# Pharmaceutical R&D: Why invest?

- Attractive ROI
- High-quality assets available
- Contribute to the betterment of humankind
  - Prevent, treat or cure disease
  - Save lives
  - Improve patient Quality-of-Life (QoL)

# Why now? What has changed?

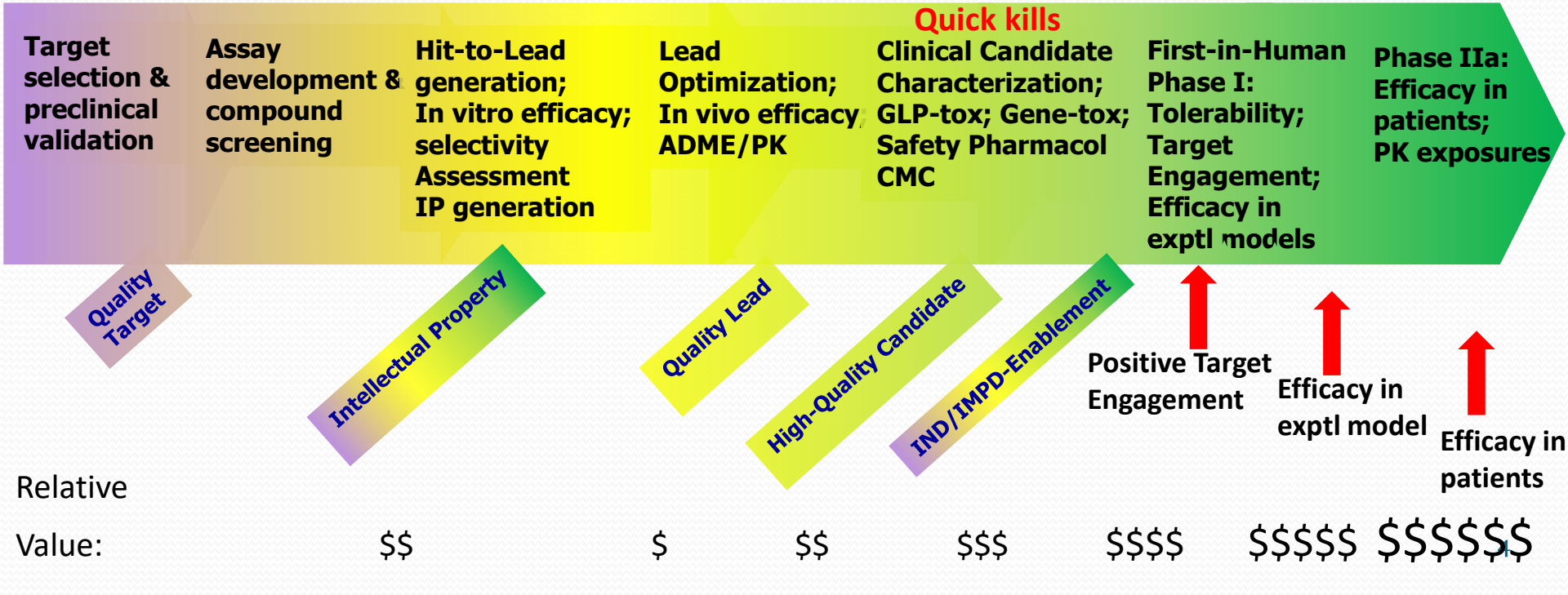
- Unparalleled culmination of knowledge / recent intersection of advances across disciplines
  - Genomics, Proteomics, Epigenetics track, even predict disease progression
  - Chemical Biology to probe complex cellular signaling mechanisms
  - Tools to assess 'drug-ability' with meaningful predictability
  - Ability to not only capture but also analyze massive amounts of data to decipher subtle differences among disease states, between patients
  - 'Evolution' from decades-old high-throughput, single target mindset
    - Molecular biology techniques, pharmacological target screening, combinatorial chemistry, etc. are valuable technologies but not geared towards treating diseases
- Focus shifting towards holistic approaches to treat & prevent disease; high expectations
  - Patients demand more than palliative treatments
  - Therapeutics offering marginal improvements will not be reimburse-able
- Big Pharma divestiture of early R&D
  - Risk-averse; shifted towards internal / external ventures to share risk; spread $ across multiple opportunities (VC model); buy-in later even if more $$$
- Public / patient awareness & willingness to participate
- Philanthropy, foundations, HNW individuals ready to contribute
- Assets + $$ = Opportunity

# Identifying opportunities of high value


- Disease cure / 'disruptive' therapy or technology
  - Therapeutic agent, device or (surgical) technique that cures the patient
- Disease interception
  - Stop progression
- QoL Improvement
  - Lasting & measurable, not merely prolongation
- Disease modification
  - Favorably alter disease progression with alleviation of symptoms
- Accompanying diagnostic / biomarker
  - Selection of likely responders from patient population
- Standard-of-Care (SoC) replacement
  - Garners favorable reimbursement
- Orthogonal to existing therapeutic mechanisms
  - Works in an additive (minimally) or synergistic manner with other Rx's
- Best-in-Class
  - BIC may not become SoC
- First-in-Class
  - 'White-space' can be challenging with respect to regulatory bodies
  - But can capture initial market
- Differentiated follow-on

# The Strike-Zone

- Minimal value creation until High-Quality Candidate is identified
- First notable inflection point comes upon IND enablement (x $M – xx $M)
- ROI from demo of target engagement (xx $M) & positive efficacy readouts (xxx $M)
- **Proposed strike-zone:**
  - **Consider High-Quality Candidates & above only; must have Back-up; IP position must be robust**
  - **Deal structure ideally back-loaded (min upfront; willing to give some equity?; no VC!)**
  - **Focus on quick-kill experiments to de-risk before large clinical spend; push for 'efficacy' in Ph1**



# Assumptions & Questions

- Base-case assumption
  - A typical High-Quality Candidate (with Back-up) will require $2-4 M and 18-24 months to advance through IND-enablement and into Humans for first clinical readout
  - Positive demonstration of target engagement, if target allows, is expected to generate marginal ROI (2-4x), depending upon pharmacological target/ therapeutic area
  - Efficacy in experimental models in healthy human volunteers (HV), if possible, would be expected to increase ROI more significantly (4-8x)
  - Efficacy in patients in PhIIa (or PhI if possible) would produce the largest ROI (10+x)