



15.482 Healthcare Finance

Spring 2017

Andrew W. Lo, MIT

Unit 9, Part 2: Clinical Trial Success Rates

Unit Outline

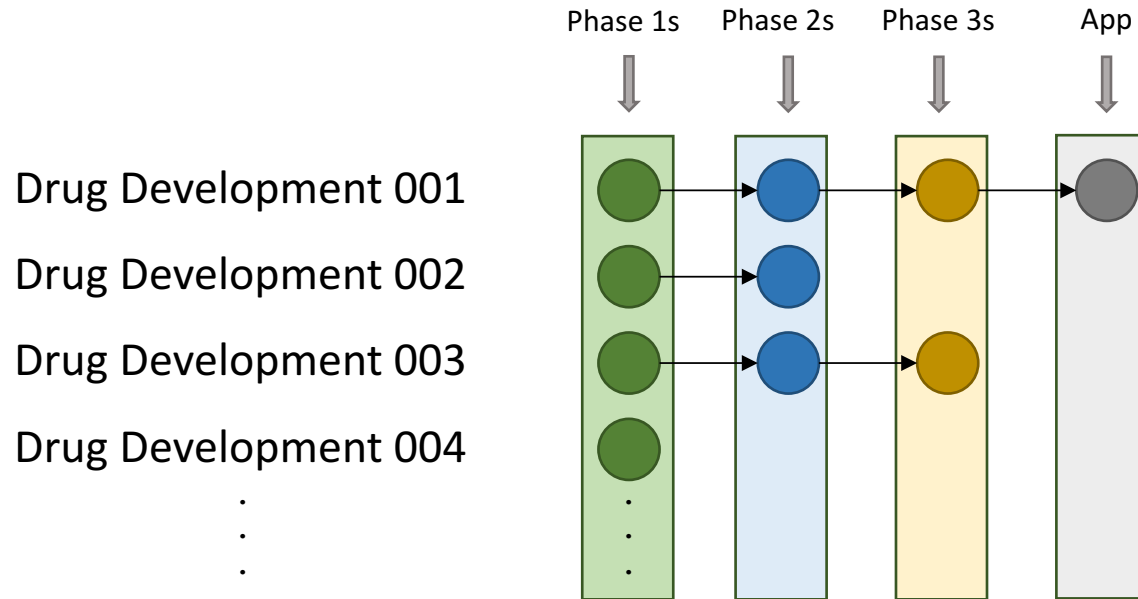
- Risk and Return in the Biopharma Industries, 1930-2015
- Estimating Clinical Success Rates
- Predicting Phase Transitions and Approvals
- Patient-Centered Clinical Trials

Estimation of Clinical Trial Success Rates and Related Parameters

Chi Heem Wong, Kien Wei Siah, Andrew W. Lo (2017)

Clinical Trials Success Rates

- Given trial data, we compute the probability of a drug development making it from Phase i to Phase j



Clinical Trials Success Rates

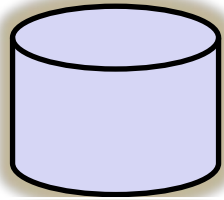
Data Sample

TrialID	Therapeutic Area	Drug Name	Phase	Disease Type	Start Date	End Date	Sponsor	Drug Development ID	Move on to the next phase?
48391	Autoimmune/ Inflammation	Loratadine	1/2	Allergic Rhinitis	NULL	2003-06-07	(Other Hospital/ Academic/ Medical Center)	?	?
70538	Autoimmune/ Inflammation	Loratadine	3	Allergic Rhinitis	NULL	2007-09-18	(Other Hospital/ Academic/ Medical Center)	?	?
100378	Autoimmune/ Inflammation	Loratadine	3	Asthma	NULL	2008-10-29	Merck & Co.	?	?
122164	Autoimmune/ Inflammation	Loratadine	4	Allergic Rhinitis	2010-01-01	2012-03-01	(Other Hospital/ Academic/ Medical Center)	?	?
151465	CNS	Loratadine	3	Pain (nociceptive)	2011-05-01	2014-05-14	Cancer and Leukemia Group B (CALGB)	?	?
153368	Autoimmune/ Inflammation	Loratadine	1	Asthma	NULL	2006-07-01	(Other Hospital/ Academic/ Medical Center)	?	?

- Trivial task if we could know whether a phase i trials for a drug development led to trial(s) in phase $i+1$

Clinical Trials Success Rates

More information in trial level data



Our study



Thomas et. al (2016)



Hay et. al (2016)

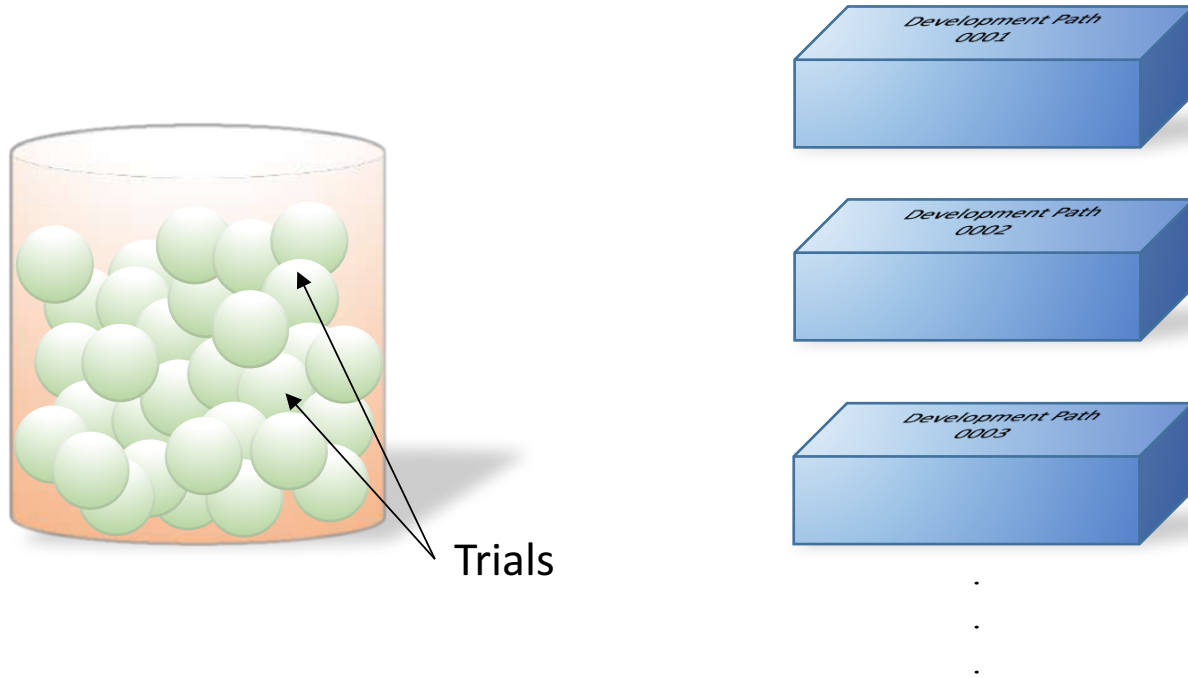


Dimasi et. al (2010)

Number of Drugs	15,102	?	5,820	1,316
Years of source data (time-span)	2000- 2015 (15 years)	2006-2015 (9 years)	2003-2011 (9 years)	1993-2009 (17 years)
Number of Companies	5,764	1,103	835	50
Phase Transitions	175,535	9,985	7,372	?
Analysis	Lead / All	Lead / All	Lead / All	Lead only
Methodology	“Path-by-path”	“Phase-by-phase”	“Phase-by-phase”	“Phase-by-phase”

Clinical Trials Success Rates

- Step 1: Identification of drug development paths



Clinical Trials Success Rates

- Step 1: Identification of drug development paths
 - We filtering by company, drug and indication to isolate trials that belong to the same drug development.
 - But, there is noise in the data. Consider the fictitious example:

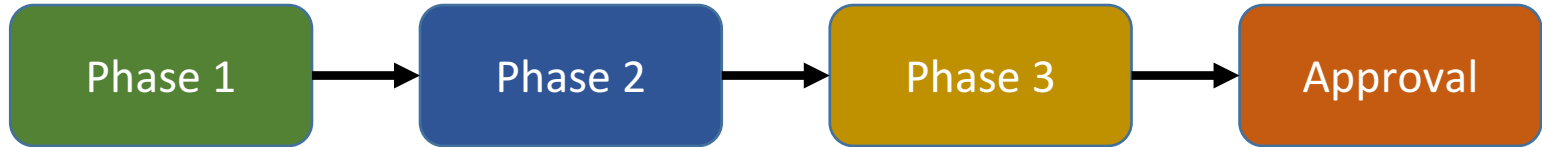


Drug Development #0001	
Id = 000234	Phase 1
Id = 029847	Phase 1
Id = 038562	Phase 3

- No phase 2! Did this development do so well in Phase 1 that it skipped Phase 2? Does it matter?

Clinical Trials Success Rates

- Step 1: Identification of drug development paths



Idealized drug development path: Every drug development **MUST** have gone through the lower stages to reach the higher stages.

Examples:

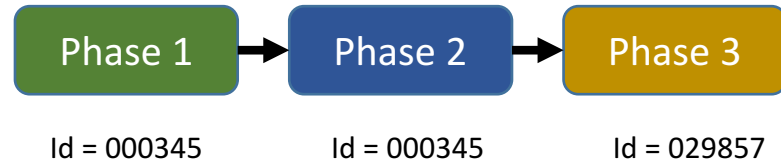
- To reach approval, the development must have gone through Phase 1, 2, 3.
- To reach phase 3, the development must have had a Phase 2 (or equivalent)

Clinical Trials Success Rates

- Step 1: Identification of drug development paths

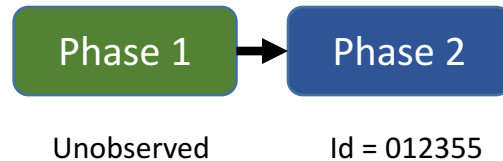
Drug Development #0002	
Id = 000345	Phase 1/2
Id = 029857	Phase 3

Drug development implied by model:



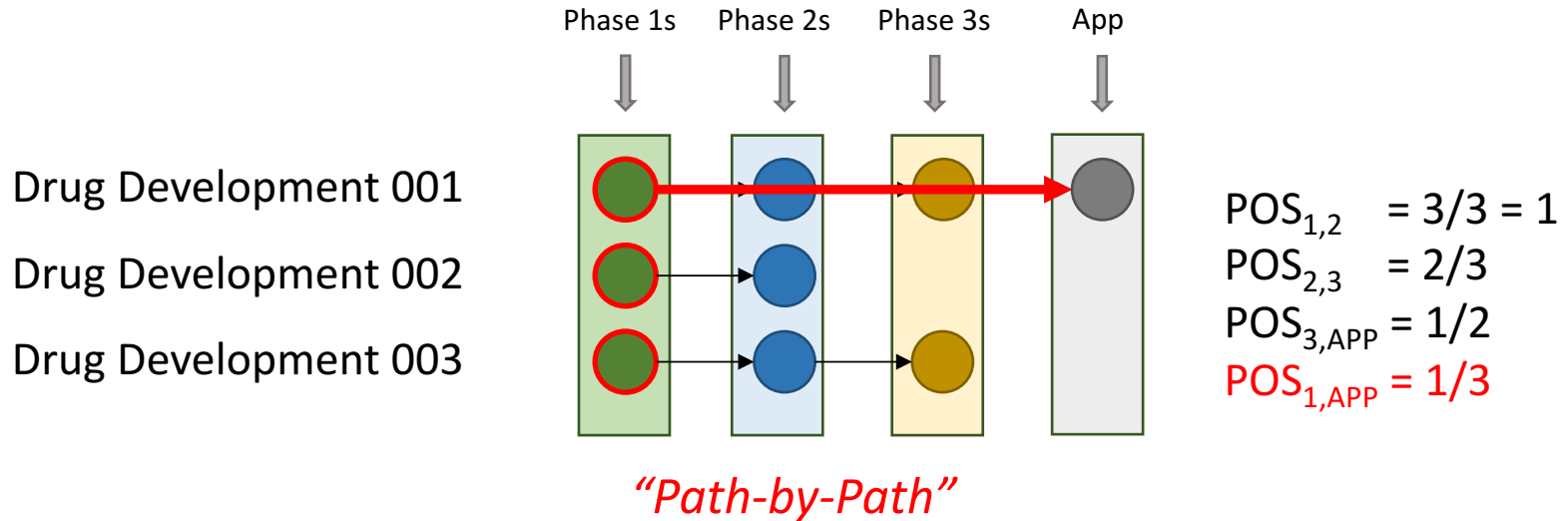
Drug Development #0003	
Id = 012355	Phase 2

Drug development implied by model:



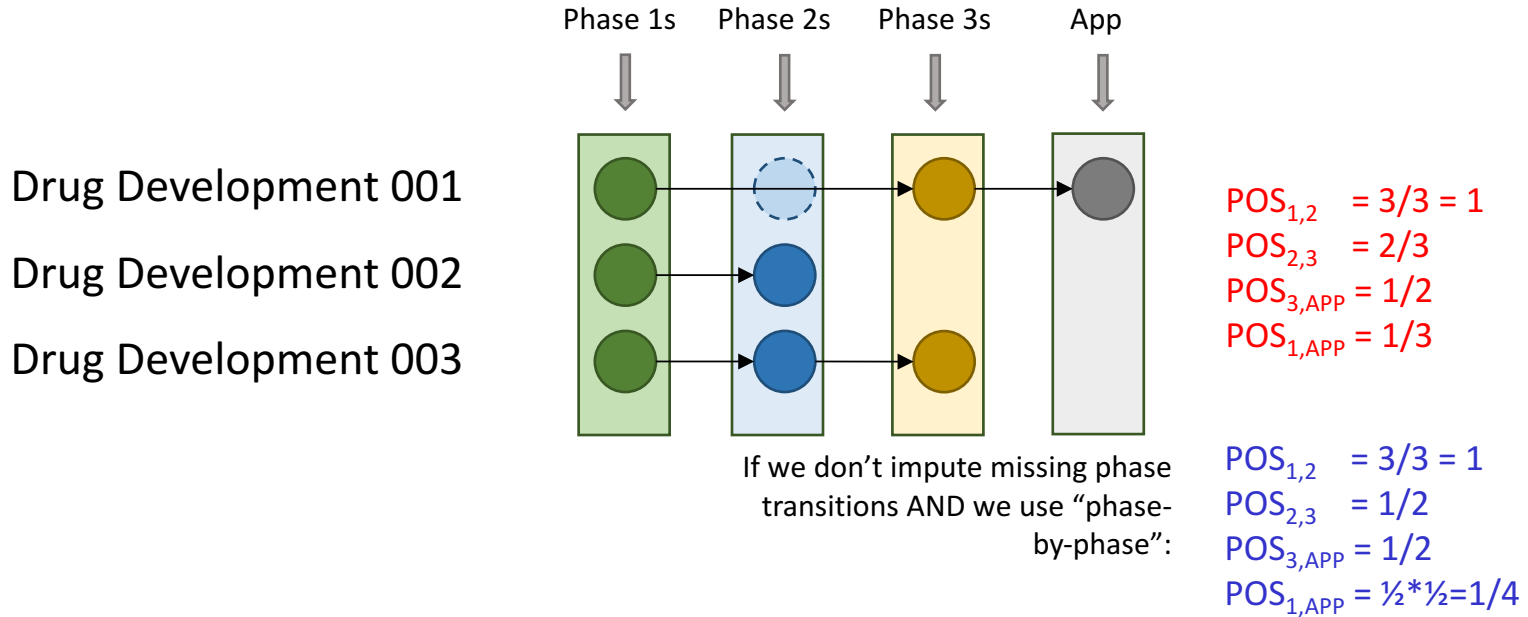
Clinical Trials Success Rates

- Step 2: Count proportion of development paths that make it to a phase



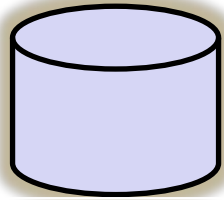
Clinical Trials Success Rates

■ Missing data imputation



Clinical Trials Success Rates

More information in trial level data



Our study



Thomas et. al (2016)



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Dimasi et. al (2010)

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Number of Companies	5,764	1,103	835	50
Phase Transitions	67,752	9,985	7,372	?
Analysis	Lead / All	Lead / All	Lead / All	Lead only
Methodology	“Path-by-path”	“Phase-by-phase”	“Phase-by-phase”	“Phase-by-phase”

Clinical Trials Success Rates

■ POS – Comparison with other studies

	This study - All Indications (Industry)		This study - Lead Indications (Industry)		Thomas et. al (2016) - All Indications		Hay et. al (2014) - All Indications		Hay et. al (2014) - Lead Indications		DiMasi et. al (2010) - Lead Indications	
	$POS_{i,i+1}$	$POS_{i,APP}$	$POS_{i,i+1}$	$POS_{i,APP}$	$POS_{i,i+1}$	$POS_{i,APP}$	$POS_{i,i+1}$	$POS_{i,APP}$	$POS_{i,i+1}$	$POS_{i,APP}$	$POS_{i,i+1}$	$POS_{i,APP}$
Phase 1 to 2	66.4%	13.8%	81.7%	15.7%	63.2%	9.6%	64.5%	10.4%	66.5%	15.3%	71%	19.0%
Phase 2 to 3	58.3%	35.1%	50.0%	20.5%	30.7%	15.2%	32.4%	16.2%	39.5%	23.1%	45%	26.8%
Phase 3 to APP	59.0%	59.0%	46.9%	46.9%	49.6%	49.6%	50.0%	50.0%	58.4%	58.4%	60%	59.5%
Phase 1 to APP		13.8%		15.7%		9.6%		10.4%		15.3%		19.0%
Number of Drugs	15,102				?		5,820		4,736		1,316	
Years of source data (time-span)	2000- 2015 (15 years)				2006-2015 (9 years)		2003-2011 (9 years)				1993-2009 (17 years)	
Number of Companies	5764				1103		835				50	

Clinical Trials Success Rates

■ POS – All Indications

All indications (Industry)								
Therapeutic Groups	Phase 1 to Phase 2		Phase 2 to Phase 3			Phase 3 to Approval		Overall
	Total Paths	POS _{1,2} , % (SE, %)	Total Paths	POS _{2,3} , % (SE, %)	POS _{2,APP} , % (SE, %)	Total Paths	POS _{3,APP} , % (SE, %)	POS, % (SE, %)
Oncology	17,368	57.6 (0.4)	6,533	32.7 (0.6)	6.7 (0.3)	1,236	35.5 (1.4)	3.4 (0.2)
Metabolic/ Endocrinology	3,589	76.2 (0.7)	2,357	59.7 (1.0)	24.1 (0.9)	1,101	51.6 (1.5)	19.6 (0.7)
Cardiovascular	2,810	73.3 (0.8)	1,858	65.7 (1.1)	32.3 (1.1)	964	62.2 (1.6)	25.5 (0.9)
CNS	4,924	73.2 (0.6)	3,037	51.9 (0.9)	19.5 (0.7)	1,156	51.1 (1.5)	15.0 (0.6)
Autoimmune/ Inflammation	5,086	69.8 (0.6)	2,910	45.7 (0.9)	21.2 (0.8)	969	63.7 (1.5)	15.1 (0.6)
Genitourinary	757	68.7 (1.7)	475	57.1 (2.3)	29.7 (2.1)	212	66.5 (3.2)	21.6 (1.6)
Infectious Disease	3,963	70.1 (0.7)	2,314	58.3 (1.0)	35.1 (1.0)	1,078	75.3 (1.3)	25.2 (0.8)
Ophthalmology	674	87.1 (1.3)	461	60.7 (2.3)	33.6 (2.2)	207	74.9 (3.0)	32.6 (2.2)
Vaccines (Infectious Disease)	1,869	76.8 (1.0)	1,235	58.2 (1.4)	42.1 (1.4)	609	85.4 (1.4)	33.4 (1.2)
Overall	41,040	66.4 (0.2)	21,180	58.3 (2.3)	35.1 (2.2)	7,532	59.0 (0.6)	13.8 (0.2)
All without oncology	23,672	73.0 (0.3)	14,647	27.3 (0.4)	27.3 (0.4)	6,296	63.6 (0.6)	20.9 (0.3)

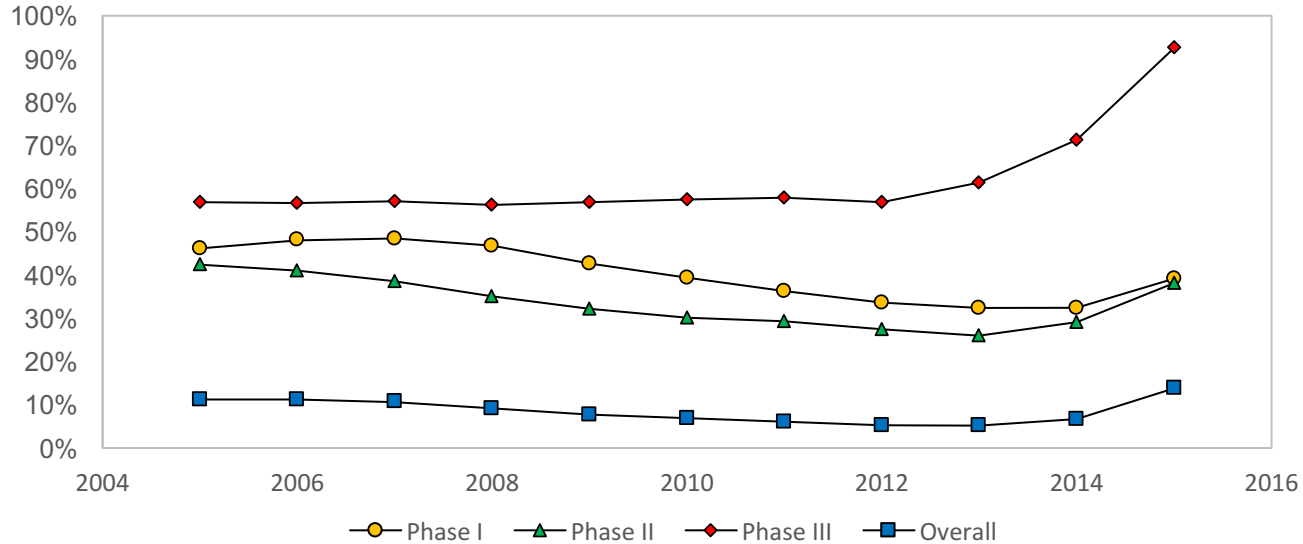
Clinical Trials Success Rates

■ POS – Lead Indications

Lead indications (Industry)								
Therapeutic Groups	Phase 1 to Phase 2		Phase 2 to Phase 3			Phase 3 to Approval		Overall
	Total Paths	POS _{1,2} , % (SE, %)	Total Paths	POS _{2,3} , % (SE, %)	POS _{2,APP} , % (SE, %)	Total Paths	POS _{3,APP} , % (SE, %)	POS, % (SE, %)
Oncology	3,107	78.7 (0.7)	1,601	53.9 (1.2)	13.1 (0.8)	431	48.5 (2.4)	11.4 (0.7)
Metabolic/ Endocrinology	2,012	75.2 (1.0)	1,273	57.0 (1.4)	26.4 (1.2)	535	62.8 (2.1)	21.3 (1.0)
Cardiovascular	1,599	71.1 (1.1)	1,002	64.9 (1.5)	34.1 (1.5)	473	72.3 (2.1)	26.6 (1.2)
CNS	2,777	75.0 (0.8)	1,695	54.5 (1.2)	24.1 (1.0)	648	63.0 (1.9)	19.3 (0.9)
Autoimmune/ Inflammation	2,900	78.9 (0.8)	1,862	48.7 (1.2)	24.3 (1.0)	659	68.6 (1.8)	20.3 (0.9)
Genitourinary	568	73.4 (1.9)	382	59.2 (2.5)	31.9 (2.4)	176	69.3 (3.5)	25.3 (2.0)
Infectious Disease	2,186	74.6 (0.9)	1,326	58.0 (1.4)	34.3 (1.3)	594	76.6 (1.7)	26.7 (1.1)
Ophthalmology	437	89.0 (1.5)	302	57.6 (2.8)	30.5 (2.6)	124	74.2 (3.9)	30.7 (2.7)
Vaccines (Infectious Disease)	881	75.8 (1.4)	567	57.1 (2.1)	40.4 (2.1)	269	85.1 (2.2)	31.6 (1.7)
Overall	16,467	75.8 (0.3)	10,010	55.9 (0.5)	26.4 (0.4)	3,478	70.0 (0.8)	21.6 (0.4)
All without oncology	13,360	75.8 (0.4)	8,409	29.0 (0.5)	29.0 (0.5)	3,478	70.0 (0.8)	23.4 (0.4)

Clinical Trials Success Rates

■ POS – Time Series



Clinical Trials Success Rates

■ POS – Biomarkers

Therapeutic Groups		Phase 1 to Phase 2			Phase 2 to Phase 3			Phase 3 to Approval			Overall	
		Total Phase Transitions	POS _{1,2} , %	(SE, %)	Total Phase Transitions	POS _{2,3} , %	(SE, %)	Total Phase Transitions	POS _{3,APP} , %	(SE, %)	POS, %	(SE, %)
Oncology	No Biomarker	5,499	26.3	(0.6)	3,190	16.2	(0.7)	903	33.6	(1.6)	1.4	(0.2)
	With Biomarker	4,986	33.5	(0.7)	2,325	25.8	(0.9)	333	40.8	(2.7)	3.5	(0.4)
	All	10,485	29.7	(0.4)	5,515	20.3	(0.5)	1,236	35.5	(1.4)	2.1	(0.2)
Metabolic/ Endocrinology	No Biomarker	1,424	45.5	(1.3)	1,214	34.5	(1.4)	865	54.1	(1.7)	8.5	(0.9)
	With Biomarker	115	33.0	(4.4)	226	31.0	(3.1)	236	42.4	(3.2)	4.3	(1.5)
	All	1,539	44.6	(1.3)	1,440	34.0	(1.2)	1,101	51.6	(1.5)	7.8	(0.8)
Cardiovascular	No Biomarker	1,117	38.1	(1.5)	711	36.8	(1.8)	673	67.5	(1.8)	9.5	(1.1)
	With Biomarker	131	55.0	(4.3)	321	41.1	(2.7)	291	50.2	(2.9)	11.3	(2.5)
	All	1,248	39.9	(1.4)	1,032	38.2	(1.5)	964	62.2	(1.6)	9.5	(1.0)
CNS	No Biomarker	2,011	40.3	(1.1)	1,858	29.9	(1.1)	1,049	51.2	(1.5)	6.2	(0.6)
	With Biomarker	212	43.9	(3.4)	234	32.5	(3.1)	107	50.5	(4.8)	7.2	(2.1)
	All	2,223	40.7	(1.0)	2,092	30.2	(1.0)	1,156	51.1	(1.5)	6.3	(0.6)
Autoimmune/ Inflammation	No Biomarker	2,227	37.7	(1.0)	1,765	24.9	(1.0)	867	64.0	(1.6)	6.0	(0.6)
	With Biomarker	288	49.0	(2.9)	355	28.5	(2.4)	102	60.8	(4.8)	8.5	(2.0)
	All	2,515	39.0	(1.0)	2,120	25.5	(0.9)	969	63.7	(1.5)	6.3	(0.6)
Genitourinary	No Biomarker	354	33.9	(2.5)	271	28.4	(2.7)	204	65.2	(3.3)	6.3	(1.5)
	With Biomarker	10	70.0	(14.5)	16	37.5	(12.1)	8	100.0	(0.0)	26.3	(15.7)
	All	364	34.9	(2.5)	287	28.9	(2.7)	212	66.5	(3.2)	6.7	(1.5)
Infectious Disease	No Biomarker	1,888	40.1	(1.1)	1,372	34.1	(1.3)	1,007	75.1	(1.4)	10.3	(0.9)
	With Biomarker	79	32.9	(5.3)	108	44.4	(4.8)	71	78.9	(4.8)	11.5	(4.2)
	All	1,967	39.8	(1.1)	1,480	34.9	(1.2)	1,078	75.3	(1.3)	10.5	(0.9)
Ophthalmology	No Biomarker	172	54.7	(3.8)	256	35.2	(3.0)	186	72.0	(3.3)	13.8	(3.0)
	With Biomarker	9	0.0	(0.0)	21	28.6	(9.9)	21	100.0	(0.0)	0.0	(0.0)
	All	181	51.9	(3.7)	277	34.7	(2.9)	207	74.9	(3.0)	13.5	(2.8)
Vaccines (Infectious Disease)	No Biomarker	718	41.4	(1.8)	748	33.2	(1.7)	597	85.8	(1.4)	11.8	(1.4)
	With Biomarker	15	13.3	(8.8)	18	11.1	(7.4)	12	66.7	(13.6)	1.0	(2.3)
	All	733	40.8	(1.8)	766	32.6	(1.7)	609	85.4	(1.4)	11.4	(1.3)
Overall	No Biomarker	15,410	35.3	(0.4)	11,385	27.0	(0.4)	6,351	60.7	(0.6)	5.8	(0.2)
	With Biomarker	5,845	35.0	(0.6)	3,624	28.8	(0.8)	1,181	50.0	(1.5)	5.0	(0.4)
	All	21,255	35.2	(0.3)	15,009	27.4	(0.4)	7,532	59.0	(0.6)	5.7	(0.2)

Clinical Trials Success Rates

■ POS – Orphan Drugs

Orphan Drugs (Industry, All indications)								
Therapeutic Groups	Phase 1 to Phase 2		Phase 2 to Phase 3			Phase 3 to Approval		Overall
	Total Paths	POS _{1,2} , % (SE, %)	Total Paths	POS _{2,3} , % (SE, %)	POS _{2,APP} , % (SE, %)	Total Paths	POS _{3,APP} , % (SE, %)	POS, % (SE, %)
Oncology	1,245	72.0 (1.3)	535	39.4 (2.1)	2.8 (0.5)	104	14.4 (3.4)	1.9 (0.4)
Metabolic/ Endocrinology	89	84.3 (3.9)	45	66.7 (7.0)	31.1 (4.9)	18	77.8 (9.8)	29.8 (4.8)
Cardiovascular	115	69.6 (4.3)	58	77.6 (5.5)	43.1 (4.6)	30	83.3 (6.8)	32.1 (4.4)
CNS	160	85.0 (2.8)	96	56.3 (5.1)	8.3 (2.2)	25	32.0 (9.3)	8.8 (2.2)
Autoimmune/ Inflammation	228	76.3 (2.8)	114	57.0 (4.6)	8.8 (1.9)	32	31.3 (8.2)	7.4 (1.7)
Genitourinary	14	100.0 (0.00)	13	46.2 (13.8)	38.5 (13.0)	6	83.3 (15.2)	38.5 (13.0)
Infectious Disease	157	89.2 (2.5)	104	53.8 (4.9)	28.8 (3.6)	39	76.9 (6.7)	28.8 (3.6)
Ophthalmology	19	73.7 (10.1)	7	71.4 (17.1)	0.0 (0.00)	0	0.0 (0.00)	0.0 (0.00)
Vaccines (Infectious Disease)	57	89.5 (4.06)	43	53.5 (7.6)	51.2 (6.6)	22	100.0 (0.0)	45.8 (6.6)
Overall	2,084	75.9 (0.9)	1,015	48.8 (1.6)	12.7 (0.7)	276	46.7 (3.0)	9.9 (0.7)
All except oncology	839	81.5 (1.3)	480	59.2 (2.2)	23.8 (1.5)	172	66.3 (3.6)	21.8 (1.4)