Valuing Pharmaceutical Drug Innovations

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Objective:

“Valuing Pharmaceutical Drug Innovations”

Why?

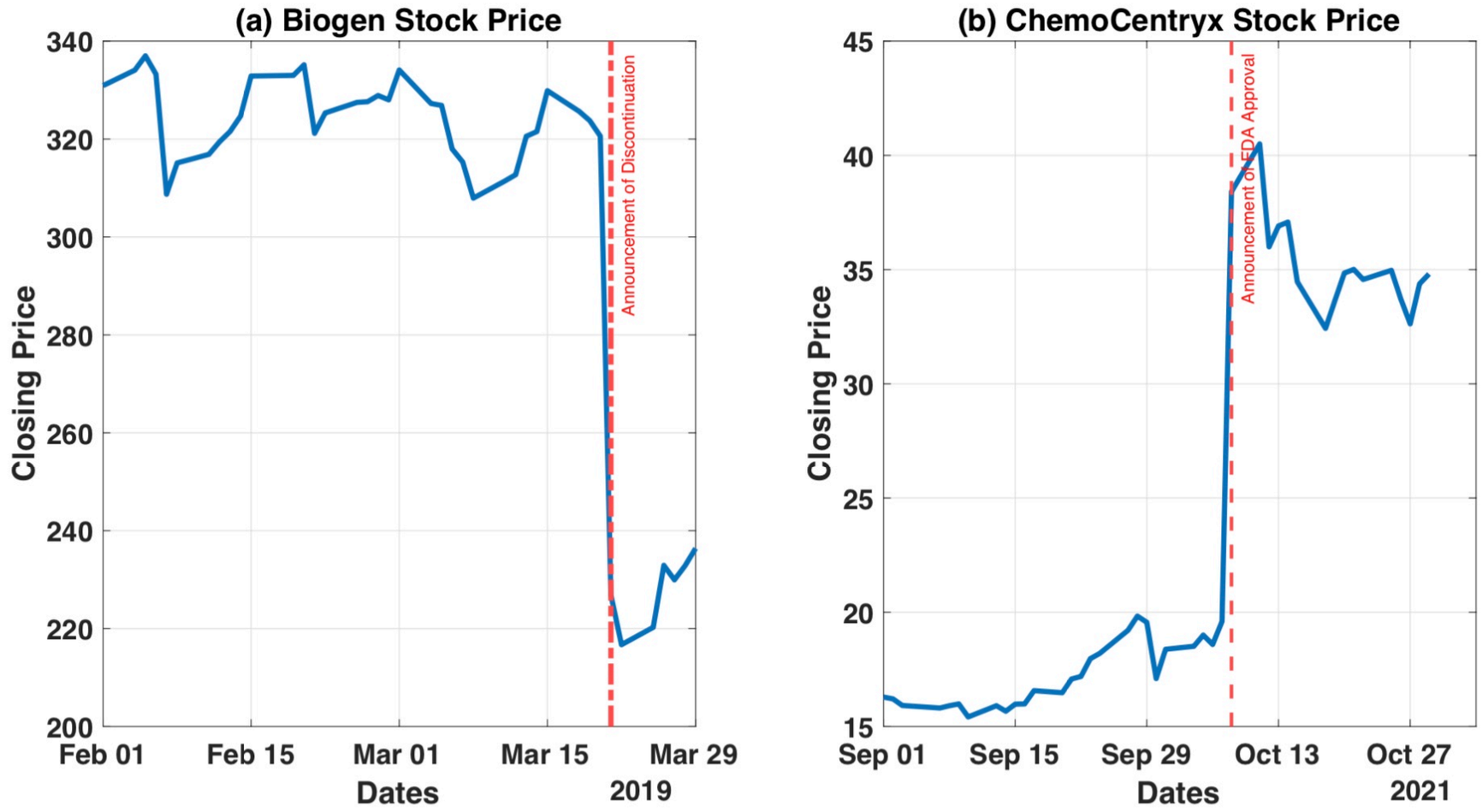
Policy: pre-requisite to incentivise drug innovations in practice (e.g. prizes, patents, licensing…)

How?

Using abnormal returns when announcements concerning drugs’ development are made

First Glance at the "How":

Figure 1: **Examples of Drug Announcements**



Note: Panels (a) and (b) display the time series of stock prices for Biogen and Merck around the announcement dates, respectively. On March 21, 2019, Biogen discontinued the Phase III clinical trial for a drug to treat Alzheimer's disease. On October 8, 2021, ChemoCentryx announced its FDA approval for a vasculitis drug.

First Glance at the Results:

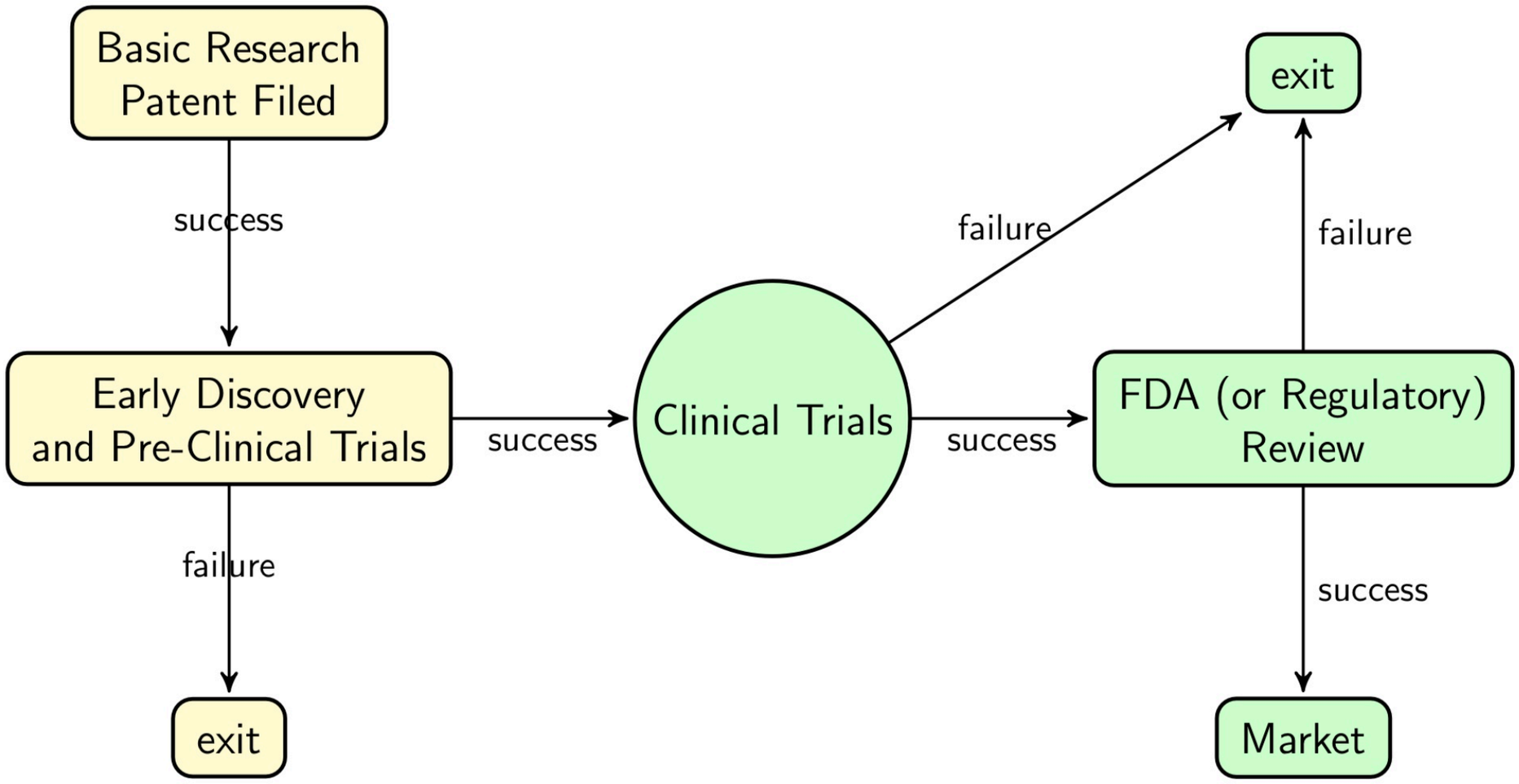
- Average market **value** of a successful drug: **$1.62 billion**
- At the discovery, average **value**: **$64.3 million**
- “ “ “ , average **cost**: **$58.5 million**

Roadmap

1. Institutional Background + Data (§ 3)
2. Model (§ 4)
3. Results (§ 5, 6)
4. Policy Implications (§ 7)

Institutional Background + Data

Figure 2: **Drug Development Process.**



Data: collect **dates of each success/failure announcement** to compare with stock market

... assuming homogeneous probabilities across drugs:

Table 2: **Transition Probabilities**

Stages	**Probability of Reaching a Stage** Marginal	Conditional
Phase I Clinical Trials	51.2%	51.2%
Phase II Clinical Trials	31.9%	62.4%
Phase III Clinical Trials	16.7%	52.4%
FDA Application	12.1%	72.3%
FDA Approval	10.8%	89%

Note: The unit of observation is a development project, i.e., a specific firm-drug-disease combination, associated with at least one announcement. The column labeled *Marginal* denotes the shares of all the initiated development projects, and the column labeled *Conditional* denotes the shares of the development projects that made it to the next stage. For example, 16.7% of all projects reached Phase III, and conditional in reaching Phase II, 52.4% made it to Phase III.

(They are used later in the model)

Remarks:

- Unreliable date of the start of clinical trials
    - Drop these announcements
- US focused (but EU similar)
- Possibility of bundling bad and good news:
    - Drop announcements that are bundled

Data on the market value of a firm:

- Daily returns from US pharma public firms
  - Including dividends
- Drop large firms (>95pc):
  - Increased chance of success
  - Different selection of drugs to develop

Model

I. From abnormal returns to values and costs

II. Identifying abnormal returns

III. Estimating discount rates

Big Remark

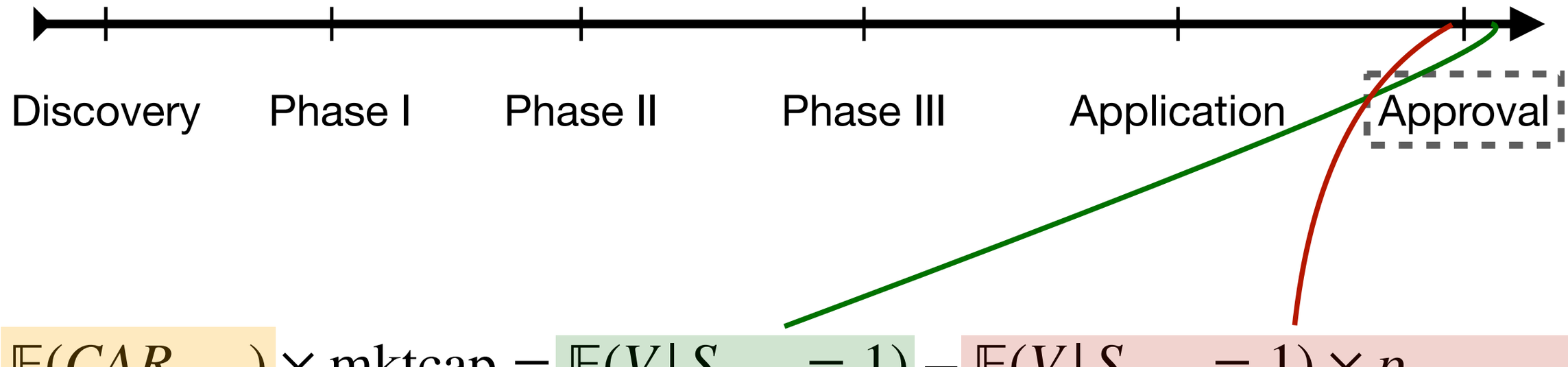
Everything is Homogeneous

E.g.: The expected value of a discovery, cost of development, probability of success, effects on the stock markets…

are homogenous across drugs and firms

I. From abnormal returns to values and costs

A. *Value at FDA approval stage*



$$\underbrace{\mathbb{E}(CAR_{appr})}_{\text{(Assume we know this)}} \times \text{mktcap} = \underbrace{\mathbb{E}(V \mid S_{appr} = 1)}_{\text{after announcement}} - \underbrace{\mathbb{E}(V \mid S_{appr} = 1) \times p_{appr|appl}}_{\text{just before announcement}}$$

$$= \underbrace{\mathbb{E}(V \mid S_{appr} = 1)}_{\text{We can get this!}}(1 - p_{appr|appl})$$

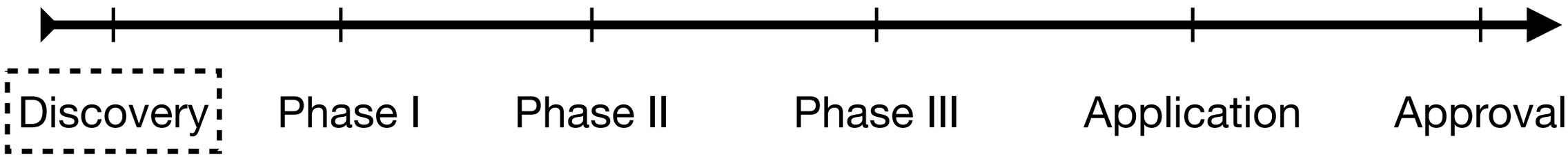
Remark: No development costs at this stage!

V : value

S_k : stage k?

I. From abnormal returns to values and costs

B. *Value at Discovery Stage*



$$\mathbb{E}(V \mid S_{disc}=1) = \left(\sum_{\tau \geq 0} \sum_{t=\tau}^{\infty} \delta^t \pi \times \mathbb{P}(\tau \mid S_{disc}=1) \right) \times p_{appr|appl} \times p_{appl|disc}$$

$$= \frac{\pi}{1-\delta} \times \left(\sum_{\tau \geq 0} \delta^t \times \mathbb{P}(\tau \mid S_{disc}=1) \right) \times p_{appr|appl} \times p_{appl|disc}$$

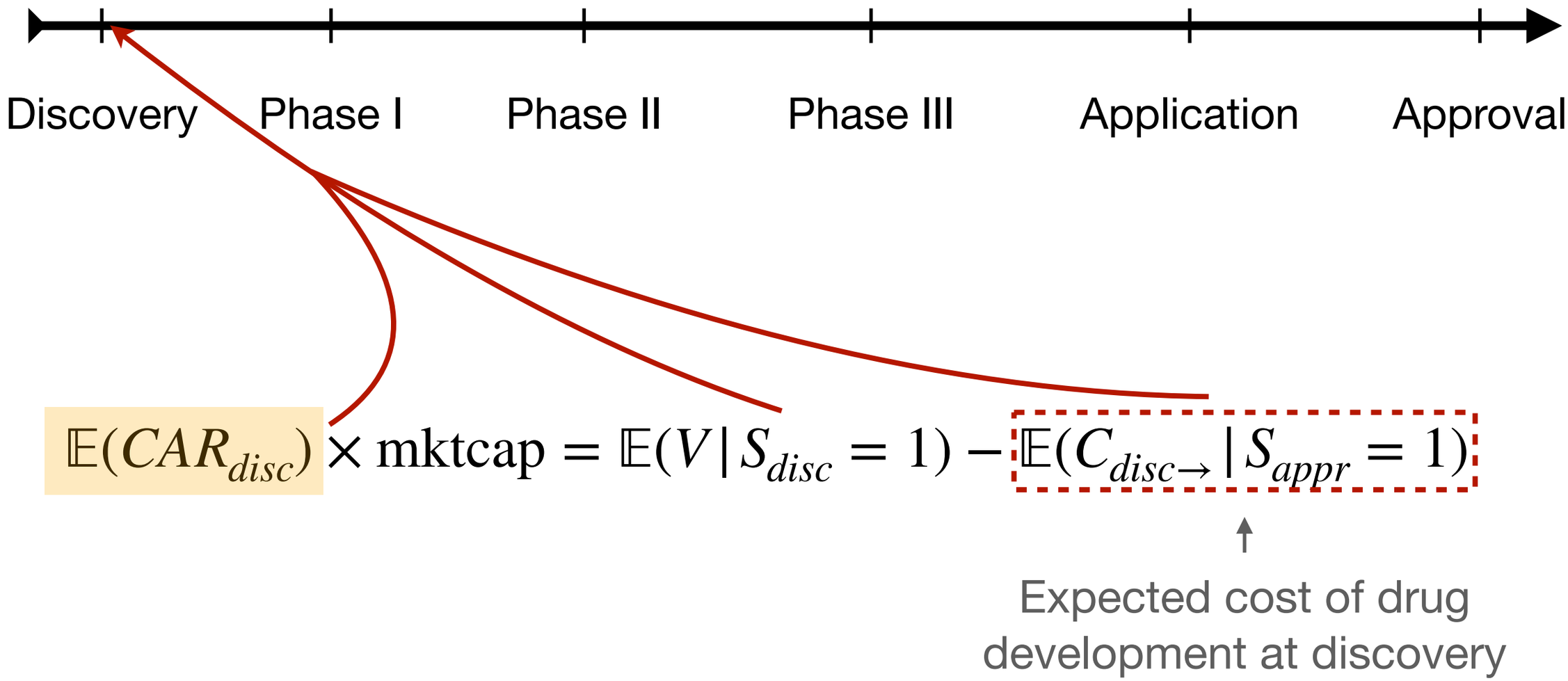
$$= \mathbb{E}(V \mid S_{appr}=1) \times \mathbb{E}(\delta^{\tau_{disc\rightarrow}}) \times p_{appr|appl} \times p_{appl|disc}$$

(Expected discount rate at discovery)
(Assume we know this)

π - yearly profits (average)

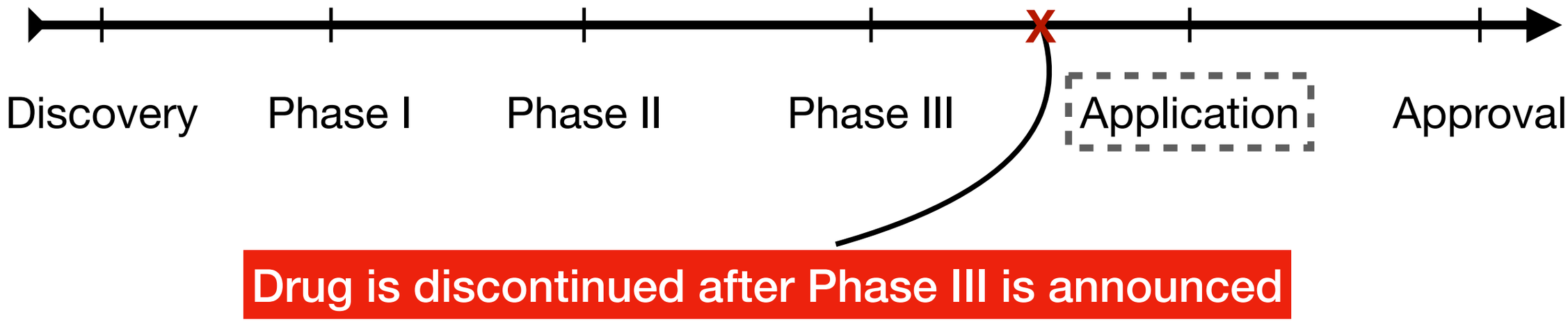
I. From abnormal returns to values and costs

C. *Cost at discovery stage*



I. From abnormal returns to values and costs

D. *Cost of FDA Application*



Can solve for this

$$\mathbb{E}(CAR_{drop\ after\ phase\ III}) \times \text{mktcap} = -\underbrace{\mathbb{E}(V \mid S_{phaseIII} = 1)}_{\text{value lost after discontinuation}} + \underbrace{\mathbb{E}(C_{appl\rightarrow} \mid S_{appl} = 1) \times p_{appl|phaseIII}}_{\text{cost savings}}$$

$$= \mathbb{E}(V \mid S_{appr} = 1) \times \mathbb{E}(\delta^{\tau_{appl\rightarrow}}) \times p_{appr|appl} \times p_{appl|phaseIII}$$

+ similar derivations for **expected costs of**

Phase I, II, III, and clinical trials

II. Identifying (cumulative) abnormal returns

Strategy: abnormal r = actual r - expected r

Procedure:

$r_{i,t}$ = log(returns) firm i, period t; j announcements

(i) Fit $r_{i,t} = \alpha_i + \beta_i r_t + \varepsilon_{i,t}$ for $t = -110, \ldots, -10$ (before announcement)

(ii) Define abnormal returns: $\hat{\varepsilon}_{i,j,t} \equiv r_{i,t} - \hat{r}_{i,j,t}$

(iii) $\widehat{CAR}_{i,j,t} = \sum_{\tau=t-w_l}^{t+w_u} \hat{\varepsilon}_{i,j,\tau}$

w_u, w_l: upper, lower window length
(1 and 2, in their estimation)

(iv) $\widehat{CAR}_{i,j,t} = \beta_{disc} \times \text{disc}_{i,j,t} + \beta_{appl} \times \text{appl}_{i,j,t} + \ldots + \omega_{i,j,t}$

Table 6: **Effects of Announcements on CAR**

	Full Sample	**Middle 90%**	**Bottom 95%**
Discovery	0.213	0.37	0.401
	[0.029, 0.420]	[0.029, 0.420]	[0.029, 0.420]
Discontinued during Discovery	-0.921	-2.429	-2.43
	[-2.239, 0.255]	[-2.238, 0.254]	[-2.238, 0.254]
Discontinued during Phase I	-1.150	-2.33	-2.319
	[-2.191, -0.157]	[-2.191, -0.157]	[-2.191, -0.157]
Discontinued during Phase II	-3.637	-7.63	-7.813
	[-5.199, -2.252]	[-5.198, -2.252]	[-5.198, .2.252]
Discontinued during Phase III	-7.310	-15.8	-15.809
	[-9.963, -4.626]	[-9.962, -4.625]	[-9.962, -4.625]
FDA Application	0.496	0.672	0.683
	[0.047, 0.953]	[0.047, 0.953]	[0.047, 0.953]
Discontinued after FDA Application	-1.384	-3.451	-3.451
	[-3.736, 0.850]	[-3.736, 0.849]	[-3.736, 0.849]
FDA Approval	1.158	4.017	4.017
	[0.547, 1.836]	[0.546, 1.836]	[1.836, 1.985]
Observations	8,281	3,968	4,032
$\overline{R}^2$	0.021	0.047	0.048

Note: The table presents estimated coefficients from Equation (7) using only single announcements. Each coefficient is followed by a 90% bootstrap confidence interval estimated using 1,000 bootstrap samples.

III. Estimating Discount Rates

Follows Aalen (1976), rather technical.

Intuition: *(I hope, you may help me here)*

- Let $\mathbb{P}$ be the **prob of time** for a drug to get from discovery to approval
- If $\mathbb{P}$ is **known**, $\mathbb{E}(\delta^{disc\rightarrow}) \approx \frac{1}{L}\sum_{l=1}^{L} \delta^{\tau_l}$; $\tau_l \sim \mathbb{P}$, Montecarlo draw
- To **estimate** $\mathbb{P}$:
  - Divide the process into 5: time of discovery to phase I, phase I to phase II, etc.
  - For each subprocess, divide the time into small intervals $[y, y+\eta]$,
    - s.t. at most one change in the drug status
  - For each interval, possible to estimate: $\frac{P(\text{success before } t)}{P(\text{no change before } t)}$ only with counting data
  - Use this to estimate $\mathbb{P}$ process-by-process

Results

Table 8: **Expected Value of Drugs**

	Full Sample	**Middle 90%**	**Bottom 95%**
At Approval			
All Drugs	\$6.83 bil	\$1.62 bil	\$1.6 bil
Drugs with Complete Path	\$7.43 bil	\$1.89 bil	\$1.99 bil
At Discovery			
All Drugs	\$331.12 mm	\$63.37 mm	\$65.97 mm
Drugs with Complete Path	\$360.16 mm	\$74.05 mm	\$82.21 mm

Note: The table presents the mean of the expected value of individual drugs at the time of approval, $\mathbb{E}(V|S_{\texttt{appr}} = 1)$, and at discovery, $\mathbb{E}(V|S_{\texttt{disc}} = 1)$. The 90% sample refers to the drugs developed by firms with real market capitalization between 5% and 95% of the entire sample. The row, "Drugs with Complete Path" refers to the sample of drugs for which we observe discovery, FDA application, and FDA approval announcements. Of the 84 such drugs, 29 belong to the Middle 90% and Bottom 95% samples. The row "Average" refers to drugs for which we observe only a few stages.

Table 11: **Total Development Costs, at Discovery**

	Middle 90%	**Bottom 95%**
All Drugs	\$58.51 mm	\$60.72 mm
Drugs with Complete Path	\$69.24 mm	\$77.01 mm

Note: The table presents the mean of the expected cost of clinical trials and the FDA application and review process (in millions of U.S. dollars) at the time of discovery. The 90% sample refers to the drugs developed by firms with real market capitalization between 5% and 95% of the entire sample. The row "Drugs with Complete Path" refers to the sample of drugs for which we observe discovery, FDA application, and FDA approval announcements. There are 84 such drugs, out of which 29 belong to the Middle 90% and Bottom 95% samples. The row "Average" refers to drugs for which we do not observe the complete path but only a subset.

Table 13: **Costs of Clinical Trials**

	Middle 90%	**Bottom 95%**
Phase I	\$0.62 mm	\$0.22 mm
Phase II	\$30.48 mm	\$34.46 mm
Phase III	\$41.09 mm	\$39.71 mm

Note: The table presents the mean of the expected cost of the three phases of clinical trials. Middle 90% sample refers to the drugs developed by firms with real market capitalization between 5% and 95% of the entire sample.

Table 12: **Cost of FDA Review and Application**

Middle 90%	**Bottom 95%**
\$638.75 mm	\$648.04 mm

Note: The table presents the mean of the expected cost of FDA review and FDA application at the time of discovery. Middle 90% sample refers to the drugs developed by firms with real market capitalization between 5% and 95% of the entire sample.

Policy Discussion

With the estimates, government could:

1. **Buyout drugs**
   - A. After FDA Approval
     Problem: Lucas Critique
   - B. At Discovery Stage
     Problem: Moral Hazard
2. **Share the cost**

   Problems:
   - Crowd out private investment
   - Promote socially wasteful R&D
   - Difficult to target “right” drugs

Conclusion

This *simple* paper gives what it promises:

“Valuing Pharmaceutical Drug Innovations”