Supplementary Online Content

Michaeli DT, Yagmur HB, Achmadeev T, Michaeli T. Valuation and Returns of Drug Development Companies: Lessons for Bioentrepreneurs and Investors. Therapeutic Innovation & Regulatory Science. doi:10.1007/s43441-021-00364-y

This supplementary material has been provided by the authors to give readers additional information about their work.

	Overall	Orphan	Oncology	CNS	Small-molecule	Biologic OR gene/cell therapy	Single-indication	Multi-indication
Phase 1 to 2	75.8%	96.1%	78.7%	75.0%	74.5%	84.4%	75.8%	66.4%
Phase 2 to 3	55.6%	86.1%	53.9%	54.5%	52.5%	60.1%	55.6%	58.3%
Phase 3 to FDA Approval	67.7%	63.5%	48.5%	63.0%	71.0%	80.4%	67.7%	59.0%
Phase 1 to FDA Approval	**28.5%**	**52.5%**	**20.6%**	**25.8%**	**27.8%**	**40.8%**	**28.5%**	**22.8%**

Table e1 Drug development success rates by subgroups

Data extracted from Wong et al. [1]. For the purposes of our analyses, success rates for orphan, small-molecule, and biologic drugs were adjusted to lead drugs only [1, 2]. *CNS* central nervous system, *FDA* US Food and Drug Administration.

	N	Mean	Median	SD	Min.	Max.	Sum
A) Valuation							
Up-front payment	303	958	257	2,270	0	22,434	290,417
Milestone payment	290	159	0	330	0	2,945	46,144
Total deal value	300	1,119	458	2,285	12	22,434	335,662
B) Lead drug							
Development stage							
Pre-Clinic	311	0.15	0.00	0.36	0	1	46
Phase 1	311	0.13	0.00	0.34	0	1	40
Phase 2	311	0.33	0.00	0.47	0	1	103
Phase 3	311	0.19	0.00	0.39	0	1	59
Approved	311	0.20	0.00	0.40	0	1	63
No. of indications	311	1.83	1.00	1.88	1	16	569
Biologic OR gene/cell therapy	311	0.21	0.00	0.41	0	1	66
Disease area							
Oncology	311	0.30	0.00	0.46	0	1	93
CNS	311	0.16	0.00	0.37	0	1	51
Others	311	0.53	0.00	0.50	0	1	167
FDA orphan designation	311	0.16	0.00	0.37	0	1	51
C) Other products							
Total no. of drugs	311	2.96	2.00	2.19	1	10	921
Average no. of indications	311	1.46	1.00	1.09	1	12	455
D) Acquisition characteristics							
Target headquarter US	311	0.76	1.00	0.43	0	1	235
Spin-off / single drug deal	311	0.11	0.00	0.31	0	1	34

Table e2 Descriptive statistics for the entire sample of Biopharma acquisitions

All valuation metrics are inflation adjusted to 2020. *CNS* central nervous system, *FDA* US Food and Drug Administration, *SD* standard deviation.

	Pre-Clinic		Phase 1		Phase 2		Phase 3		Approved	
	Mean	*P* Value	Mean	*P* Value	Mean	*P* Value	Mean	*P* Value	Mean	*P* Value
FDA orphan designation status										
Orphan	NA[a]	*NA* [a]	227	*p=0.257*	744	*p=0.373*	2,166	*p=0.317*	3,703	*p<0.05*
Non-orphan	88		370		673		1,648		1,964	
No. of indications										
Multi-indication	87	*p=0.484*	594	*p<0.05*	1,058	*p<0.05*	2,249	*p=0.208*	3,438	*p<0.01*
Single-indication	88		230		522		1,578		1,670	
Molecule type										
Small-molecule	71	*p<0.05*	325	*p=0.139*	517	*p<0.05*	1,536	*p=0.103*	2,105	*p=0.161*
Biologic OR gene/cell therapy	109		341		811		3,759		2,088	
Disease area										
Oncology	70	*p=0.176*	403	*p=0.242*	1,068	*p<0.05*	1,747	*p=0.490*	4,561	*p<0.01*
CNS	67	*p=0.346*	233	*p=0.204*	314	*p<0.001*	1,740	*p=0.490*	2,066	*p=0.372*
Other [b]	104		343		607		1,775		1,747	
Mean	**99**		**479**		**856**		**2,255**		**1,964**	

Table e3 Stage-specific Biopharma company valuation (in million US dollars) by FDA orphan status, number of indications, molecule type, and disease area

All valuation metrics are inflation adjusted to 2020. *P* Values calculated based on nonparametric bootstrapped *t* tests (resampling of 1,000 iterations with replacement). *CNS* central nervous system, *FDA* US Food and Drug Administration, *NA* not applicable.

[a] No valuation data exists for the Pre-Clinic orphan category given that the FDA only issues the orphan designation status after IND approval.
[b] The disease category "other" includes immunology, infectious disease, cardiovascular, dermatology, internal medicine, ophthalmology.

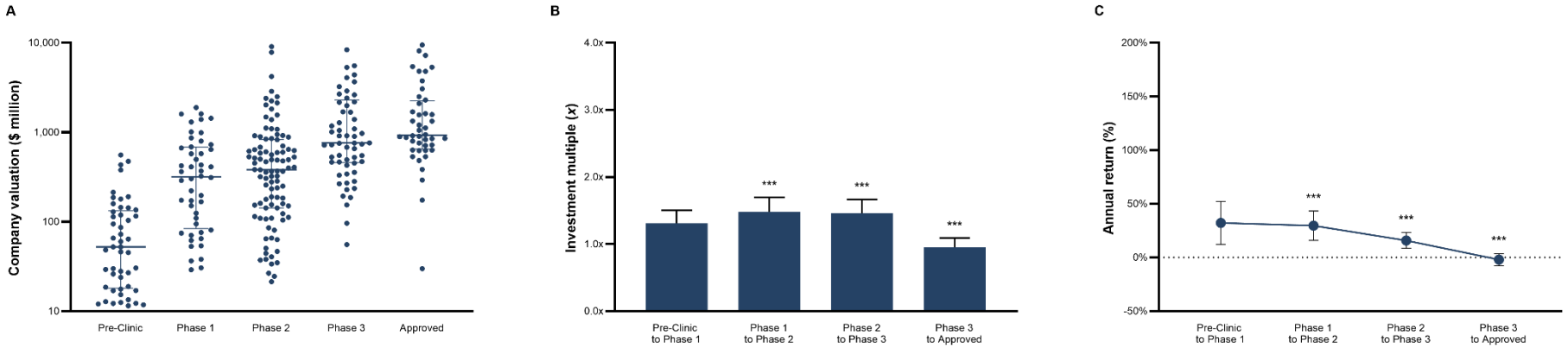

Figure e1 Company valuation (**A**), investment multiples (**B**), and annual returns (**C**) by development stage for the entire sample

All valuation metrics are inflation adjusted to 2020. *P* Values calculated based on ANOVA with Dunnett's test compared to Pre-Clinic to Phase 1: *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.