Tufts Center for the Study of Drug Development

Briefing

Cost of Developing a New Drug

November 18, 2014

Tufts Center for the Study of Drug Development
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Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs

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R&D Cost Study Briefing
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Agenda

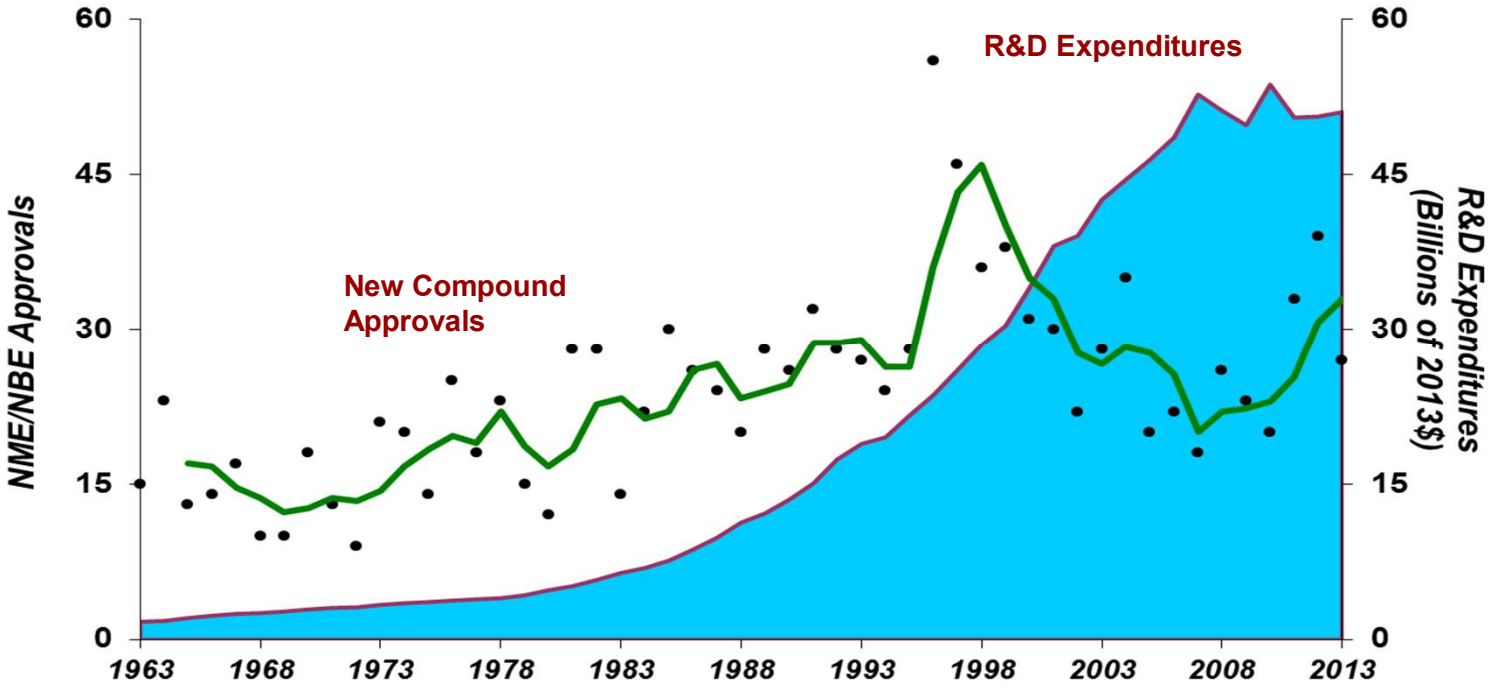
- Main Finding
- Data and Methods
- Clinical approval rates, phase transition rates, and out-of-pocket costs per approved compound
- Development times, the discount rate, and capitalized costs per approved compound
- Post-approval cost estimates
- R&D cost growth rates
- Cost drivers

Main Finding:

The estimated average pre-tax industry cost per new prescription drug approval (inclusive of failures and capital costs) is:

$2,558 million

New Drug and Biologics Approvals and R&D Spending



R&D expenditures are adjusted for inflation; curve is a 3-year moving average for NME/NBEs

Sources: Tufts CSDD; PhRMA, 2014 Industry Profile

Data and Methods

Outline of Study Cost Dataset

- 106 investigational new drugs and biologics from 10 firms first tested in humans anywhere in the world, 1995-2007
- Clinical period development cost data up to 2013
- Five compounds still active at the time of data collection.
- Compounds that lasted late in development oversampled to increase the amount of information for late development stages. Results then weighted to reflect the population distribution.
- Annual company biopharmaceutical R&D expenditures from 1990 to 2010 broken down in various ways (used to estimate pre-human R&D costs).

Elements Used to Determine Fully Allocated New Compound R&D Costs

- Out-of-pocket clinical costs (all indications, long-term animal testing, overhead, CMC during clinical testing and prior to first approval)
- Out-of-pocket discovery research and preclinical development costs
- Clinical approval success and phase attrition rates
- Development times
- Cost of capital

Out-of-Pocket Clinical Costs

- Survey data on costs by phase and year for a sample of investigational compounds.
- Oversampled compounds that proceeded to late-stage testing: stratified random sample.
- Weight survey response to reflect actual population distribution for strata.
- Calculate weighted average phase costs.

Out-of-Pocket Discovery and Preclinical Development Costs

- Cannot attribute all pre-human R&D costs to specific compounds.
- Use time series data on company annual aggregate spending on pre-human and clinical R&D.
- Apply lag structure on data based on gap between pre-human and clinical expenditures (difference in median phase times).
- Determine ratio of pre-human to clinical expenditures from lagged data.
- Apply ratio to clinical phase cost estimate to obtain a pre-human cost estimate.

Clinical Approval Success Rates

- Since many compounds fail in testing, phase costs must be weighted by the probability of entering the phase (expected costs) to obtain costs per investigational compound.
- Overall clinical approval success rates used to translate cost per investigational compound to cost per approved compound.
- Tufts CSDD database of investigational compounds used to estimate these probabilities (subset relevant to cost study sample period).
- Other interesting results obtained: attrition rates and distribution of failures by phase.

Phase Development Times

- Use survey data to find average time in phase (across indications).
- Use survey data to find average time between start of one phase and beginning of the next phase.
- Average phase-to-phase times used to establish a representative development time profile from synthesis to approval.
- Representative time profile, along with average phase lengths, used to determine how expenditures are distributed over time.

Cost of Capital and Capitalization

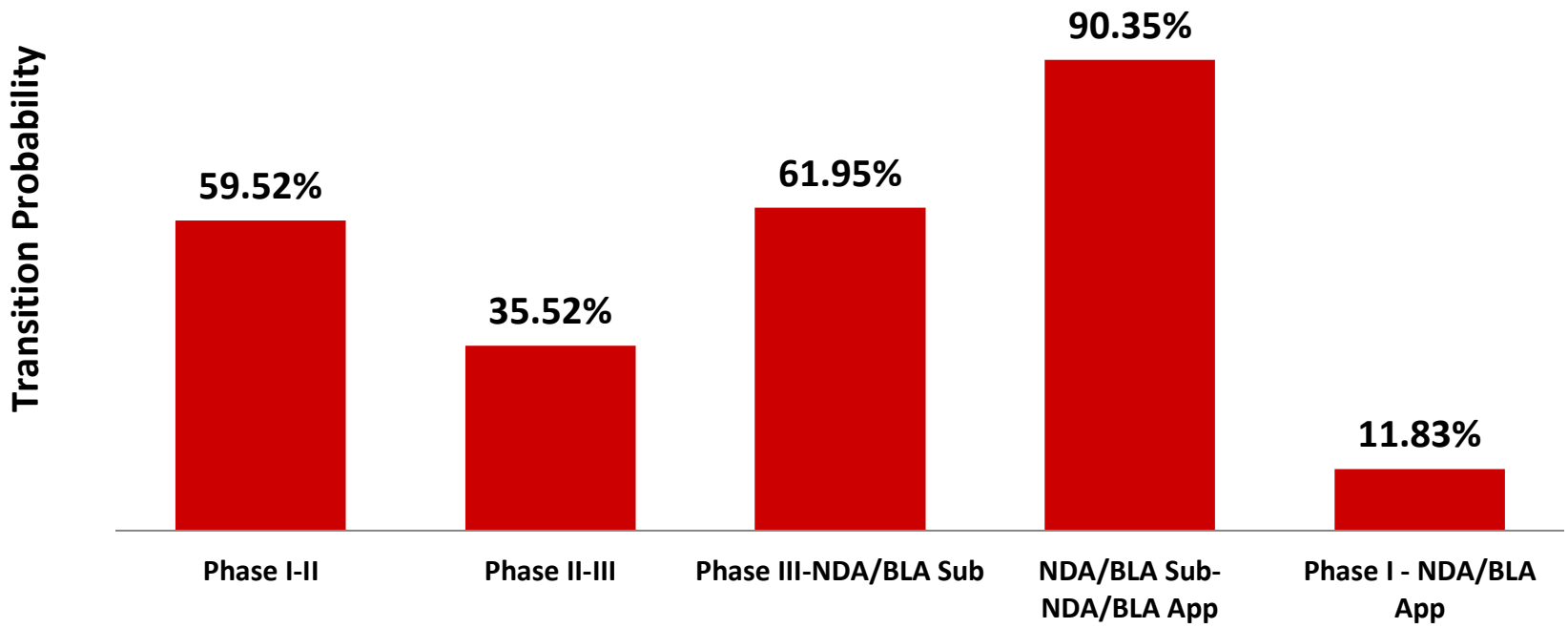
- Cost of capital is the expected return required by investors to get them to invest in drug development.
- Capital Asset Pricing Model (CAPM) applied to data on biopharmaceutical firms over relevant period to determine an industry cost of capital.
- Estimate is based on data on stock market returns and debt-equity ratios for a sample of biopharmaceutical firms.
- Used as the discount (interest) rate to capitalize R&D expenditures to marketing approval according to the estimated development timeline.

Results

Data for Phase Transition and Approval Success Rate Estimates

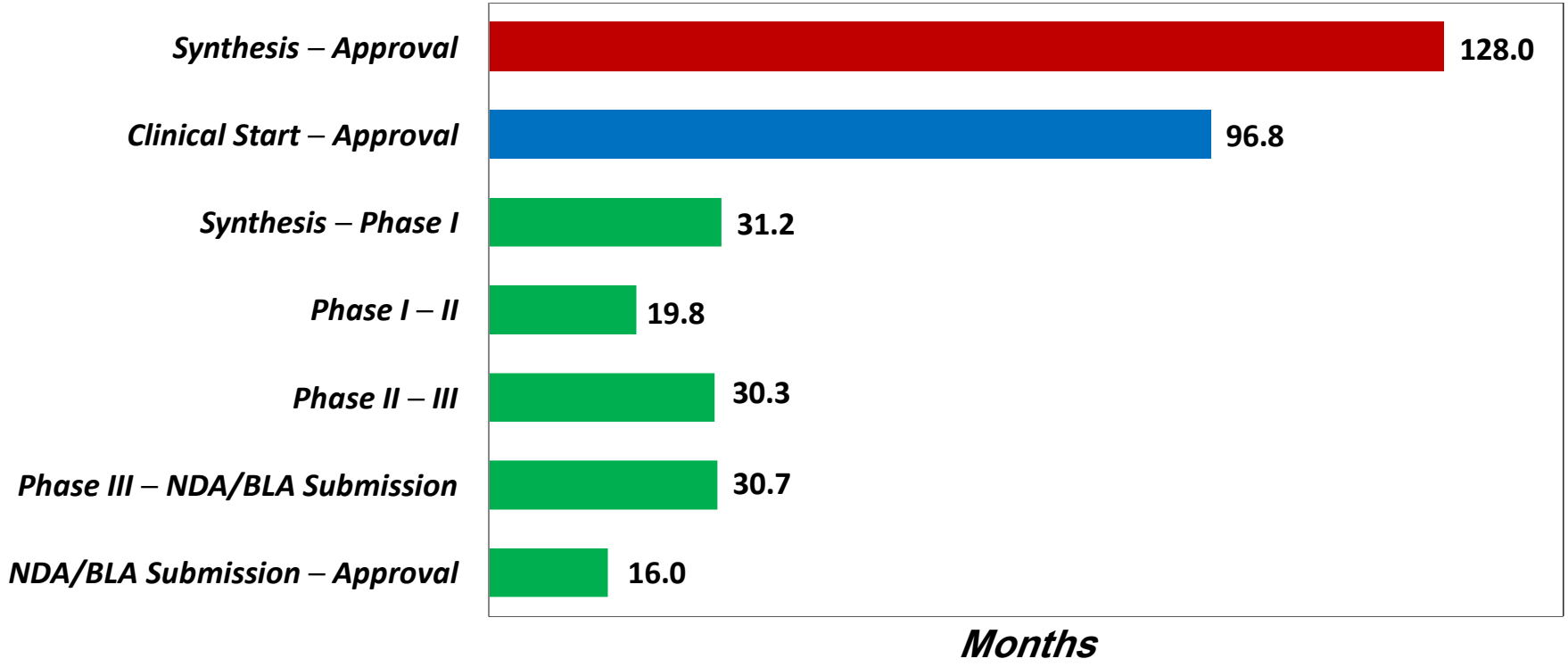
- Dataset of investigational compounds in the portfolios of top 50 firms (several commercial pipeline databases, published company pipelines, clinicaltrials.gov, web searches).
- Subset of self-originated compounds first tested in humans anywhere in the world from 1995 to 2007.
- 1,442 compounds met study inclusion criteria.
- Development status checked through end of 2013.
- For this set of compounds, 7.1% were approved, 80.3% had been discontinued in some phase, and 12.6% were still active in some phase.

Clinical Phase Transition Probabilities and Overall Clinical Approval Success Rate*



*Therapeutic new molecular entities and new therapeutically significant biologic entities first tested in humans, 1995-2007

Representative Development and Regulatory Review Time Profile (synthesis to approval)



Pre-human Cost Estimates

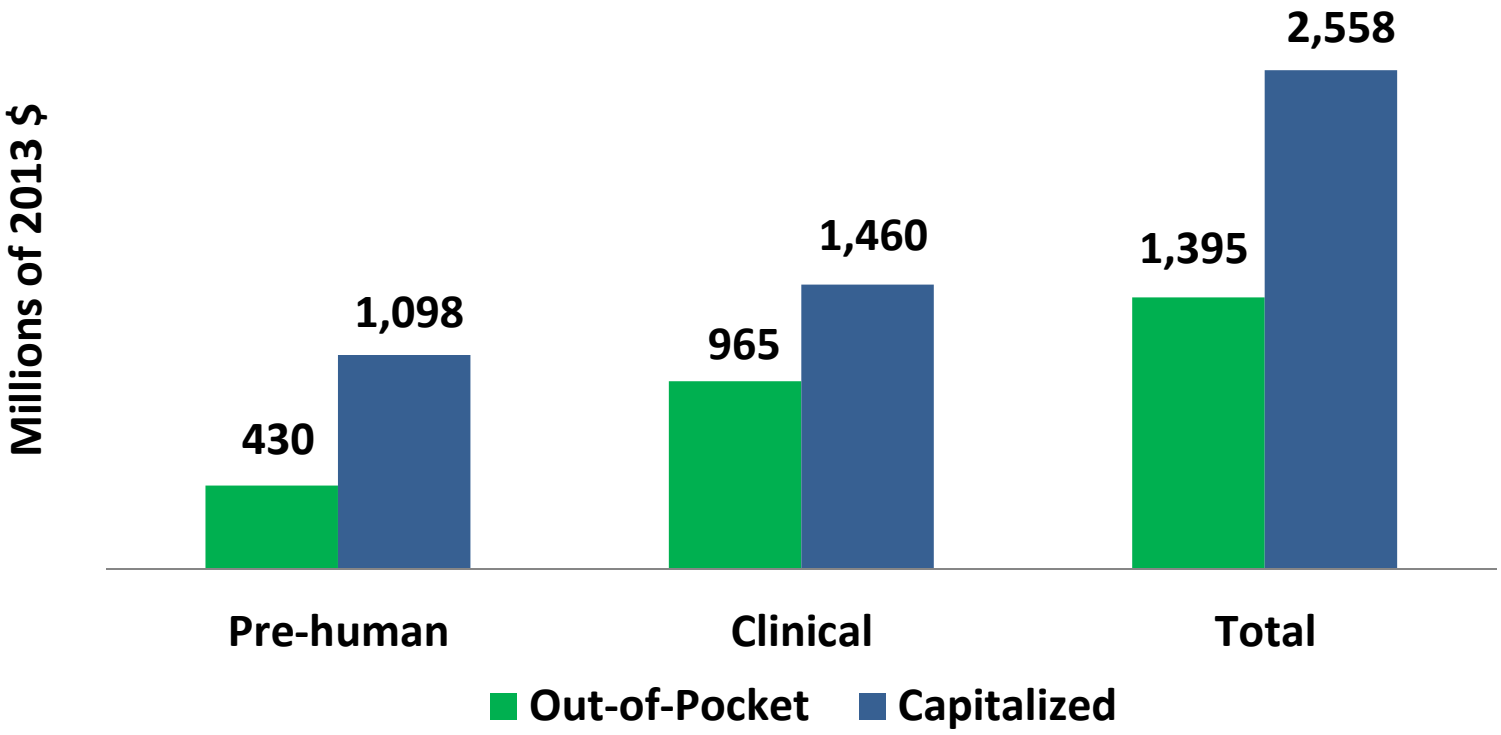
- **Annual data on pre-human and clinical period company R&D expenditures on self-originated investigational compounds aggregated across companies.**
- **Need to impose a lag structure between pre-human and clinical expenditures.**
- **Based on development time data, we used a 5-year lag between median pre-human and median clinical expenditures .**
- **Implies that pre-human expenditures are 30.8% of costs per approved compound.**
- **Results are not very sensitive to assumed lag within reason (4 and 6-year lags applied in sensitivity analysis)**

Nominal and Real Cost of Capital (COC) for the Biopharmaceutical Industry, 1994-2010

	1994	2000	2005	2010
Nominal COC	14.2%	14.9%	13.3%	11.4%
Inflation Rate	3.1%	3.1%	2.5%	2.0%
Real COC	11.1%	11.8%	10.8%	9.4%

Implication: R&D costs were capitalized at a 10.5% real COC

Out-of-Pocket and Capitalized Cost per Approved New Compound



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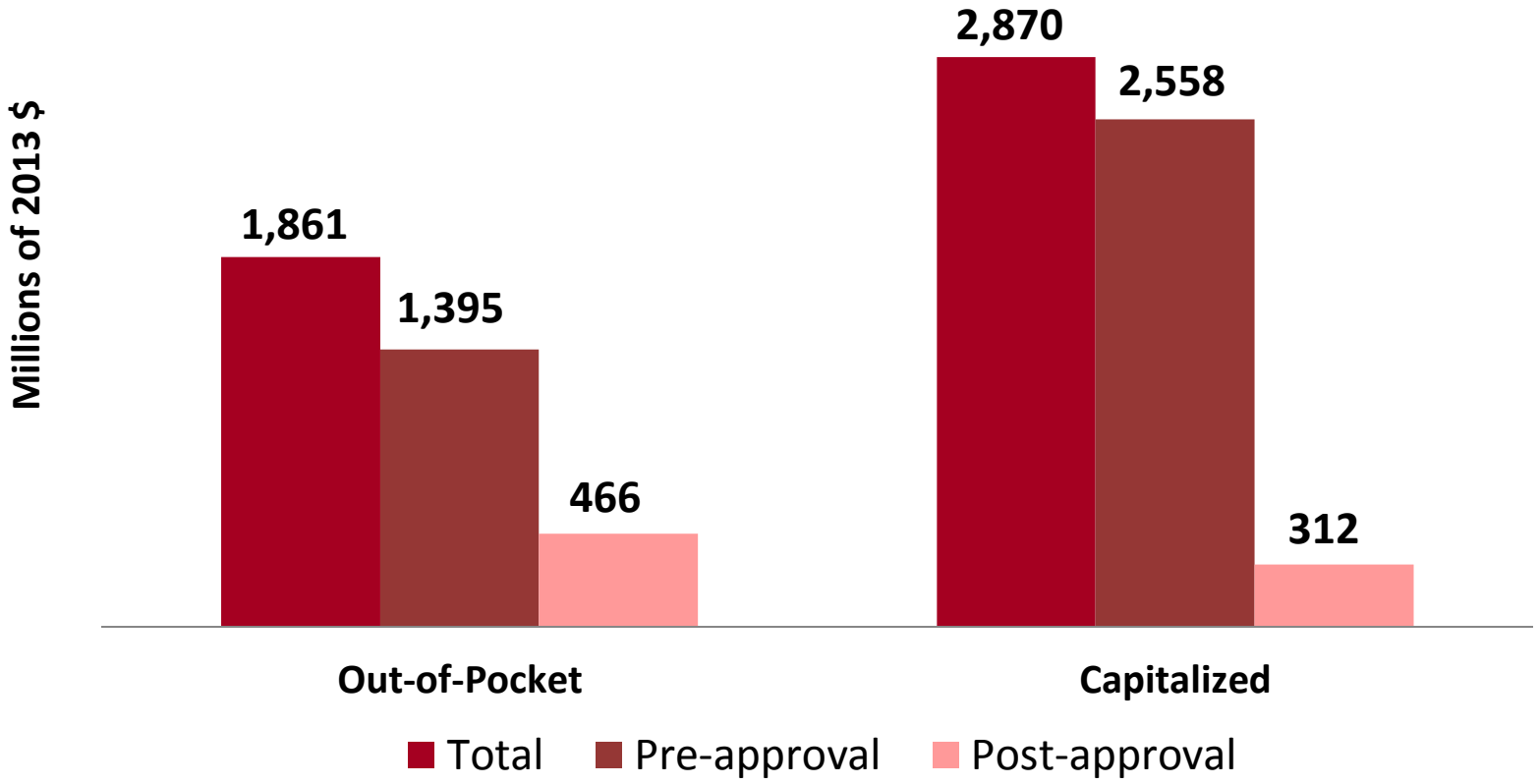
Pre-approval, Post-approval and Total Lifecycle Cost per Approved New Compound



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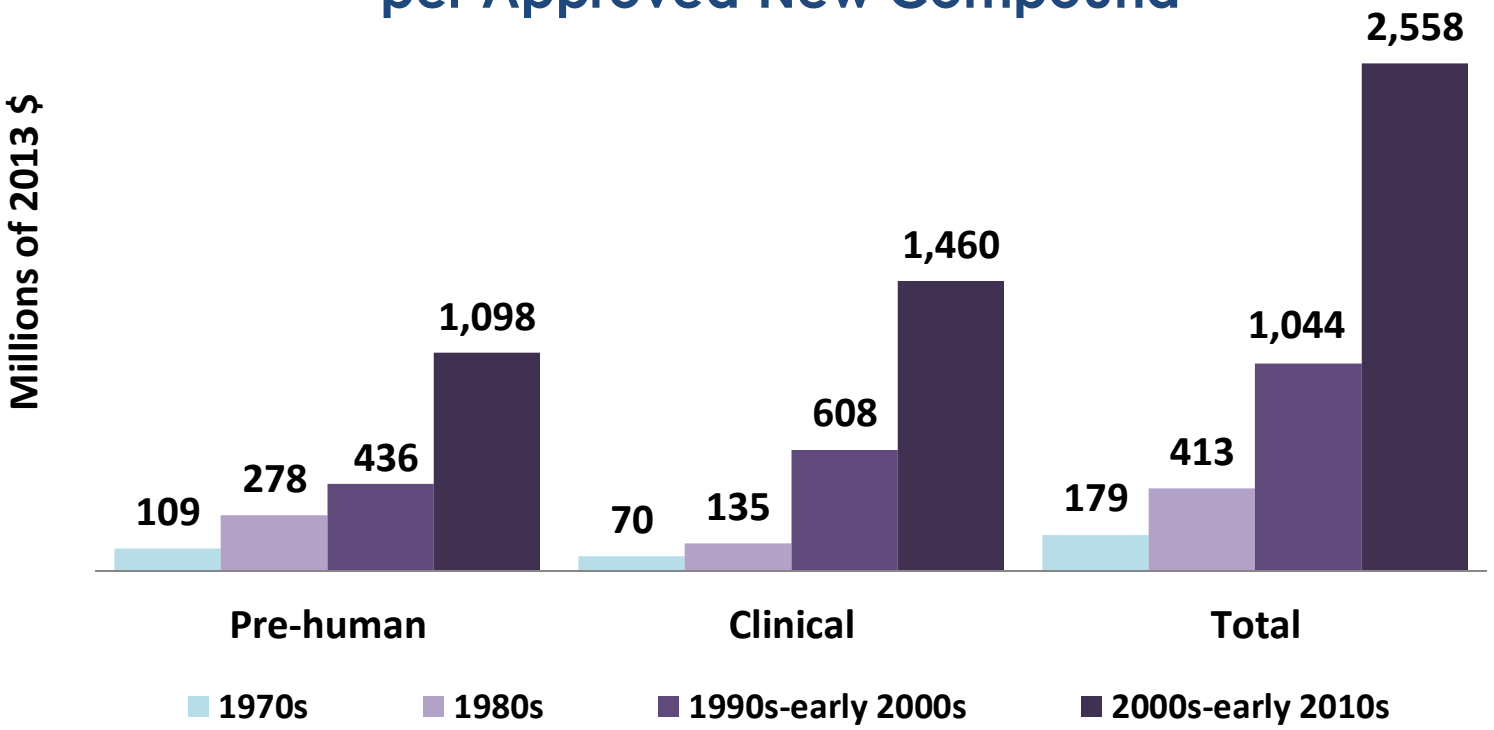
Growth in Capitalized R&D Costs per Approved New Compound



Sources: 1970s, Hansen (1979); 1980s, DiMasi et al. (1991); 1990s-early 2000s, DiMasi et al. (2003); 2000s-early 2010s, Current Study

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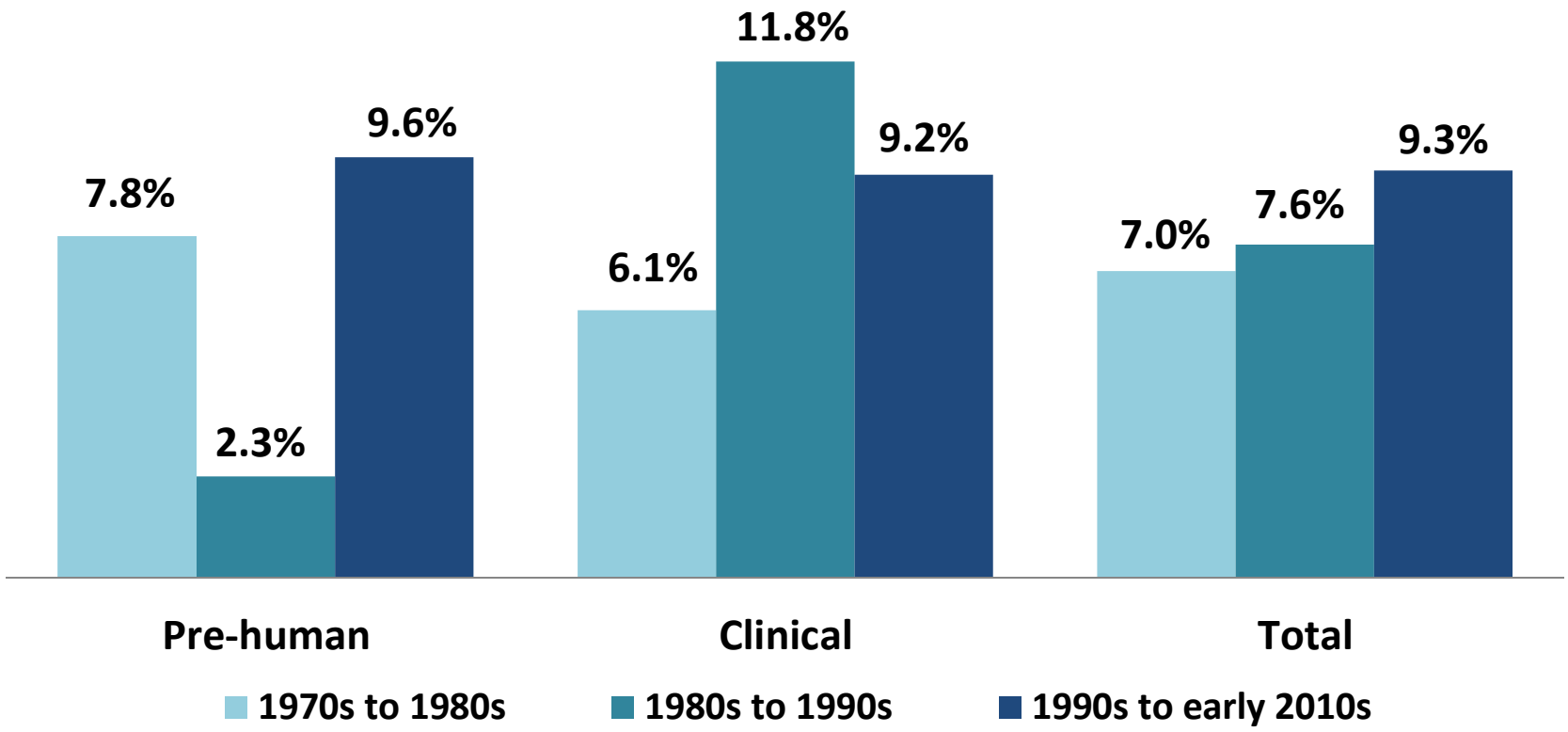
Compound Annual Inflation-Adjusted Growth Rates for Out-of-Pocket R&D Costs



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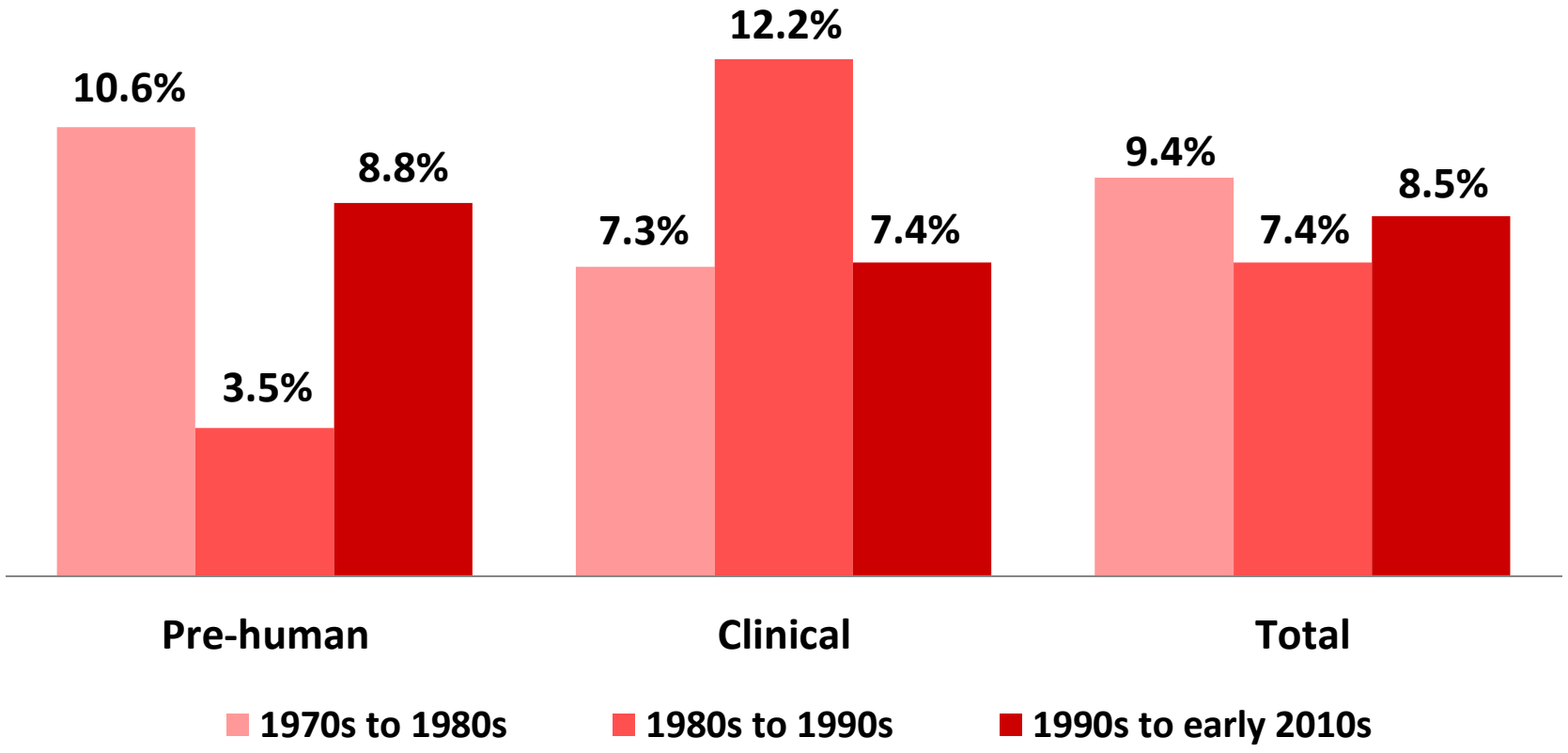
Compound Annual Inflation-Adjusted Growth Rates for Capitalized R&D Costs



Cost Drivers: Change in Capitalized Cost per Approved Compound by Factor (direct cash outlays)*

Factor Category	Factor	Percentage Change in Cost
Cash Outlays	Out-of-Pocket Clinical Phase Costs	82.5%
	Pre-human/Clinical Cost Ratio	1.6%
	Overall Out-of-Pocket Costs	85.5%

*** Factor impact on current study cost relative to prior study cost ($1,044 million in 2013 dollars)**

Cost Drivers: Change in Capitalized Cost per Approved Compound by Factor (development risk)*

Factor Category	Factor	Percentage Change in Cost
Risk	Clinical Approval Success Rate with Prior Study Distribution of Failures	57.3%
	Distribution of Failures with Prior Study Clinical Approval Success Rate	-6.0%
	Overall Risk Profile: Clinical Approval Success Rate plus Distribution of Failures	47.3%

*** Factor impact on current study cost relative to prior study cost ($1,044 million in 2013 dollars)**

Cost Drivers: Change in Capitalized Cost per Approved Compound by Factor (time and cost of capital)*

Factor Category	Factor	Percentage Change in Cost
Time	Pre-human Phase	-4.9%
	Clinical Phase	0.2%
	Regulatory Review	-3.0%
	Overall Development Timeline	-5.6%
Cost of Capital	Discount Rate	-3.1%

*** Factor impact on current study cost relative to prior study cost ($1,044 million in 2013 dollars)**

Summary

- Total capitalized cost per approved new compound grew at an 8.5% compound annual rate; out-of-pocket cost per approved new compound grew at a 9.3% annual rate.
- Clinical approval success rates have declined significantly.
- Increases in the cash outlays used to conduct clinical development and higher drug failure rates during clinical testing have contributed most to the estimated increase in R&D costs.
- Changes in the time to develop and get new drugs approved and in the cost of capital had modest moderating effects on the increase in total R&D cost.

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