The Real Effects of Equity Markets on Innovation

Internet Appendix

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I. Alternative Specification of Drug Suspension

In my main specification, the variable *SuspendDummy* is a binary variable that takes the value of 1 if the drug does not continue onto the next phase of clinical trials. This does not mean the firm actively announced that the drug was suspended, but rather the drug never announces a phase II start date (which is required by law). For example, from 2012 to 2014 The Medicines Company conducted Phase I trials on the drug candidate MDCO-216. Although Phase I trial results were reported, The Medicines Company never initiated a Phase II trial. As a result, drug candidate MDCO-216 is assigned a $SuspendDummy_{dpit}$ value equal to 1. To ensure sufficient time has passed to allow companies the opportunity to start Phase II trials, the sample ends in 2015, even though clinical trial data ends in 2018.

An alternative specification, utilized by Krieger (2021), codes a drug as suspended if a drug suspension is announced, or if Pharma Intelligence codes the drug as suspended as a result of a drug being removed from a product pipeline, a conference call, or directly contacting the firm.

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Table IA1 reports the effect of market downturns on phase I clinical trial success probability using the Krieger (2021) definition of drug suspension. I find that market downturns still drive drug suspensions 60 and 90 days following trial announcement, although the magnitude is a little lower (0.07 vs 0.12).

II. Clustering by From and Firm X Indication

It is likely that drugs developed within the same firm share some dependence. As a robustness check, Tables IA2 and IA3 cluster my main results by firm and firm x drug indication. The results are identical to regressions only clustered by drug indication in terms of magnitude and only differ slightly in statistical significance.

III. Drug Suspensions at the Firm Level

Table IA4 examines the effect of collapsing my panel of drug-year observations to firm-year observations in order to examine the propensity of a firm to suspend drugs following a market downturn. Similar to my main results, Column 1 shows that market downturns 30 days following a clinical trial announcement have no effect on drug suspension probability. Unlike my panel of drug-year observations, firm-year observations show that market downturns 60 days following a clinical trial announcement have a similar economic significance of 9.3% increase, however, the statistical significance is lacking. Columns 3 and 4 show that market downturns 90 and 120 days following trial announcement lead to a 19% and 17% increased probability of drug suspension.

In sum market downturns still lead to a significant increase in drug suspension probability when my panel is collapsed to the firm-year level. These results continue to indicate that public firms respond to market downturns by suspending early-stage drug development.

IV. Do Market Returns Predict Clinical Trial Initiations?

I next examine whether market returns predict also predict the starts of clinical trials. On one hand, firms may be less likely to start trials if the market is down because of financial constraints. On the other hand, because clinical trials are scheduled months in advance of the trial start date, firms may be less sensitive to market returns. Table IA5 provides evidence of the latter as market returns in the 30-120 days before trial announcement do not affect the probability of a firm starts a clinical trial.

V. Logit vs Linear Probability Model

Table IA6 examines the effect of market downturns on phase I clinical trial success probability using a logit model instead of a linear probability model. Results are nearly identical to those of the linear probability model reported in the main paper, with the exception that interpretation of the logit coefficients is less straightforward. While coefficients in a linear probability model can be seen as percent changes in the dependent variable, coefficients in a logit model represent changes in the log odds ratio of suspension. Additionally, logit models are less flexible to the inclusion of fixed effects and clustering standard errors on multiple dimensions.

VI. Pre-Announcement Returns and Volatility

If market downturns following trial announcements are driving drug suspensions, it should be that market downturns prior to trial announcements do not drive my results. Table IA7 Columns 1 and 2 verifies this is the case. Market downturns or firm returns 60 days prior to trial announcements do not predict post-announcement suspension probability.

Columns 3-5 show that market downturns following trial announcements, rather than

increased volatility, drive my results. $MarketVolatility_{Realized}$is the standard deviation of S&P returns over the sixty days following trial announcement; $FirmVolatility_{Realized}$ is the standard deviation of firm returns over the same period; and $MarketVolatility_{Expected}$ is the value of the VIX index when the trial was announced. I find that when these various measures of volatility are accounted for, the probability of drug suspension remains statistically and economically significant.

VII. Observing Clinical Trial Announcements

The Food and Drug Administration Amendments Act of 2007 (FDAAA) requires firms to report the beginning of phase II and phase III clinical trials within 21 days of the first clinical trial enrollment. As shown in Figure IA1, all phases of clinical trial announcements sharply increased following 2007. This increased consistency in the timing and reporting of clinical trials enables me to track whether market fluctuations influence the probability of continuing to the next phase of clinical trials, even if a company does not announce, or delays announcing, a decision to discontinue drug development. As such, I only include post-2007 data in my analysis.

VIII. Frequency of Market Downturns

Figure IA2 graphically shows the relationship between trial announcements, eventual drug suspensions, and market downturns. I show that trial announcements are relatively constant over my sample period, and that there are many instances in which a trial could be announced and markets would be down in the 60 days that followed.

IX. Bond Yields and Market Returns

Figure IA3 graphically shows the relationship between pharmaceutical company bond yields and S&P 500 returns. When the market is down bond yields for pharmaceutical companies tend to increase.

X. Market Reactions to Drug Suspensions by Stage

Why are market-driven drug discontinuations limited to Phase 1 of clinical trials? Event studies shown in the internet appendix show that suspensions of later-stage drugs results in significant drops in market value. Figure IA4 shows that stage III suspensions result in a drop of 1.5% of firm value following a suspension announcement. Stage II suspensions result in approximately 1.2% drop in firm value, and Stage I suspensions result in a lower 0.5% drop in firm value, although the drop is not statistically significant. Furthermore, since the FDAAA only requires that results of Phase II and III drugs be reported, firms are incentivized to under-report phase I discontinuations.

REFERENCES

Krieger, Joshua L, 2021, Trials and terminations: Learning from competitors' R&D failures, *Management Science* .

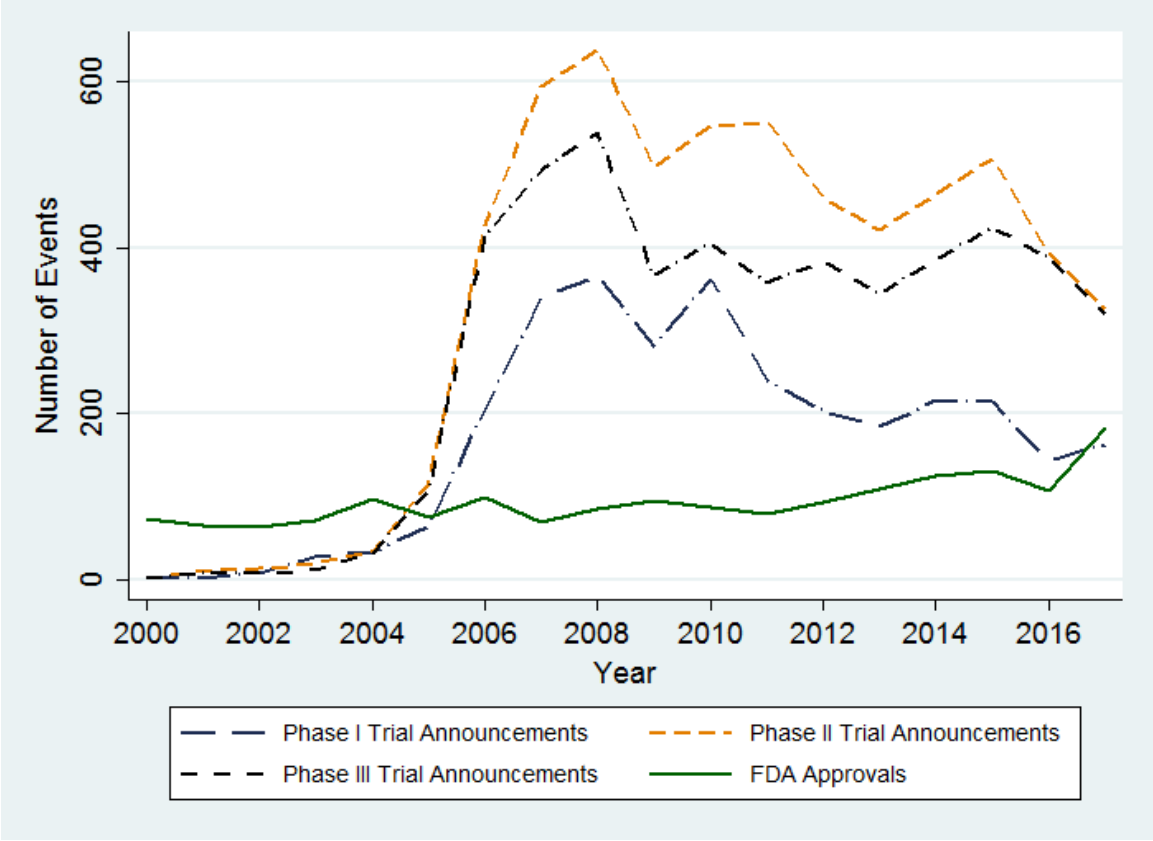

Figure IA1.
Trends in Clinical Trial Announcements
The above figure shows yearly trends in clinical trial announcements. The Food and Drug Administration Amendments Act of 2007 (FDAAA) required firms to publicly disclose a clinical trial within 21 days of patient enrollment. Observations prior to 2007 are also limited by the incomplete coverage of the Pharma Intelligence database up to that point.

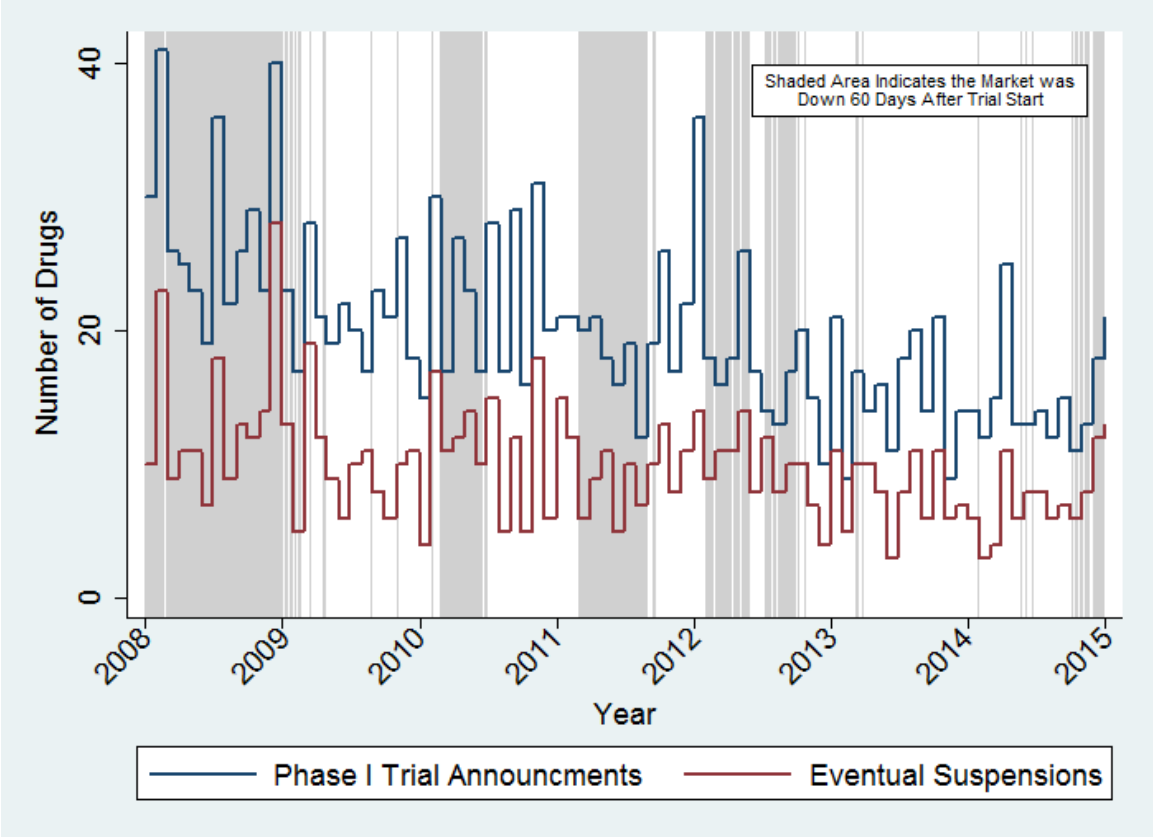

Figure IA2.
Market Fluctuations and Drug Suspensions
Blue lines represent the number of phase I clinical trial announcements per month, while red lines represent the number of those trials that were eventually suspended. Shaded areas represent potential trial announcement days which would have resulted in the market being down 60 days following announcement. The sample begins in 2008, as firms were not required to disclose the start of clinical trials prior to the Food and Drug Administration Amendments Act of 2007. As a result, there is limited coverage of phase I trials announcements in the Pharma Intelligence database pre-2008.

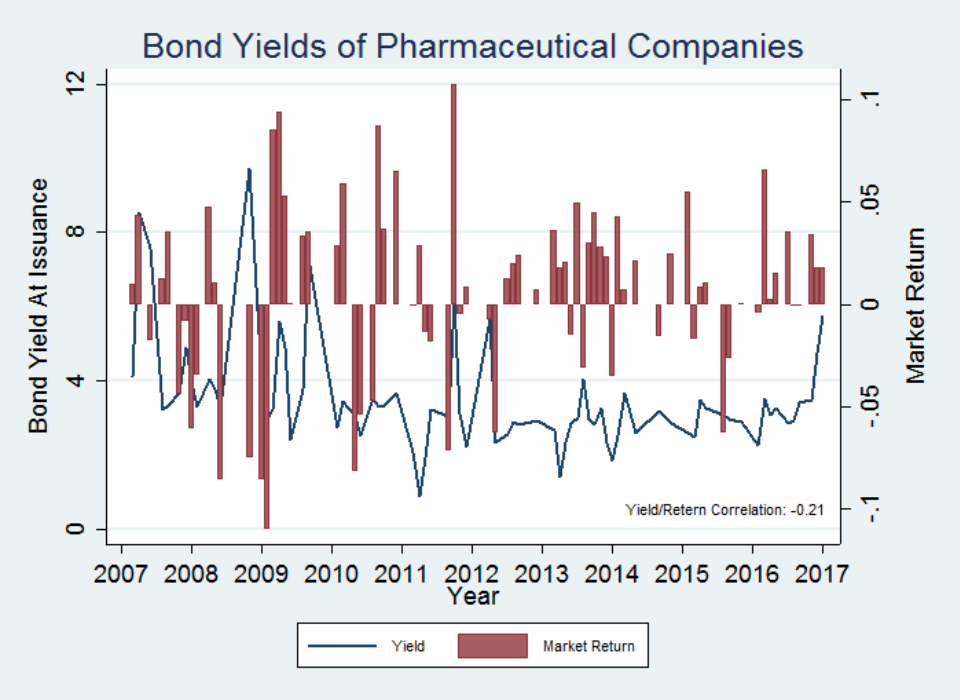

Figure IA3.
Pharmaceutical Bond Yield Trends
Blue lines indicate the monthly average bond yields of pharmaceutical companies (four-digit NAICS 3254) over time. Red bars show monthly returns of the S&P 500 index over the same period.

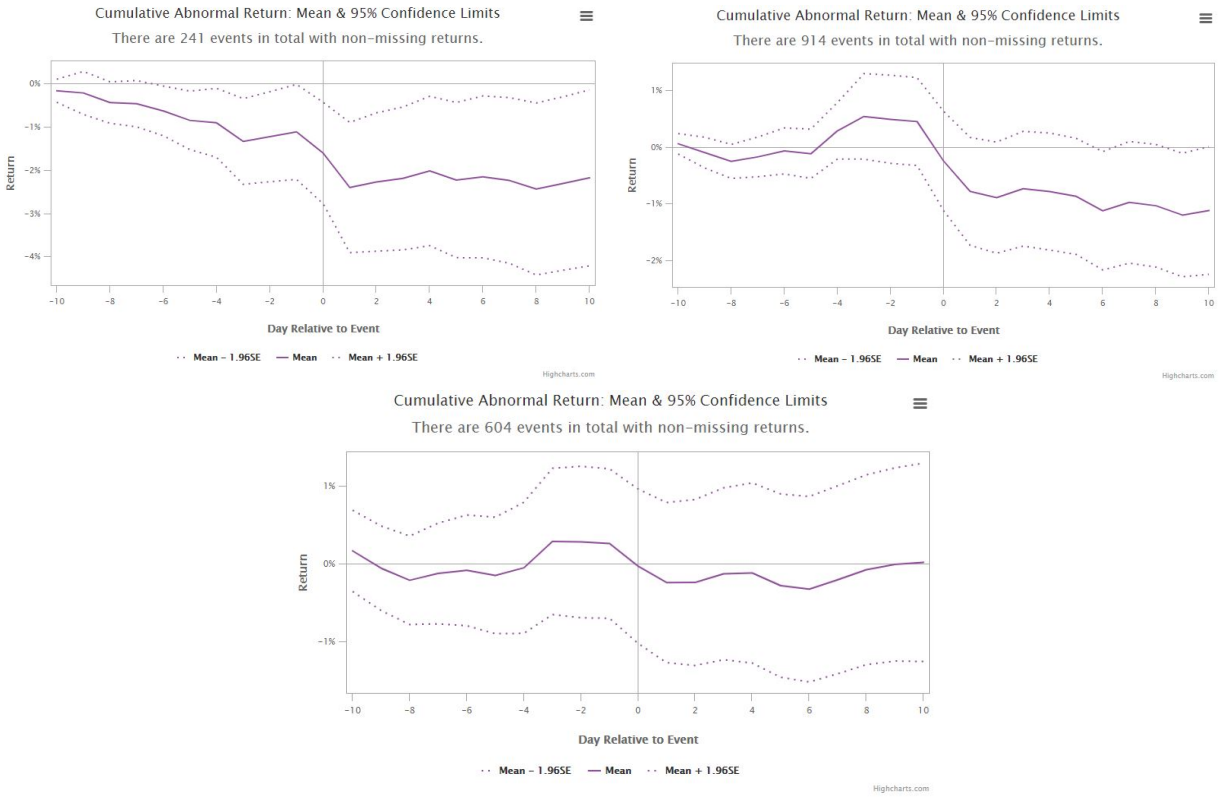

Figure IA4. Event studies shown in the internet appendix show that suspensions of later stage drugs results in significant drops in market value. Back of the envelope calculations show that stage III suspensions result in a drop of 1.5% of firm value following a suspension announcement (top left frame). Stage II suspensions result in approximately 1.2% drop in firm value, and Stage I suspensions result in a lower 0.5% drop in firm value, although the drop is not statistically significant (top right, bottom frames). Furthermore, since the FDAAA only requires that results of Phase II and III drugs be reported, firms are incentivized to under report phase I discontinuations, as seen in the internet appendix.

Table IA1
Effect of Market Downturns on Trial Success For Public Firms Alternative Definition of Drug Suspension

This table reports the effect of market downturns on phase I clinical trial success probability using the Krieger (2021) definition of drug suspension. The sample is limited to drugs developed by public firms. *SuspendDummy* is a binary variable set to one if a drug does not continue on to the next phase of clinical trials. *MarketDown* is a binary variable set to one if the S&P 500 returns were negative over the *DownturnPeriod* of $t, t+n$ days following clinical trial announcement. Standard errors are robust and are clustered by drug indication. The characters *, **, and *** denote significance at the 10%, 5%, and 1% level, respectively.

$$SuspendDummy_{dpit} = \alpha + \beta \cdot MarketDown_{t,t+n;d} + \sigma_T + \mu_{dpit}$$

	Phase I Clinical Trials			
	(1)	(2)	(3)	(4)
	SuspendDummy	*SuspendDummy*	*SuspendDummy*	*SuspendDummy*
Downturn Period (Days)	t, t+30	t,t+60	t,t+90	t,t+120
MarketDown	0.0064	0.072**	0.073**	0.0095
	(0.1)	(2.1)	(2.1)	(0.2)
Observations	502	576	575	573
Adjusted R-squared	0.099	0.065	0.065	0.059
Year FE	Yes	Yes	Yes	Yes

Table IA2
Effect of Market Downturns on Trial Success For Public Firms Clustering by Firm

This table reports the effect of market downturns on phase I, II, and III clinical trial success probability. The sample is limited to drugs developed by public firms. *SuspendDummy* is a binary variable set to one if a drug does not continue on to the next phase of clinical trials. *MarketDown* is a binary variable set to one if the S&P 500 returns were negative over the *DownturnPeriod* of $t, t+n$ days following clinical trial announcement. *Standard errors are robust and are clustered by firm.* The characters *, **, and *** denote significance at the 10%, 5%, and 1% level, respectively.

$$SuspendDummy_{dpit} = \alpha + \beta \cdot MarketDown_{t,t+n;d} + \sigma_T + \mu_{dpit}$$

Panel A: Phase I Clinical Trials

	(1)	(2)	(3)	(4)
	SuspendDummy	*SuspendDummy*	*SuspendDummy*	*SuspendDummy*
Downturn Period (Days)	t, t+30	t,t+60	t,t+90	t,t+120
MarketDown	0.051	0.11***	0.12**	0.094*
	(1.2)	(2.8)	(2.4)	(1.9)
Observations	575	574	573	571
Adjusted R-squared	0.071	0.078	0.078	0.072
Year FE	Yes	Yes	Yes	Yes

Panel B: Phase II Clinical Trials

	(1)	(2)	(3)	(4)
	SuspendDummy	*SuspendDummy*	*SuspendDummy*	*SuspendDummy*
DownturnPeriod	t,t+30	t,t+60	t,t+90	t,t+120
MarketDown	0.015	0.044	0.028	-0.011
	(0.4)	(0.9)	(0.5)	(-0.2)
Observations	674	674	673	671
Adjusted R-squared	0.054	0.055	0.054	0.054
Year FE	Yes	Yes	Yes	Yes

Panel C: Phase III Clinical Trials

	(1)	(2)	(3)	(4)
	SuspendDummy	*SuspendDummy*	*SuspendDummy*	*SuspendDummy*
DownturnPeriod	t,t+30	t,t+60	t,t+90	t,t+120
MarketDown	0.12***	0.055	0.036	0.0053
	(3.1)	(1.1)	(0.7)	(0.1)
Observations	414	414	414	413
Adjusted R-squared	0.027	0.011	0.009	0.007
Year FE	Yes	Yes	Yes	Yes

Table IA3
Effect of Market Downturns on Trial Success For Public Firms Clustering by Firm and Drug Indication

This table reports the effect of market downturns on phase I, II, and III clinical trial success probability. The sample is limited to drugs developed by public firms. *SuspendDummy* is a binary variable set to one if a drug does not continue on to the next phase of clinical trials. *MarketDown* is a binary variable set to one if the S&P 500 returns were negative over the *DownturnPeriod* of $t, t+n$ days following clinical trial announcement. *Standard errors are robust and are clustered by firm and drug indication.* The characters *, **, and *** denote significance at the 10%, 5%, and 1% level, respectively.

$$SuspendDummy_{dpit} = \alpha + \beta \cdot MarketDown_{t,t+n} + \sigma_T + \mu_{dpit}$$

Panel A: Phase I Clinical Trials

	(1)	(2)	(3)	(4)
	SuspendDummy	*SuspendDummy*	*SuspendDummy*	*SuspendDummy*
Downturn Period (Days)	t, t+30	t,t+60	t,t+90	t,t+120
MarketDown	0.051	0.11***	0.12***	0.094**
	(1.1)	(3.2)	(2.9)	(2.1)
Observations	575	574	573	571
Adjusted R-squared	0.071	0.078	0.078	0.072
Year FE	Yes	Yes	Yes	Yes

Panel B: Phase II Clinical Trials

	(1)	(2)	(3)	(4)
	SuspendDummy	*SuspendDummy*	*SuspendDummy*	*SuspendDummy*
DownturnPeriod	t,t+30	t,t+60	t,t+90	t,t+120
MarketDown	0.015	0.044	0.028	-0.011
	(0.3)	(0.9)	(0.5)	(-0.2)
Observations	674	674	673	671
Adjusted R-squared	0.054	0.055	0.054	0.054
Year FE	Yes	Yes	Yes	Yes

Panel C: Phase III Clinical Trials

	(1)	(2)	(3)	(4)
	SuspendDummy	*SuspendDummy*	*SuspendDummy*	*SuspendDummy*
DownturnPeriod	t,t+30	t,t+60	t,t+90	t,t+120
MarketDown	0.12***	0.055	0.036	0.0053
	(2.7)	(1.1)	(0.7)	(0.1)
Observations	414	414	414	413
Adjusted R-squared	0.027	0.011	0.009	0.007
Year FE	Yes	Yes	Yes	Yes

Table IA4
Effect of Market Downturns on Trial Success For Public Firms Collapsing Panel to Firm-Year Observations

This table reports the effect of market downturns on phase I, II, and III clinical trial success probability. The sample is limited to drugs developed by public firms. *SuspendDummy* is the fraction of drugs that do not continue onto the next phase of clinical trials in year t. *MarketDown* is the fraction of the time the S&P 500 returns were negative over the *DownturnPeriod* of $t, t+n$ days following clinical trial announcement. Standard errors are robust and are clustered by drug indication. The characters *, **, and *** denote significance at the 10%, 5%, and 1% level, respectively.

$$SuspendDummy_{pit} = \alpha + \beta \cdot MarketDown_{t,t+n} + \sigma_T + \mu_{pit}$$

Panel A: Phase I Clinical Trials

	(1)	(2)	(3)	(4)
	SuspendDummy	*SuspendDummy*	*SuspendDummy*	*SuspendDummy*
Downturn Period (Days)	t, t+30	t,t+60	t,t+90	t,t+120
MarketDown	0.062	0.093	0.19***	0.17**
	(0.8)	(1.6)	(2.7)	(2.2)
Observations	248	247	246	245
Adjusted R-squared	0.129	0.126	0.152	0.139
Year FE	Yes	Yes	Yes	Yes

Panel B: Phase II Clinical Trials

	(1)	(2)	(3)	(4)
	SuspendDummy	*SuspendDummy*	*SuspendDummy*	*SuspendDummy*
DownturnPeriod	t,t+30	t,t+60	t,t+90	t,t+120
MarketDown	0.0099	0.074	0.055	0.088
	(0.1)	(1.0)	(0.7)	(0.8)
Observations	261	261	260	258
Adjusted R-squared	0.064	0.067	0.066	0.070
Year FE	Yes	Yes	Yes	Yes

Panel C: Phase III Clinical Trials

	(1)	(2)	(3)	(4)
	SuspendDummy	*SuspendDummy*	*SuspendDummy*	*SuspendDummy*
DownturnPeriod	t,t+30	t,t+60	t,t+90	t,t+120
MarketDown	0.088	0.10	0.083	-0.029
	(1.4)	(1.4)	(1.1)	(-0.4)
Observations	209	209	209	208
Adjusted R-squared	-0.009	-0.008	-0.012	-0.019
Year FE	Yes	Yes	Yes	Yes

Table IA5
Do Market Returns Predict Clinical Trial Starts

This table reports the effect of market returns on phase I, II, and III clinical trial *start* probability. The sample is limited to drugs developed by public firms. Pr(Start Phase I Trail) is the probability a firm will start a new drug on day t. $MarketReturn_{t-n,t-1}$ the return of the market $t-n$ to $t-1$ days before clinical trial initiation announcement. Standard errors are robust and are clustered by firm. The characters *, **, and *** denote significance at the 10%, 5%, and 1% level, respectively.

$$TrailStart_{pit} = \alpha + \beta \cdot MarketDown_{t,t+n} + \sigma_T + \mu_{pit}$$

	(1) Pr(Start Phase I Trail)	(2) Pr(Start Phase II Trail)	(3) Pr(Start Phase III Trail)
$MarketReturn_{t-30,t-1}$	0.0000178	-0.0002172	-0.000691
	(0.01)	(-0.15)	(-0.70)
$MarketReturn_{t-60,t-1}$	-0.0001725	0.0000404	0.0006227
	(-0.14)	(0.03)	(0.61)
$MarketReturn_{t-90,t-1}$	-0.0004378	0.000881	0.0007176
	(-0.48)	(0.80)	(0.97)
$MarketReturn_{t-120,t-1}$	-0.0006603	0.0012271	0.0008001
	(-0.77)	(1.28)	(1.24)
Year FE	Yes	Yes	Yes

Table IA6
Effect of Market Downturns on Trial Success: Logit Specification
This table reports the effect of market downturns on phase I clinical trial success probability using a logit model instead of a linear probability model. *SuspendDummy* is a binary variable set to one if a drug does not continue on to phase II of clinical trials. $MarketDown$ is a binary variable set to one if the S&P 500 returns were negative over the 60 days following phase I clinical trial announcement. $FirmReturn$ is the return of the firm over the 60 days following phase I clinical trial announcement. *Orphan* is a binary variable set to one if a drug is approved for potential orphan status. $Pr(Approval)$ is the likelihood that a drug will reach the market given drug and firm characteristics. *Firm-Year Controls* include ROA, $BookLeverage$, $log(MarketBook)$, $R\&D/Assets$, $log(Assets)$, $CapEx/Assets$, $SG\&A/Assets$, and $Cash/Assets$. Standard errors are robust and are clustered by drug indication. The characters *, **, and *** denote significance at the 10%, 5%, and 1% level, respectively.

	(1)	(2)	(3)	(4)	(5)	(6)
	Dependent Variable = SuspendDummy					
$MarketDown$	0.61***	0.60***		0.58**	0.63**	0.54*
	(2.6)	(2.7)		(2.3)	(2.0)	(1.7)
$FirmDown$		0.033		0.024	-0.066	-0.13
		(0.2)		(0.1)	(-0.2)	(-0.4)
$MarketReturn$			-3.91***			
			(-2.6)			
$FirmReturn$			0.58**			
			(2.0)			
Orphan			-2.23***	-2.50***	-1.75***	-1.73***
			(-3.4)	(-2.9)	(-4.2)	(-3.9)
$pr(Approval)$			0.0069	-0.0095	-0.0056	-0.022
			(0.3)	(-0.4)	(-0.2)	(-0.8)
Observations	576	576	576	498	492	425
Firm-year Controls	No	No	No	Yes	No	Yes
Drop 2008	No	No	No	No	Yes	Yes
Year FE	Yes	Yes	Yes	Yes	Yes	Yes
Pseudo R-squared	0.013	0.013	0.065	0.10	0.047	0.087

Table IA7
Pre-Announcement Returns and Volatility

This table examines whether returns prior to trial announcements affect drug suspension probability. $MarketDown$ is a binary variable set to one if the S&P 500 returns were negative over the 60 days following phase I clinical trial announcement. $FirmDown$ is a binary variable set to one if firm returns were negative over the 60 days following phase I clinical trial announcement. $MarketDown_{pre}$ is a binary variable set to one if the S&P 500 returns were negative in the 60 days prior to phase I clinical trial announcement. $FirmDown_{pre}$ is a binary variable set to one if firm returns were negative over the 60 days prior to phase I clinical trial announcement. $MarketVolatility_{Realized}$ is the standard deviation of S&P returns over the sixty days following trial announcement. $FirmVolatility_{Realized}$ is the standard deviation of firm returns over the same period. $MarketVolatility_{Expected}$ is the value of the VIX index when the trial was announced. Standard errors are robust and are clustered by drug indication. The characters *, **, and *** denote significance at the 10%, 5%, and 1% level, respectively.

	(1)	(2)	(3)	(4)	(5)
	Dependent Variable = SuspendDummy				
$MarketDown$	0.11***	0.11***	0.099***	0.097***	0.083**
	(3.3)	(3.1)	(2.9)	(2.9)	(2.3)
$MarketDown_{pre}$	-0.046	-0.046			
	(-1.2)	(-1.2)			
$FirmDown$		0.0065			
		(0.2)			
$FirmDown_{pre}$		0.00			
		(0.0)			
$MarketVolatility_{Realized}$			0.034	0.048*	0.067**
			(1.4)	(1.8)	(2.3)
$FirmVolatility_{Realized}$				-0.038	-0.037
				(-1.4)	(-1.4)
$MarketVolatility_{Expected}$					-0.037
					(-1.3)
Observations	576	572	576	576	559
Adjusted R-squared	0.080	0.077	0.081	0.086	0.088
Year FE	Yes	Yes	Yes	Yes	Yes