Impact of Patient Engagement on Project Valuation

Bennett Levitan, MD-PhD
Epidemiology, Janssen Research and Development

CTTI Patient Groups & Clinical Trials Expert Meeting

January 22, 2015
Disclosures

- Bennett Levitan is employed by Janssen R&D, a health care company developing numerous pharmaceuticals.

- Bennett Levitan owns stock in Johnson & Johnson and is invested in financial portfolios that own stock in companies undertaking clinical development of pharmaceuticals.
Agenda

• An approach to project valuation

• Impact of patient engagement on valuation drivers
5 Key Drivers of Pharmaceutical Project Value

- **Revenue**
  - What financial benefits accrue from project success?

- **Cost**
  - Resource: What resources are expended developing the project?
  - Opportunity: What is not done while resources are committed?

- **Time**
  - When do the costs, revenue and risks occur?
  - Can risks be resolved before major resource commitment?

- **Risk** ...

- **Intangibles**
  - Patient health and satisfaction
  - Strategic relevance
  - Precedent
  - Reputation
  - ...
Many Manifestations of Risk as a Key Driver

- **Technical risk**
  - Will we choose to advance development after each study?
    - Efficacy, safety, competitors, management, payers, etc.
- **Regulatory risk**
  - Will the health authorities approve this treatment and as planned?
- **Operational risk**
  - Will we complete each study in the expected time?
  - Will the regulatory review complete in the expected time?
- **Resource risk**
  - Will the studies cost what we expected?
  - Will the staffing requirements be what we planned for?
- **Forecasting risk**
  - How will actual revenue compare to predicted revenue?
How can we consider these drivers collectively?
One General Approach for Project Valuation

- Break apart the different paths towards success and failure
- Assess the costs, revenue, risks and timing associated with each separately
- Calculate metrics associated with the paths collectively

- Two metrics we will consider
  - Probability of technical and regulatory success (PTRS)
  - Expected net present value (ENPV)
Break apart the different paths towards success and failure

- **Circles represent studies or other key risky events**
  - Branches indicate success or failure of the event
- **Success of one event brings the opportunity to attempt the next**
  - Definition of success generally based on study protocol, target product profile, good clinical practices

![Diagram showing the paths towards success and failure in drug development](image)
Real World is Often More Complex

- Multiple indications
- Parallel development paths
- Multiple regulatory agencies
- Multiple definitions of success

- Despite complexity, approach is used
Break apart the different paths towards success and failure

- **Circles represent studies or other key events**
  - Branches indicate success or failure of the event
- **Success of one study brings the opportunity to attempt the next**
  - Definition of success generally based on study protocol, target product profile, good clinical practices
Including Technical and Regulatory Risk

- Characterize the technical uncertainty of each event with probabilities of success (POS or PTS)
- Several means to assess probabilities
  - Benchmarks
  - Company history
  - Subjective assessments
  - PK/PD modeling

Probability of technical and regulatory success (PRTS)

- Probability of regulatory approval: 90% (Succeed) - 10% (Fail)
- Probability of phase 3: 60% (Succeed) - 40% (Fail)
- Probability of phase 2: 40% (Succeed) - 60% (Fail)

Overall probability: 22%
Is Regulatory Approval a “Success”? 

- Increasingly, regulatory approval is insufficient
  - Need patients and physicians to value the product
  - Need approval to reimburse
  - Needs payers to place product on formulary
- Should incorporate forecasting risk
Interaction of Revenue and Time

- **Time value of money**
  - $1000 next year is worth less than $1000 today
  - $1000 in two years is worth even less
- **Why?**
  - Can invest the $1000 in less risky opportunities and have more funds in the future
- **How characterize the effect of time?**
  - “Present value” of money and “net present value” (NPV)
  - Calculation is straightforward
  - Critical point: Delaying the launch of a product can greatly reduce the value of the product
  - Impact can be tremendous.
    - A year’s delay can reduce NPV by 10%!
    - Old saw: “A million dollars a day”
Additional Impacts of Time of Forecast

- **First to market**
  - The first treatment in a given disease a higher chance of achieving large market share and being reimbursed
  - Also advantages to second to market vs. third, etc.

- **More time until patent expiration**

  ![Time vs. Revenue Diagram]

  - Huge impact at patent expiration
  - Earlier launch increases time until revenue curve decays
Each development path has an associated cost or reward
Characterize these costs/rewards in present value terms
More steps → more cost
Putting it all together: ENPV

Expected Net Present Value

**ENPV** = “Expected Net Present Value”

= Average NPV adjusted for regulatory & technical risk

= \( 0.22 \times 400 - 0.02 \times 45 - 0.16 \times 40 - 0.60 \times 3 = 77 \text{ MM} \)
Role of ENPV

- Encapsulates cost, revenue, time, technical risk and regulatory risk
- Can be augmented to account for operational and resource risk
- Extremely valuable metric for
  - Choosing between different plans for a product
  - Comparing products
  - Assessing a portfolio of products
- And
  - Assessing the impact of patient engagement
Agenda

• An approach to project valuation

• Impact of patient engagement on valuation drivers
Patient Group Engagement Across the Clinical Trial Continuum

Building a model to evaluate impact

Pre-Discovery
- Interest of research question to patient community
- Provide data on unmet need and therapeutic burden
- Direct funding and fund raising for research or product development
- Understanding mechanisms of action relevant to disease and symptom burden

Pre-Clinical
- Network recruitment / outreach
- Direct funding and fund raising for research or product development
- Infrastructure support
- Provide input on study design (barriers to participation)
- Support trial awareness and recruitment
- Peer advocate during informed consent procedure

Phase 1
- Direct funding and fund raising for trial operations support
- Network recruitment / outreach
- Serve on a Data Safety Monitoring Board
- Report on patient feedback regarding sites, investigators, and study participant experience
- Serve in preference studies for benefit-risk assessment

Phase 2/3
- Natural history database / registry support
- Provide feedback on how the patient community views results
- Help return study results to participants
- Write newsletter articles or blog about results
- Co-present results
- Serve on post-market surveillance initiatives

FDA review & approval
- Serve on FDA advisory committees
- Provide testimony at FDA hearings
- Feedback on meaningful clinical endpoints

PAS/Outcomes

Provided by CTTI
*Adapted from Parkinson’s Disease Foundation materials for CTTI’s Patient Groups & Clinical Trials Project
Provide information on unmet need, therapeutic burden, benefit-risk of available treatments (therapeutic context)

- **Impact on valuation**
  - Selection of treatments with greater medical need → less regulatory risk
  - Increased medical need → Increased patient/HCP interest
  - More likely to select the right projects → less opportunity cost

⇒ Improves regulatory risk, revenue, opportunity cost and intangibles

→ Need to talk with patient early
Help finalize eligibility criteria within the study protocol; Assist in creating the informed consent form;

- **Impact on valuation**
  - Easier to obtain patients $\rightarrow$ increased rate of enrollment $\rightarrow$ shorter studies
  - Improves cost, timing, operational risk and intangibles (patients benefit earlier, reputation boost)

$\Rightarrow$ Need to talk with patient early

### Prob (\$MM)

- **Succeed**
  - **Phase 3**
    - **Succeed**: 40%  
      - **Succeed**: 90%  
        - **Prob**: 22%  
          - **NPV ($MM)**: 400
    - **Fail**: 60%  
      - **Fail**: 10%  
        - **Prob**: 2%  
          - **NPV ($MM)**: -45

- **Fail**
  - **Phase 2**
    - **Succeed**: 60%  
      - **Fail**: 40%  
    - **Fail**: 40%  
    - **Succeed**: 60%  
    - **Fail**: 40%  
      - **Fail**: 60%  
        - **Prob**: 16%  
          - **NPV ($MM)**: -40  
        - **Fail**: 60%  
          - **Prob**: 60%  
            - **NPV ($MM)**: -3
Provide input on study design, barriers to participation

- **Impact on valuation**
  - Increased rate of enrollment → shorter studies
  - Fewer amendments → shorter studies
  - Easier to participate → higher compliance with protocol and fewer dropouts → better efficacy and safety and less chance of too much missing data → higher probabilities of success

⇒ Improves cost, timing, technical/regulatory/operational risk, intangibles (patients benefit earlier, reputation boost)

Need to talk with patient early

<table>
<thead>
<tr>
<th>Prob</th>
<th>NPV ($MM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>22%</td>
<td>400</td>
</tr>
<tr>
<td>2%</td>
<td>-45</td>
</tr>
<tr>
<td>16%</td>
<td>-40</td>
</tr>
<tr>
<td>60%</td>
<td>-3</td>
</tr>
</tbody>
</table>
How Patient Engagement Impacts Risk:

Typical model for key events in a clinical study

- Present (planning)
- Start Protocol Outline
- Issue Protocol
- First Patient In
- Last Patient In
- Last Patient Out
- Database Lock
- Final Study Report

Patient engagement steps that improve enrollment impact here

- Sponsors have models/estimates for each interval
- Can model the impact of patient engagement with changes to the probability that a patient is recruited in a given time
Serve as a peer advocate during the informed consent procedure

- **Impact on valuation**
  - Better understanding of what to expect → higher compliance with protocol and fewer dropouts → better efficacy and safety and less chance of too much missing data
  
  ⇒ Improves technical risk, regulatory risk, operational risk, intangibles (patients benefit earlier, reputation boost)
Provide feedback on how the patient community will view results

- **Impact on valuation**
  - Increased patient uptake of treatment → higher revenue
  - Improves revenue and intangibles (reputation boost)
Participate in preference studies for endpoint weighting

Preferences for Anticoagulants in Atrial Fibrillation

**US Physician**
- Death
- Disabling Stroke
- Non-Disabling Stroke
- Major Bleeding
- Heart Attack
- Blood Clot

**US Patient**
- Death
- Disabling Stroke
- Non-Disabling Stroke
- Major Bleeding
- Heart Attack
- Blood Clot

Levitan, Yuan, González, et al., ISPOR 18th Ann Int Mtg, 2013
Participate in preference studies for endpoint weighting

- **Impact on valuation**
  - Improved compound strategy and defense of benefit-risk assessment
  - Stronger case to patients/physicians for use
  - Stronger argument to payers for reimbursement

⇒ Improves regulatory risk and revenue
Work with sponsor to ensure study participants get feedback from study

- **Impact on valuation**
  - Stronger case to patients/physicians for use
  - Stronger argument to payers for reimbursement
  ⇒ Improves technical/regulatory risk and revenue
Summary of Valuation Impacts of Patient Engagement (1 of 4)

- **Improves enrollment → Reduces time to launch → increases NPV**
  - Study design
    - Help define eligibility criteria within the study protocol
    - Provide input on study design (barriers to participation)
    - Advise on study recruitment
  - Recruiting
    - Network outreach
    - Support trial awareness and recruitment
  - Enrolling
    - Assist in creating the informed consent form
    - Peer advocate during informed consent procedure
Summary of Valuation Impacts of Patient Engagement (2 of 4)

- **Increases probability of technical success (PTS)**
  - Provide input on study design
  - Assist in creating the informed consent form
  - Peer advocate during informed consent procedure
  - Report on patient feedback regarding sites, investigators, and study participant experience

- **Increases probability of regulatory success (PRS)**
  - Provide data on unmet need and therapeutic burden
  - Serve in preference studies for benefit-risk assessment
Summary of Valuation Impacts of Patient Engagement (3 of 4)

- **Reduces dropout → PRS, PTS**
  - Assist in creating the informed consent form
  - Provide input on study design (barriers to participation)
  - Peer advocate during informed consent procedure
  - Report on patient feedback regarding sites, investigators, and study participant experience

- **Increases adherence → PTS, PRS**
  - Assist in creating the informed consent form
  - Provide input on study design (barriers to participation)
  - Peer advocate during informed consent procedure
  - Report on patient feedback regarding sites, investigators, and study participant experience
Summary of Valuation Impacts of Patient Engagement (4 of 4)

* Increases revenue
  * Interest of research question to patient community
  * Provide data on unmet need and therapeutic burden
  * Feedback on meaningful clinical endpoints
  * Serve in preference studies for benefit-risk assessment
  * Feedback on meaningful clinical endpoints
  * Write newsletter articles or blog about results
Conclusions

- Main drivers of treatment valuation are cost, revenue, timing, risk and intangibles
- Expected net present value modeling can account for most drivers in a clear and well-accepted summary metric
- Patient engagement activities impact on all drivers for treatment valuation
- Many of these driver impacts can be characterized quantitatively and can support sponsor decisions to increase patient engagement in trial development