Strategic Considerations for Clinical Development Programs in Emerging Biopharma Companies

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Quintiles

Improve your probability of success™
Congratulations!

- Your scientific hypothesis has been validated in animal studies.
- You’ve identified a lead compound or biologic (and back-ups).
- You’ve understood some preliminary animal pharmacology and have negative preliminary toxicology findings.
- You’ve decided to start (or have begun) human clinical testing!

... and your Investors are thrilled, but daunted (because now the “fun” starts)
Why are you here today?

What we will discuss:

• The importance of designing your clinical program with the end in mind, from First-in-Man through approval and commercialization
• Perspectives: Investors vs. stakeholders vs. market
• Balancing risk with investment opportunity
• Understanding the specific landscape and market for your product
• Thinking ahead without investing major resources

Key takeaways:

• Recognize the opportunity: Align clinical & commercial intentions
• Design to build evidence: Integrate key program elements to inform stakeholder requirements
• Optimize execution & operations: Balance current spend against future return by leveraging capabilities of a partner
• Deliver value: Planning for the future now helps optimize ROI
Activities of “Today”: Pre-clinical development

The next investment ($7-10M) frontier...

**ADME:** absorption, distribution, metabolism, and excretion
**API:** active pharmaceutical ingredient
**PK:** pharmacokinetics
**Prep:** preparation
**Tox:** toxicity
**FIH:** First-In-Human
Early clinical development realities
An investor’s (and potential partner’s) perspective

Stakeholders want to understand the value (opportunity, ROI) of a compound. They also want to understand the risk.

Better, faster decision-making about whether a (or which) compound should progress has become even more critical.

Optimal investment return requires early-phase studies that deliver quality data & insights to make the correct decisions.

New approaches needed to:

- Rapidly assess the clinical & market viability of the NME
- Identify risks
- Decrease time to “kill-progress” decisions
An investor’s/partner’s “long-haul” perspective

**Capitalized costs per new drug approval:** $1460M

<table>
<thead>
<tr>
<th>Phase</th>
<th>Mean 80.8 mo.</th>
<th>16 mo.</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>I</td>
<td>II</td>
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<tr>
<td>Mean Out-of-Pocket Cost ($M)</td>
<td>$25.3</td>
<td>$58.6</td>
</tr>
<tr>
<td>Phase Transition Probability</td>
<td>59.5%</td>
<td>35.5%</td>
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Polling question #1
Which statement below best fits your team’s understanding of “long haul” point of view on your product and the incorporation a “design with the end in mind” principle in planning activities?

› We have a strong understanding of the long haul view and actively incorporate it into our design principles and planning activities.

› We have a strong understanding of the long haul view, but struggle to bring it into design principles and planning activities.

› We are working towards better understanding of this view, and expect to incorporate it into our design principles and planning activities this year.

› Our view of the long haul is limited and therefore not a part of our design principles and planning activities.
Value creation in biopharma

Preclinical R&D

Clinical Development
- Phase I
- Phase II
- Phase III

Regulatory Submission

Post-Approval

Stakeholders?

Future Landscape?

Market Drivers?

Comparators?

Endpoints?

Positioning?

Launch strategy?

Lifecycle strategy?

$ Time

Value creation in biopharma
The Market Perspective: What shapes return?

Value is in the eye of the stakeholder / decision-makers

Value Definition

- Payers
- Prescribers
- Healthcare Providers
- Regulators
- Regional & Local Agencies
- Public
- Patients
The challenge of meeting multiple stakeholder needs

Patient
- Need to maintain health
- Benefit/risk tradeoffs
- Affordability of care

Policymaker
- Balance of quality and cost
- Societal considerations
- Health system statutes and guidelines

Manufacturer
- Incentives to develop evidence
- Reimbursement commensurate with value
- Return on investment
- Reward for innovation

Payer & HTA
- Balance of quality and cost
- Evidence-based care
- Provision of appropriate care to appropriate populations
- Balancing care across the population

Provider & Hospital
- Provision of appropriate care
- Provision of reimbursed services
- Financial efficiency & viability
- Managing with a budget

Laboratory
- Better, faster, cheaper
- Staff resource requirements and turn around
- Managing with a budget

Value
Investment view: Can the molecule deliver value?

Value is built from the documented and expected performance of the molecule.

Therefore, the “strategy” for development must focus on demonstrating the asset’s unique capabilities in the language of decision-makers.
Polling question #2

Which statement below best aligns with your organization’s abilities to address, understand, and incorporate the full range of stakeholder requirements into your product and program plans?

› We’re fully staffed and structured to address this today.

› We have limited abilities to do this today, but are confident in the different options to get there.

› We have limited abilities to do this today, and are uncertain how to approach it.

› We haven’t really considered this at all.
## Defining the opportunity: Key early development questions

*Deliverables and the tools used to answer them*

<table>
<thead>
<tr>
<th>Question</th>
<th>Deliverable</th>
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<tbody>
<tr>
<td><strong>Entering Pre-clinical</strong></td>
<td></td>
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<tr>
<td>? What indication(s)?</td>
<td>✔ Landscape analysis</td>
</tr>
<tr>
<td>? What patients?</td>
<td>✔ Patient pathway</td>
</tr>
<tr>
<td>? What unmet need?</td>
<td>✔ Regulatory strategy</td>
</tr>
<tr>
<td><strong>Entering PH I-II</strong></td>
<td></td>
</tr>
<tr>
<td>? What differentiation?</td>
<td>✔ HTA analysis</td>
</tr>
<tr>
<td>? Which comparators?</td>
<td>✔ TTP gap analysis</td>
</tr>
<tr>
<td>? What evidence requirements?</td>
<td>✔ Stakeholder analysis</td>
</tr>
<tr>
<td>? What endpoints?</td>
<td>✔ CDP design &amp; gap analysis</td>
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</tbody>
</table>
Early clinical strategy development

Strategic Question (What?)

Is it ‘druggable’? (Go/No-Go)

Is the Disease Area Attractive?

Will this MOA Compete? (Go/No-Go)

What initial clinical focus to drive differentiation? (Go/No-Go)

Candidate

Bioavailable

Not Orally Bioavailable

Disease Area 1: Highly Competitive

‘Me-Too’ MOA

Novel, High Efficacy Likely

Disease Area 2: High Unmet Need

Non-validated MOA

High Efficacy Likely

Sub-population Biomarker Available

Sub-population Research Biomarker Only

Validate in Lab

Ph I in Patients

Ph I in HV

PK/PD

• Landscape Assessment

• Disease TPP

• Competitive Assessment

• SoC/Treatment Guidelines

• TPP Gap Analysis

• Patient Pathway

• Biomarker Assessment

• ROI Trade-off Analysis

Driving Execution Decisions (How?)
Building evidence: Optimizing evidence-generation

Building evidence requires addressing strategic questions using a stepwise approach to ensure next steps drive the highest program value

### Integrated and Iterative Steps

#### Landscape Assessment
- Evaluate market dynamics, patient pathways, medical practice, and objective competitive data
- Evaluate HTAs & proxies
- Develop perspective on evolving market 'White Space' / unmet need

#### Stakeholder Value
- Use market research to characterize stakeholder unmet needs at launch
- Identify anticipated value/differentiation drivers and acceptance thresholds
- Focus on specific evidence requirements for optimized approval/utilization

#### Gap Analysis & TPP/CDP Scenario Surfacing
- Surface gaps in program objectives in context of evolving launch environment, stakeholder needs and desired value drivers to frame TPP scenarios
- Align TPP to stakeholder evidence needs to surface evidence strategy gaps and frame CDP scenarios

#### Trade-off Analysis
- Conduct cross-functional evaluation of ROI considerations & key cost, risk and value tradeoffs associated with pursuit of select TPP and CDP scenarios
- Gain agreement around recommendations for strategic product profile focus and value demonstration plan to optimize medicine value

#### Optimized Evidence Plan(s)
- Translate recommended trade-off outputs into integrated evidence plan including regulatory and additional value evidence development
- Articulate risk plan to monitor for need to change strategic or operational plan
- Use ROI assessment to drive plan endorsement and execution

### Improving your probability of success

- Systematically gathering and analyzing the information you need
- Supporting you in analyzing options to seamlessly integrate clinical strategy and execution
Building evidence: Integrated Asset Development

Demonstrating and delivering the full value of your therapy to the marketplace

Integrated Asset Development Plan delivers complete set of cross-functional strategic and operational outputs across the development of a pharmaceutical therapy.

Integrated and iterative process drives optimized information and risk fidelity across the life cycle.

Process clarity provides efficiencies around cross-functional interfaces, dependencies and overlap.

Cross-functional focus ensures that process drives optimized value to all critical stakeholders.
Building the early evidence-generation plan

Key deliverables and activities

Pre-Clinical

- Disease Area Strategy
  - Value Proposition
    • Indication Prioritization
    • Financial Trade-off Decision Analytics
    • Pricing Analysis
  - Target Product Profile
    • Competitive Landscape Analysis
    • Patient Pathway Analysis
    • Stakeholder Analysis
    • Policy Landscape
    • Payer / Provider / Patient Research
    • HTA Analysis
    • KOL Analysis / Interviews
    • Draft Launch Label

Phase I

- Regulatory Plan
  - NDA Submission Plan
- Clinical Development Plan
  • Translational Science plan
  • Clinical Pharmacology
  • Clinical Trial Landscape
  • Regulatory Pathway Assessment
  • Benefit-Risk Value Proposition
  • Endpoint Analysis

Phase II

- Clinical Development Plan
  • Generate CDP Scenarios
  • Timelines and Key Milestones
  • Endpoint Strategy
  • Regulatory Strategy
  • Statistical Modeling
  • Study Design Concept Scenario Development
  • Interim Decision Points
  • Risks/Contingencies
  • TPP/CDP Alignment
  • Protocol Development & Optimization
- Value Proposition
  • NPV/ROI Evaluation
- Market Access Plan
  • Stakeholder Needs Assessment
  • Patient Access Considerations
- Regulatory Plan
  • End-of-Phase II Planning

Develop for Launch
Accelerated approval: Development considerations

**Discovery**
- Identify unmet medical need
- Develop target candidate compound

**Pre-clinical Development**
- Start API production and scale up
- Determine formulation
- Assess GLP toxicity
- Perform non-clinical safety/pharmacology, ADME, PK
- Determine if Adaptive Pathway is applicable

**Pre-IND Meeting**

**Submit IND**

**Meet with Reg Auth.**

**Phase I**
- Identify unmet medical need
- Develop target candidate compound
- Design FIH proof of principle study to determine PK, early safety profile and biologic activity (dose range)
- Design/conduct robust POC study to establish sufficient evidence in target population
- Leverage biomarkers
- Gather sufficient evidence for expanded label approval

**File for Initial Licensure**

**Phase II**

**Confirmatory Trial(s)**

**Regulatory Action Ltd. Initial Marketing**

**Marketing**
- Optimize brand value and reimbursement
- Product safety surveillance

**Expanded Marketing**

**Regulatory Action**
Now what? Doing the work…

*Optimizing execution & operations requires balancing internal cost with delivery*

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**Keeping the “Foot in the Future” mindset while executing mission-critical activities is a challenging balancing act for a small, emerging enterprise**

- Requires multi-disciplinary expertise (Large Pharma has New Products Planning)
- Requires senior-level, forward-thinking, strategic drug development expertise
- Requires good data to support cost, time, risk and return trade-offs
- Requires integration of multiple stakeholder-related planning efforts

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**This approach can be costly, especially if built through internal staffing**

- Headcount would be added at a time of most significant product attrition risk
- Requisite expertise is expensive

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**Alternate approach: Consider a “virtual pharma model”**

- Keep in-house decision-making expertise lean and focused on strategic intent
- Leverage capabilities of an integrated, end-to-end, full-service provider
- This requires a much more strategic, end-to-end approach to sourcing
Polling question #3

What is your organizations’ primary approach to building infrastructure and operationalizing your key programs?

› We’ll build out internal teams slowly overtime at a time of most significant product attrition risk.

› We’re partnering with other pharma organizations on this.

› We’re approaching a virtual model to keep a lean in-house model paired with expertise and services from an external service provider/partner (s)

› Something in between
## Leveraging your service provider

*Comprehensive integrated clinical and regulatory sourcing support*

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<thead>
<tr>
<th>Disease Area Strategy</th>
<th>Seamless Integration with Early Development Team</th>
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<tbody>
<tr>
<td>Clinical Support for Lead Identification/Optimization or Due Diligence</td>
<td>Integration with Non-Clinical Outsourced Activities</td>
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<tr>
<td>Translation Science Strategy &amp; Implementation (Lab)</td>
<td>Rigorous Project Management Across ECD Portfolio</td>
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<tr>
<td>Candidate Drug Nomination Package (Clinical/Reg/Commercial)</td>
<td>Integrated IT infrastructure</td>
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<tr>
<td>Animal-to-Human Dose Selection &amp; Formulation (Clin Pharm/MBDD)</td>
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<tr>
<td>Preparation &amp; Submission of IND Package/Agency meetings</td>
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<tr>
<td>Preparation of Phase I/PoC Protocols</td>
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<tr>
<td>Tech transfer &amp; execution of GLP clinical assays (PK, PD, ADME, Genomic, etc.)</td>
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<tr>
<td>Early Patient &amp; Endpoint Strategies</td>
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<tr>
<td>Ongoing evolution of Integrated Asset Development Plan</td>
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<tr>
<td>Operational Start-Up and Execution of ECD Program (Data Flow)</td>
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<tr>
<td>Preparation and transition to Phase II/III Clinical Program</td>
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In Conclusion… Focus on Driving Value

Key Takeaways

The role of the Emerging Pharma leader is to balance the needs of “Today” with the requirements of “Tomorrow”:

• **Recognize the opportunity:**
  › Align clinical & commercial intentions

• **Design to build evidence:**
  › Integrate key program elements to inform stakeholder requirements

• **Optimize execution & operations:**
  › Balance current spend against future return by leveraging capabilities of a partner/service provider

• **Deliver value:**
  › Planning for the future now helps optimize the value of your asset
Thank you!

Q&A

For more information:

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