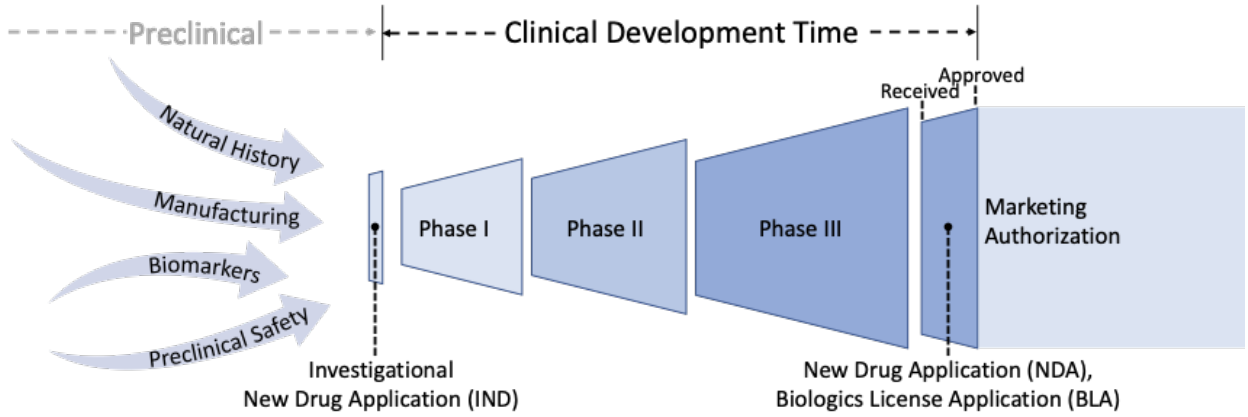
Supplementary Box 1 | **Dataset and analysis**

Data capture

Clinical development times (as shown in Supplementary Figure 1) were manually curated from public data sources for each innovative drug approval from 2010 through 2020.



Supplementary Figure 1 | **The clinical development time for a new drug covers the period between the start of clinical testing and marketing authorization.**

The FDA publishes investigational new drug application (IND) effective dates in the Federal Register as part of its determination of regulatory review period for purposes of patent extension as well as in the drug approval package summary review documents provided at Drugs@FDA. Clinical testing typically proceeds 30 days after IND submission and an initial review by the FDA. Some drug approval packages refer to an IND being 'opened' and it is unclear if this refers to its submission date or the date it became effective; these dates were used without alteration. When multiple INDs were opened by a sponsor for the same drug, we use the earliest effective date to mark the start of clinical development. Fixed dose combination products often have one IND for the combination product and an earlier IND for a single active ingredient drug. Likewise, some sponsors submit multiple INDs for the same drug in different indications. The FDA inconsistently publishes the effective dates of predecessor INDs in these cases. Also, when multiple new molecular entities are included into a single product (BLA 125462 for BAT/Botulism Antitoxin Heptavalent; NDA 206619 for VIEKIRA PAK containing ombitasvir, paritaprevir and dasabuvir; NDA 209394 for MAVYRET containing glecaprevir and pibrentasvir; NDA 208261 for ZEPATIER containing elbasvir and grazoprevir; NDA 203100 for STRIBILD containing elvitegravir and cobicistat; BLA 761169 for INMAZEB containing atoltivimab, maftivimab and odesivimab), we used the date of the first new molecular entity to enter human clinical testing. Finally, where the initial clinical characterization of a drug is done outside the US, the dates of initial clinical development may precede the effective dates of an IND. Such cases are usually described in the regulatory background section of the summary clinical review or sometimes in the chemistry, administrative or other sections of the drug approval package. The trials themselves are often described in detail within the drug approval package, especially the clinical pharmacology summary review. Where dates of such early trials are not available or substantial international development and/or marketing of a drug preceded US development, no clinical development start date is provided. Where dates of such early trials are provided within the drug

approval package, they were used as the clinical development start date. Where the trial can be cross-referenced by trial identifier or other trial descriptors including title, number enrolled, and study location, we used trial start dates provided by clinicaltrials.gov, other regulatory filings including at the Japanese Pharmaceuticals and Medical Devices Agency, European Medicines Agency, Securities and Exchange Commission, and occasionally company press releases, trial databases and peer-reviewed literature.

Data on NDA and BLA receipt dates (date the first and complete marketing application was received by the agency) and utilization of FDA's expedited development mechanisms (fast track designation, breakthrough designation, accelerated approval, priority review and priority review voucher) and orphan product designation were provided by FDA/CDER. Additional data on innovative drugs approved by the Center for Biologics Evaluation and Research (CBER) were gathered separately. 13 new vaccine products approved between 2010 and 2020 were excluded from the present study.

Non-first-cycle products are those that required a resubmission to address the agency's review concerns including manufacturing, safety or efficacy deficiencies in the original new drug application submission. This does not include products that submitted amendments and may have had review target dates adjusted accordingly, nor does it include cases where a different new drug application for the same product has been earlier submitted and not approved (for example NDA 206-334 for oritavancin which has previously been the subject of the withdrawn NDA 22-153 or NDA 211-996 for tafamidis meglumine which had previously been the subject of NDA 202-737).

Development and review time linear regression

For each innovative drug, additional details on its clinical development were captured including whether the program benefited from any FDA expedited development mechanisms. FDA expedited development mechanisms include: fast-track designation, breakthrough designation, accelerated approval, and priority review status. In addition, this study recorded whether the product had an FDA orphan product designation, whether the product approval required multiple review cycles, whether the approved product contained a black box warning, whether the product benefited from Animal Rule approval, and finally whether the product was a diagnostic imaging agent.

Two linear regression models were created in Python 3.8.5 with statsmodels ordinary least squares(OLS) method of linear regression using clinical development time as well as review time (the number of days elapsed between the receipt of a new drug application or biologics license application and product approval) for the matrix of factors outlined above.

Clinical Development Time Regression Results

Dep. Variable:	Days In Clinical Development	**R-squared:**	0.079
Model:	OLS	**Adj. R-squared:**	0.058
Method:	Least Squares	**F-statistic:**	3.783
Date:	Sat, 09 Oct 2021	**Prob (F-statistic):**	0.000136
Time:	11:29:49	**Log-Likelihood:**	-3586.4
No. Observations:	405	**AIC:**	7193.
Df Residuals:	395	**BIC:**	7233.
Df Model:	9		
Covariance Type:	nonrobust		

	coef	**std err**	**t**	**P>|t|**	**[0.025**	**0.975]**
const	3315.5883	167.378	19.809	0.000	2986.526	3644.651
fastTrack	-43.9435	198.619	-0.221	0.825	-434.427	346.540
breakthrough	-479.4227	241.053	-1.989	0.047	-953.331	-5.515
priority	76.4560	224.695	0.340	0.734	-365.291	518.203
accelerated	-1100.4155	273.289	-4.027	0.000	-1637.699	-563.132
orphan	552.4105	205.867	2.683	0.008	147.679	957.142

nonFirstCycle	642.5630	259.620	2.475	0.014	132.154	1152.972
blackBox	-10.6366	208.115	-0.051	0.959	-419.788	398.514
diagnosticImaging	60.8467	558.515	0.109	0.913	-1037.186	1158.880
animalRule	-480.5828	788.514	-0.609	0.543	-2030.792	1069.626

Omnibus:	229.732	**Durbin-Watson:**	1.905
Prob(Omnibus):	0.000	**Jarque-Bera (JB):**	2089.603
Skew:	2.273	**Prob(JB):**	0.00
Kurtosis:	13.157	**Cond. No.**	13.2

Note: Standard Errors assume that the covariance matrix of the errors is correctly specified

Review Time Regression Results

Dep. Variable:	Days In Review	**R-squared:**	0.476
Model:	OLS	**Adj. R-squared:**	0.464
Method:	Least Squares	**F-statistic:**	39.90
Date:	Sat, 09 Oct 2021	**Prob (F-statistic):**	2.50e-50
Time:	11:29:50	**Log-Likelihood:**	-2914.1
No. Observations:	405	**AIC:**	5848.

Df Residuals:	395	**BIC:**	5888.
Df Model:	9		
Covariance Type:	nonrobust		

	coef	std err	t	P>|t|	[0.025	0.975]
const	379.2022	31.825	11.915	0.000	316.634	441.770
fastTrack	6.5113	37.766	0.172	0.863	-67.736	80.758
breakthrough	-18.4881	45.834	-0.403	0.687	-108.597	71.621
priority	-102.8700	42.724	-2.408	0.017	-186.864	-18.876
accelerated	-60.8675	51.963	-1.171	0.242	-163.027	41.292
orphan	-19.0294	39.144	-0.486	0.627	-95.985	57.927
nonFirstCycle	828.7822	49.364	16.789	0.000	731.733	925.832
blackBox	-72.7698	39.571	-1.839	0.067	-150.566	5.027
diagnosticImaging	-114.2320	106.196	-1.076	0.283	-323.013	94.549
animalRule	57.6139	149.929	0.384	0.701	-237.144	352.372

Omnibus:	484.854	**Durbin-Watson:**	1.970

Prob(Omnibus):	0.000	**Jarque-Bera (JB):**	39265.195
Skew:	5.524	**Prob(JB):**	0.00
Kurtosis:	49.955	**Cond. No.**	13.2

Note: Standard Errors assume that the covariance matrix of the errors is correctly specified.

Therapeutic class and molecule type one-way ANOVA

To determine where there were significant differences between clinical development times for different therapeutic classes or different molecule types, we applied one-way ANOVA testing. We excluded therapeutic and molecule type classes with few observations in the dataset. A full listing of included classes is found below.

SUMMARY

Groups	*Count*	*Sum*	*Average*	*Variance*
Antiviral	26	66209	2546.5	1806809.38
Oncology	126	398890	3165.79365	3187246.57
Endocrinology	51	177734	3484.98039	2819988.58
Respiratory	19	78966	4156.10526	9955810.43
Neurology	63	217442	3451.46032	2570470.41
Hematology	24	92380	3849.16667	4456158.84
Antibacterial	24	87696	3654	1628162.35

ANOVA

Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	43140782.6	6	7190130.44	2.20487969	0.04229512	2.12642386

Within Groups	1063088625	326	3261008.05
Total	1106229408	332	

SUMMARY

Groups	*Count*	*Sum*	*Average*	*Variance*
Antibody	74	240414	3248.83784	1911501.7
Enzyme	16	66144	4134	13092973.2
Oligonucleotide	9	20366	2262.88889	280252.611
Peptide	26	111376	4283.69231	3224869.5
Polymer	5	24608	4921.6	5344241.3
Protein	8	23488	2936	2057781.14
Small molecule	260	862842	3318.62308	2871695.7
Virus	6	20051	3341.83333	1118820.97

ANOVA

Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	57246677.6	7	8178096.81	2.68993393	0.0098652	2.0327123
Within Groups	1203942706	396	3040259.36			
Total	1261189383	403				