Seamless Cancer Drug Development Paradigm

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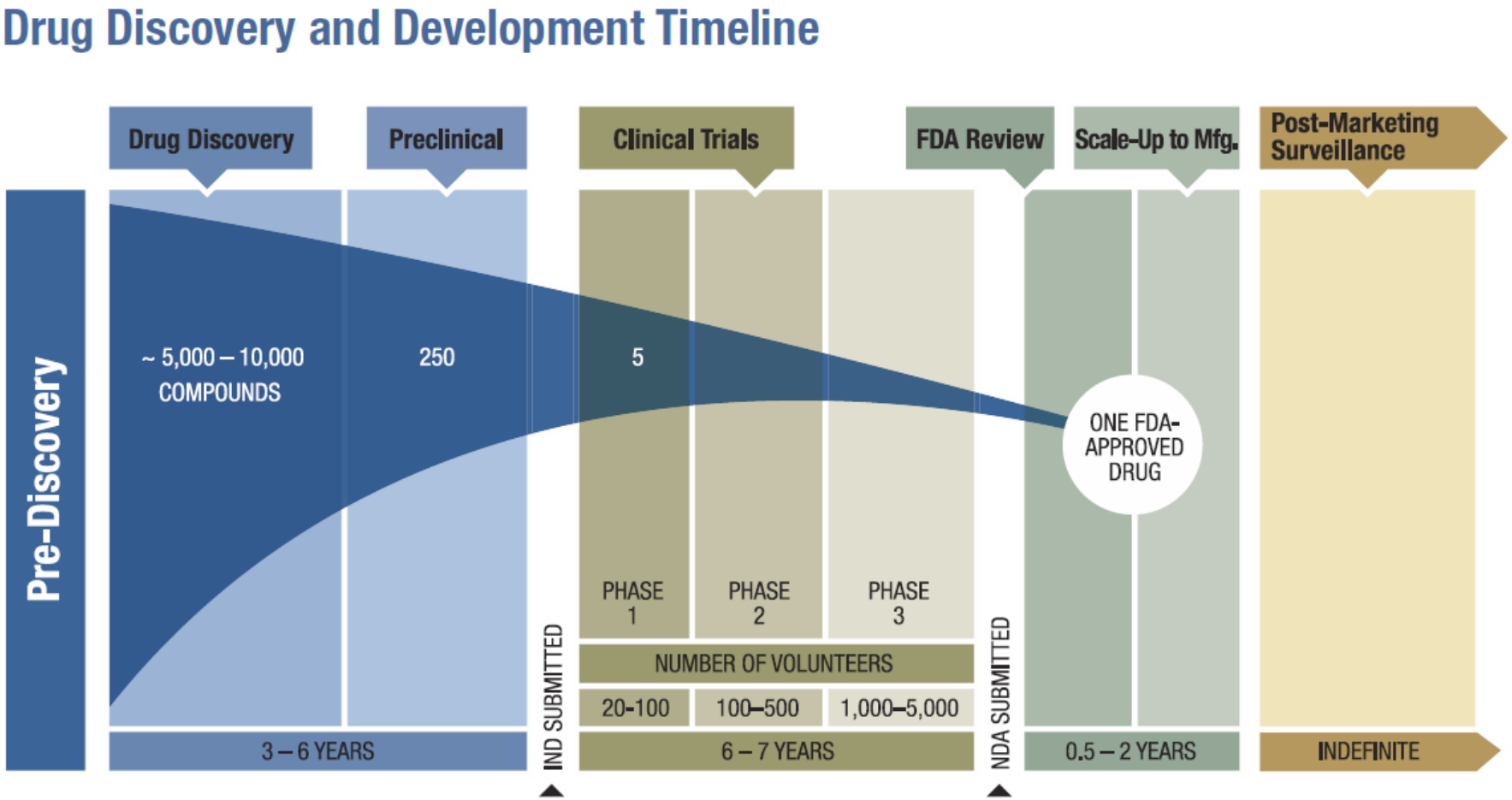
The Historic Paradigm – Can it be Enhanced?



Courtesy of the American Association of Cancer Research 2011 Cancer Progress Report

3 Ways to Add Efficiencies to Drug Development

1) Innovative Trial Designs & Operation
2) Development & Regulatory Coordination
3) Enhanced Public Policy

Innovative Trial Designs & Operation

- Several novel clinical trials have employed methodologies designed to make transition between phases of research less distinct (Adaptive designs, Phase 2/3 trials)
- Standing trial networks can make the conduct of trials more seamless by not having to launch each new study from scratch
- In order for research networks to be successful, they need to access community sites and have trials that are actually interesting to patients
- Examples:
  - Lung-MAP: Incorporates genetic screening into a master protocol to identify patients that match to different sub-studies based on biomarker expression
  - I-SPY2: Utilizes an adaptive randomization design to identify active investigational drugs, potentially paired with biomarkers predictive of response
  - GBM-AGILE: Research network to create standards-based end-to-end systems solutions for biomarker discovery, development and delivery

Development & Regulatory Coordination

- Enhanced coordination can help make development processes and regulatory review more seamless particularly for treatment regimens that involve different products from different FDA Centers
- FDA Oncology Center of Excellence included in the Cancer Moonshot and included in 21st Century Cures Initiatives
- Intended to reflect the current state of multi-modal interventions in cancer treatment
- Organize clinical aspects in a more patient-oriented approach rather than a product-oriented approach

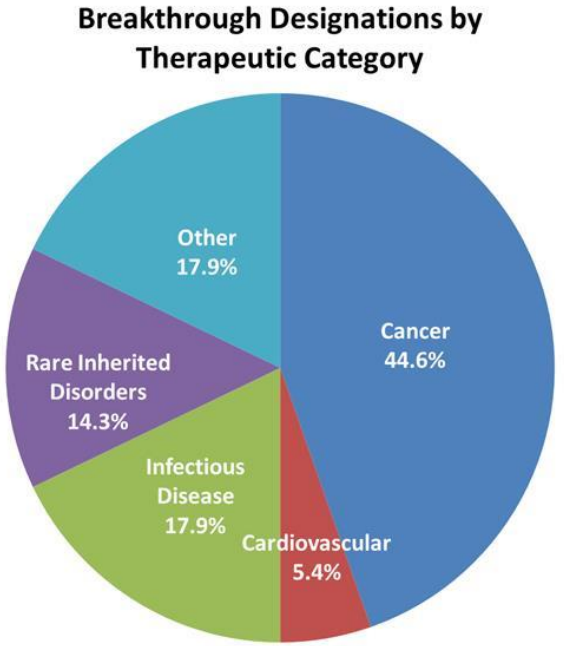
Development & Regulatory Coordination (Cont.)

- Validation & Utilization of Common Tools
  - Patient Reported Outcomes
    - Development and validation of a PRO adds a layer of complexity to any development program
    - Use of a previously validated tool that can be applied in multiple settings can provide valuable information with less logistical burden (i.e. NCI PRO-CTCAE)
- Proactive Trial Planning – Exploratory Randomized Trials
  - Randomized Phase 2 studies can be used to make “go/no-go” decisions
  - If a notable effect is seen in a small study, questions arise about the need for additional studies
  - Pre-specifying thresholds and plans to expand the patient cohort when unanticipated activity is seen can help ensure confidence in the result without necessarily requiring a brand new trial.

Enhanced Public Policy

- Successful policy needs to be reflective of current science
- This was the premise behind the Breakthrough Therapy Designation
  - When large treatment effects early in development are observed, a new approach is needed
  - The Breakthrough Program is public policy that is operationalizing seamless development
  - 441 total requests for Designation
  - 145 requests granted
  - 46 Breakthrough

    Therapies approved



Enhanced Public Policy (cont.)

- 21st Century Cures Initiative
  - Recently passed the House and the Senate and funding for Year 1 has been provided through the Continuing Resolution
  - Contains Several provisions that will enhance more streamlined development
    - Accelerate Approval Development Plans – Enhanced communication for use of surrogate endpoints
    - Biomarker Qualification – Process for validating new biomarkers
    - Hiring and Retention – Improved mechanisms to help FDA attract top talent
- PDUFA
  - Renews FDA authority to collect user fees – needs passed by Sept 30, 2017
  - Will provide funding for several projects related to 21st Century Cures
  - Will provide specific funding to support use of the Breakthrough Designation