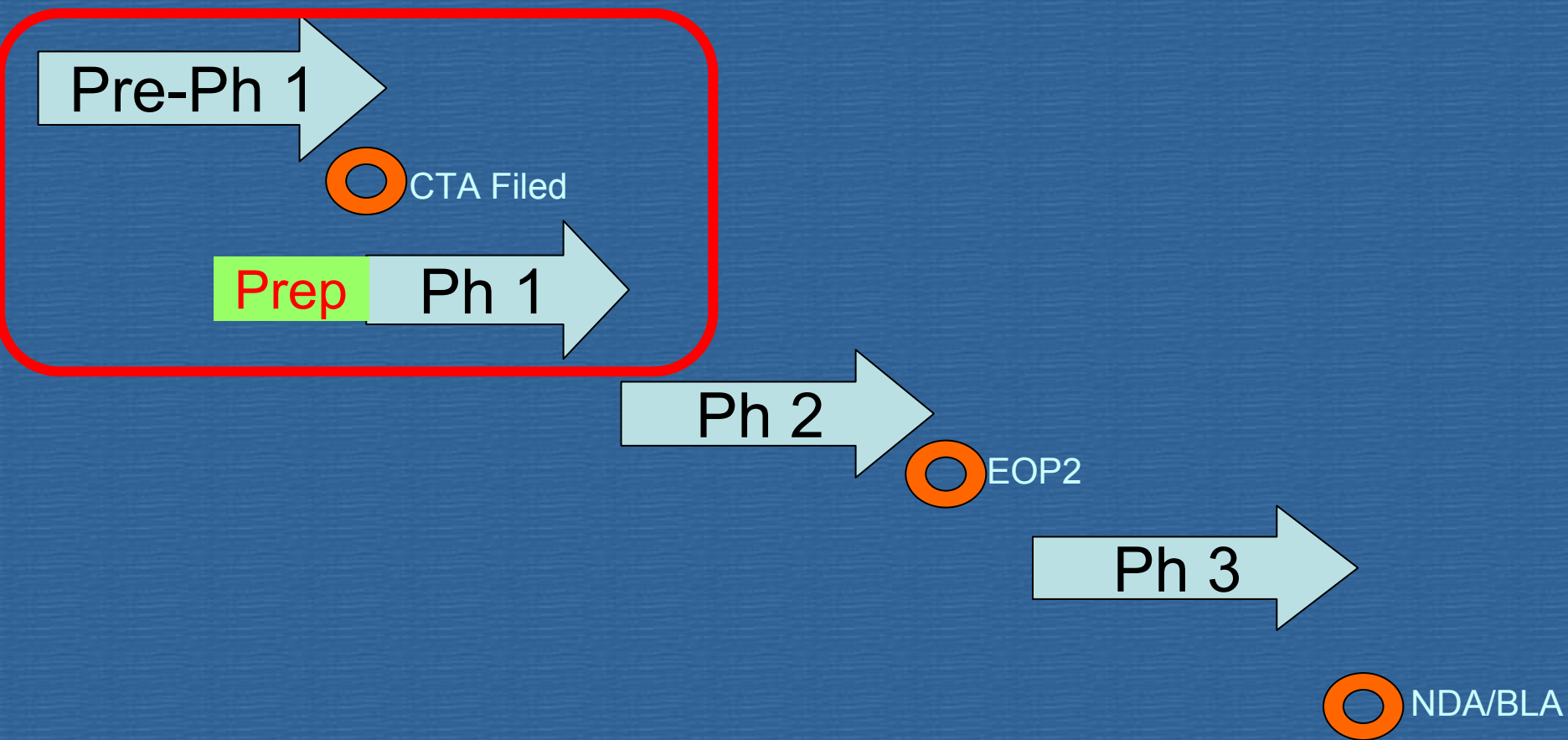


Platform Technologies

- Working definition for today's presentation
 - Technology that enables the reproducible creation of products and processes to support present and future development across multiple programs.
- Relevance to CMC
 - Methods
 - Formulations
 - Formulated drug substance/drug product
 - Product presentation
 - Manufacturing



Front-loading Considerations: CMC



Pre-Phase 1 through Phase 1

- CMC on critical path so speed is important
- Significant number of molecules developed in this phase are ultimately killed, so keeping costs down is important
 - 780 Protein candidates between 1990-2008*
 - 70 approved (globally)*
- Heavy utilization of platform technologies recommended
 - Methods do not need to be optimized
 - Drug substance process does not need to be optimized
 - Drug product does not need to be optimized

*Tufts University presentation given at 5th Annual Antibodies Conference in London UK, March 2009 (Janice Reichert, Ph.D.)

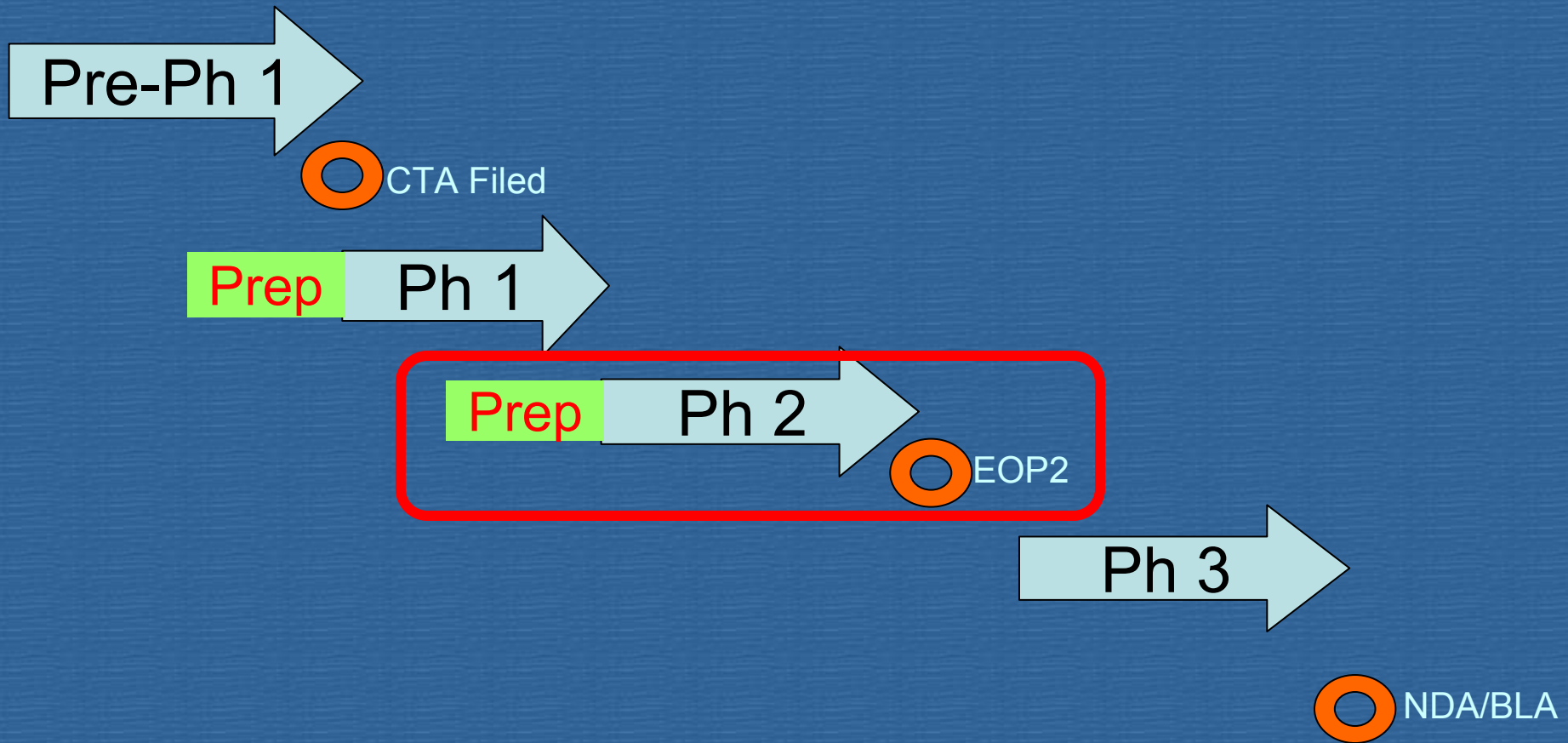


Pre-Phase 1 through Phase 1

- Key development planning variables
 - Proposed route of administration in phase 1
 - Dosing
- Potential business trigger (for phase 1 prep)
 - Decision to initiate toxicology studies
- Opportunities for front loading
 - Early stability work confirming that drug substance can be frozen
 - Formulation feasibility
 - Identifying one of your drug lots that is used in one of your tox studies as a reference std
- Maintain a minimal investment in ongoing product characterization- know your molecule (intangible but important)



Front-loading Considerations: CMC

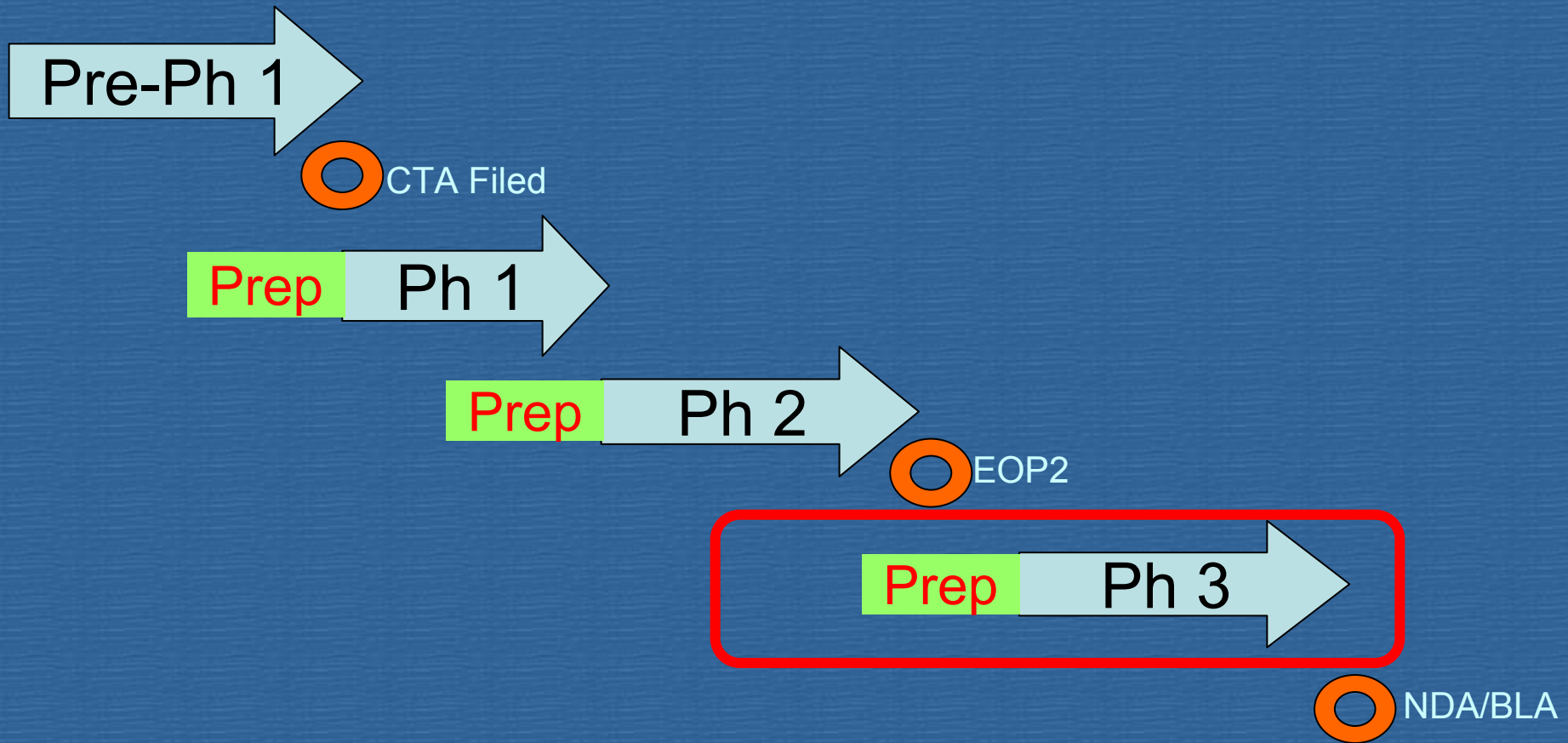


Phase 2 Prep

- Potential technical trigger
 - Initial read on phase 1 safety data
- Key development planning variables
 - Desired product presentation for phase 3 and launch
- Opportunities for front loading
 - Manufacturing
 - Scale/Location
 - Process improvements
 - Formulation
 - Viral clearance
- Expand investment in ongoing product characterization-
know your molecule (intangible but important)



Front-loading Considerations: CMC



Phase 3 Prep

- Business/Technical Triggers
 - Case by case from a company perspective
 - Case by case from a program perspective
- Key development variables
 - Desired product presentation for launch
- Opportunities for front loading
 - Manufacturing (initial launch considerations)
 - Scale
 - Process improvements
 - Location/CMO
 - Method validation



Summary Slide

- Corporate strategies do have direct bearing on the risk/benefit decisions of front loading
- From a program perspective, many drug supply activities are typically front loaded to maintain a reasonable development timeline
- Platform technologies can reduce the amount of work in development making front loading more cost/time effective
- Don't forget to invest some time and effort in understanding your molecule!



Acknowledgements

- Brian Schmidt, Senior Scientist of Analytical Chemistry, Facet Biotech
- Supriya Gupta, Associate Director of Formulation Development, Facet Biotech
- Amit Varma, Director of Process Development, Facet Biotech
- Program Management Department at Facet Biotech

