

# **A New Process for Interactions Between Sponsors and FDA To Facilitate Planning/Implementation of Adaptive Designs**

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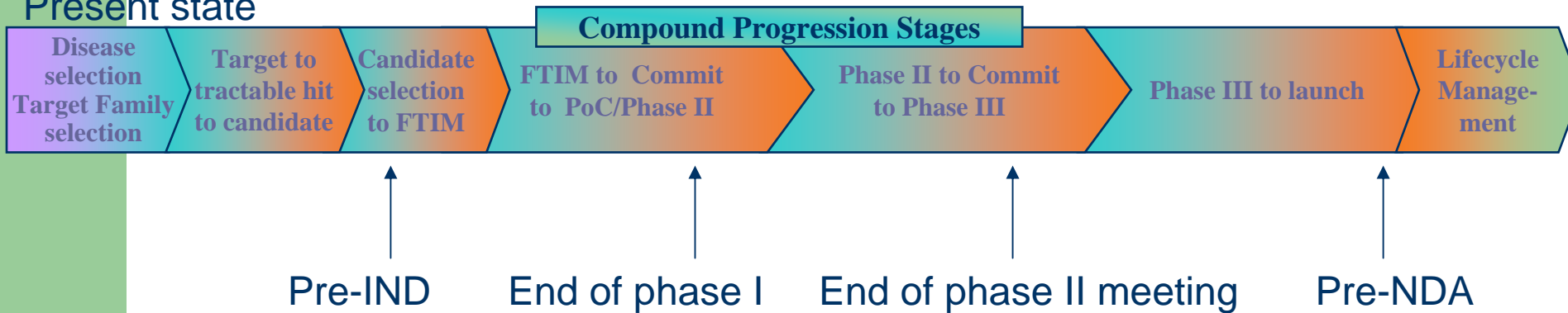
Eli Lilly and Company

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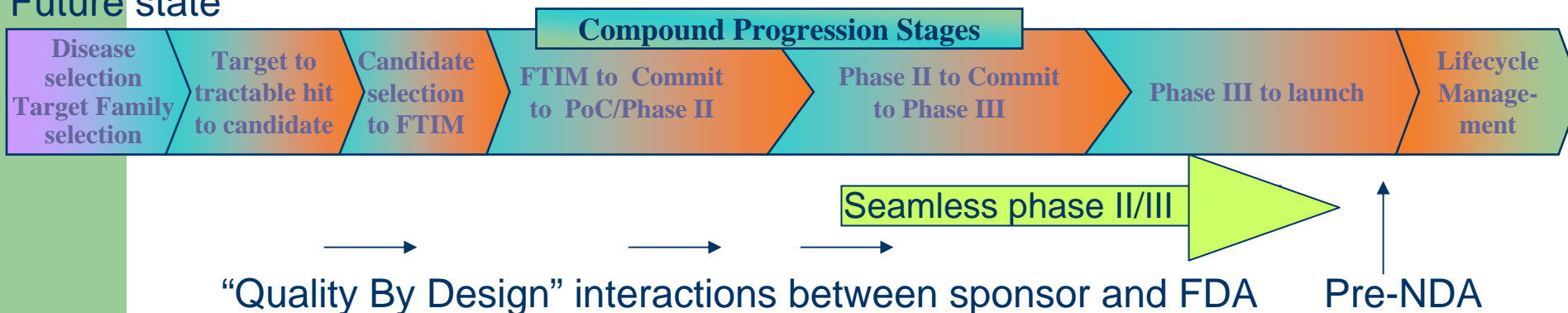


# Sponsor/FDA Interactions: Present and Future

## Present state



## Future state



# Goal (“Learn”): Sufficient evidence to make sponsor internal decisions

- Must have sufficient characterization of dose-response, enabling the
  - Correct choice of dose(s) for phase III
  - Sufficient safety database at relevant doses to underwrite confirmatory phase III trial(s)

# Goal (“Confirm”): Substantial Evidence for Efficacy and Safety

- Efficacy – Confirmatory evidence substantiated in one or more trials by rejecting a well-defined null hypothesis at a predetermined level of statistical significance.
- Safety – Evidence that potential risks are no greater than that which would outweigh the demonstrated benefits.

# How to Reach Goal Faster?

1. Practice and train hard
2. Plan your approach to win
3. Start strong
4. Jockey for Position
5. Make your move
6. Finish going away
7. Win one for the Patient!

# Practice and Train Hard

- Put infrastructure for seamless “Learn and Confirm” in place and put it through the paces
  - Strategy
    - Statistics, scenario analysis comparing alternative design options
    - Regulatory requirements
  - Logistics
    - Center the world around the data (capture/management/access/reporting)
    - Drug supply management
    - Clinical trial execution (patient availability, site capabilities)
    - Enabling integrity/validity of the clinical trial (Data Monitoring Committees, appropriate firewalls, documentation of processes in SOPs)

# Plan Your Approach to Win

- Pre IND meeting
  - Entire clinical development plan in principle
  - Agree to Quality By Design interactions
  - Introduce Target Product Profile
- Data reviewed here includes:
  - Quality Clinical Development System Attributes
  - Pre-clinical support and plan
  - Clinical plan, including scenario analyses of options

# Start Strong

- Submit IND including scenario analyses and simulation reports for clinical development plan/study protocol(s), informed by pre-IND discussion
- Generate sufficient safety data to support Proof of Concept investigation.
- Prove the Concept
- Hold Proof of Concept meeting (also known as the End of Phase 1 discussion) focused on overall safety profile and proof that the drug development concept is valid

# Jockey For Position

- “Setting the stage for success” meeting (also known as the End of Phase 2A meeting) focused on
  - PK/PD characterization
  - dose selection window
  - Pre-clinical data
- Review data from adaptive clinical trials that bracket the right patient/dose/duration, and pilot “outcomes”
- FDA Updates with unplanned positioning

# Make Your Move

- Confirmatory Meeting (also known as End of Phase 2B meeting)
  - Place your bet on
    - Right dose(s) and duration
    - Right patients
    - Right statistical model(s)
    - Right number of patients
    - Right endpoints
- Agree to future adaptation plans, if any

# Finish Going Away

- Pre NDA meeting to overview the evidence demonstrating your prediction(s) were realized and how it will be made accessible to reviewers (e.g. content and format)
- Confirm that Good Review Management Practices will be adhered to
- Propose adaptive benefit/ risk management plan (including scenario planning)?

# Win One for the Patient!

- Adaptive by Design Benefit/Risk Management will help provide for and protect public health
- More quickly get the Right dose to the right patient

# Summary

- Quality by Design (QBD) Regulatory Interactions needed to implement Adaptive by Design (ABD) development program
- May result in fewer meetings if ABD agreed to up front (e.g. greater up front planning, data sharing)
- Current regulations support and consistent with QBD interactions but guidance needed on ABD trial implementation
- Regulators and sponsors need to agree that the extra resources needed to implement QBD regulatory interactions for ABD trials are justified by the ultimate patient outcome